OPERATIONAL RESEARCH FOR IMPROVING CARE OF HIV-INFECTED TB PATIENTS IN INDIA

Presented by
Dr Ajay Kumar Madhugiri Venkatachalaiah

Promotoren:
Prof. dr. P.N.R. Dekhuijzen
Prof. dr. A.D. Harries (London School of Hygiene and Tropical Medicine, Verenigd Koninkrijk)

Copromotoren:
Dr. M.J. Boeree
Dr. R. Zachariah (World Health Organization, Zwitserland)

Manuscriptcommissie:
Prof. dr. K. van der Velden
Prof. dr. M.W. Borgdorff (Amsterdam UMC)
Dr. M. van Cleeff (KNCV Tuberculosefonds)

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door
Dr Ajay Kumar Madhugiri Venkatachalaiah
geboren op 15 maart 1977
te Bengaluru (India)

Supervisors:
Prof. dr. P.N.R. Dekhuijzen
Prof. dr. A.D. Harries (London School of Hygiene and Tropical Medicine, United Kingdom)

Co-supervisors:
Dr. M.J. Boeree
Dr. R. Zachariah (World Health Organization, Switzerland)

Doctoral Thesis Committee:
Prof. dr. K. van der Velden
Prof. dr. M.W. Borgdorff (Amsterdam UMC)
Dr. M. van Cleeff (KNCV Tuberculosis Foundation)

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by
Dr Ajay Kumar Madhugiri Venkatachalaiah
Born on March 15, 1977
in Bengaluru (India)

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LIST OF ACRONYMS

AFB	Acid Fast Bacillus
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARTC	ART Centre
BMCRI	Bangalore Medical College and Research Institute
CD4	Cluster of Differentiation 4
CI	Confidence Intervals
CNS	Central Nervous System
CPT	Cotrimoxazole Preventive Therapy
DCC	District Coordination Committees
DFID	Department for International Development
DMC	Designated Microscopy Centres
DOT	Direct Observation of Treatment
DOTS	Directly Observed Treatment Short course
EPTB	Extra-pulmonary tuberculosis
GFATM	The Global Fund Against AIDS, Tuberculosis and Malaria
HBV	Hepatitis B Virus
HIV	Human Immunodeficiency Virus
HRG	High Risk Groups
IC	Infection Control
ICF	Intensified Tuberculosis Case Finding
ICTC	Integrated Counselling and Testing Centre
IDU	Intravenous Drug Users
IPT	Isoniazid Preventive Therapy
IQR	Inter Quartile Range
ISTC	International Standards for TB Care
JIPMER	Jawaharlal Nehru Institute of Postgraduate Medical Education and Research
LED FM	Light Emitting Diode Fluorescent Microscopy
LT	Laboratory Technician
MDR TB	Multidrug Resistant Tuberculosis
MMP	Methadone Maintenance Programme
MPH	Masters in Public Health
MSF	Médecins Sans Frontières
MTB	Mycobacterium Tuberculosis
NACO	National AIDS Control Organization
NACP	National AIDS Control Programme
NAICC	National Airborne Infection Control Committee
NIRT	National Institute for Research in Tuberculosis

NNS	Number Needed to Screen
NTP	National Tuberculosis Programme
NTWG	National Technical Working Group
OR	Operational Research
OSE	On Site Evaluation
PHI	Peripheral Health Institutions
PI	Principal Investigator
PID	Patient Identification Digit
PITC	Provider-Initiated HIV Testing and Counselling
PLHIV	People living with HIV
PMDT	Programmatic Management of Drug-resistant Tuberculosis
PMR	Programme Management Report
PTB	Pulmonary Tuberculosis
RNTCP	Revised National Tuberculosis Control Programme
SACS	State AIDS Control Societies
SCC	State Coordination Committees
SORT IT	Structured Operational Research Training Initiative
STCI	Standards of TB care in India
STLS	Senior TB laboratory supervisor
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
SWG	State Working Group
TB	Tuberculosis
The Union	International Union Against Tuberculosis and Lung Disease
UK	United Kingdom
UNAIDS	The Joint United Nations Programme on HIV/AIDS
USAID	United States Aid for International Development
USD	United States Dollar
USEA	The Union South-East Asia Office
VCT	Voluntary HIV Counselling and Testing
WDF	World Diabetes Foundation
WHO	World Health Organization
WHO/TDR	Special Programme for Research and Training in Tropical Diseases at the World Health Organization

1.

Introduction and Outline of Thesis

This thesis describes operational research studies planned and conducted to improve the care and management of patients co-infected with Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) in India between 2011 and 2015, particularly in relation to improving HIV testing among patients with presumptive TB and linking HIV-infected presumptive TB to antiretroviral therapy. The thesis also describes the overarching operational research capacity building initiative under which these studies were carried out, its evolution and impact on policy and practice.

GLOBAL BURDEN OF TUBERCULOSIS AND HIV

Tuberculosis (TB) and the Human Immunodeficiency Virus (HIV) have probably taken more lives than any other infectious diseases in the history of humanity. Despite great progress over the years in the care of TB and HIV, they still remain the leading infectious causes of death globally.[1,2] In 2015, an estimated 10.4 million patients fell ill with TB implying about 20 new TB patients every minute! [1] About 1.8 million individuals with TB also died during the same year, translating to about 5000 deaths due to TB every day! [1] An estimated 1.2 million (11%) new TB cases occurred among people living with HIV (PLHIV) and 400,000 TB related deaths were among PLHIV. [1] With an estimated pool of about 3 billion people with latent TB infection,[1] the end of the TB epidemic remains rather far from sight.

Globally, 36.7 million [34.0–39.8 million] people were living with HIV at the end of 2015, and 1.1 million people died of HIV-related disease or the acquired immune deficiency syndrome (AIDS) in 2015.[2] Tuberculosis and HIV act in deadly synergy. HIV infection increases the risk of progression from latent to active TB and from disease to death if HIV and TB are not treated in a timely manner.[3] Further, the risk of TB recurrence is greater even if the patient is successfully treated. Similarly, TB remains the most common opportunistic infection and cause of mortality among PLHIV. There are challenges to diagnose and treat TB among PLHIV that include atypical clinical presentations which can lead to missed diagnoses, the high pill burden, co-toxicity of using several drugs simultaneously and drug-drug interactions.[4]

There has been great progress with TB and HIV care over the years. It is estimated that TB treatment averted 49 million deaths between 2000 and 2015, and incidence and death rates fell during this period.[1] Similarly, HIV incidence is declining in many parts of the world and access to antiretroviral therapy (ART) has increased several fold.[2] The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates showed that more than 18 million people were receiving ART in mid-2016. Buoyed by these developments, the global community has pledged to end the TB and AIDS epidemics by 2030 as part of the larger sustainable development goals.[5] To achieve this, the World Health Organization (WHO)'s Global TB Programme has formulated an 'End TB strategy' with an overall vision of a TB-free world (meaning zero deaths, zero disease and zero suffering due to TB) and a goal of ending the TB epidemic (operationally defined as reducing the annual incidence of TB to 10 new cases per 100,000 population).[6] Similarly, UNAIDS has provisionally defined ending the AIDS

epidemic as the reduction of new HIV infections, stigma and discrimination experienced by PLHIV and key populations, and AIDS-related deaths by 90% compared to 2010 levels.[7] Both the TB and HIV worlds have set themselves ambitious 90-90-90 targets to achieve by 2020.[8,9] With respect to HIV, it means diagnosing 90% of estimated PLHIV, treating 90% of those diagnosed with HIV and achieving viral suppression in 90% of those treated with ART.[8] In the case of TB, this means diagnosing and treating 90% of all people with TB (PWTB), including 90% of the key populations at risk of TB, and achieving 90% treatment success for all people diagnosed with TB. [9]

BURDEN OF TUBERCULOSIS AND HIV IN INDIA

The global TB burden is primarily driven by the large absolute numbers in India. In 2015, an estimated 2.8 million people fell ill with TB in India thus accounting for 27% of the global TB burden. Similarly, about 480,000 people died due to TB in India accounting for one-third of global TB mortality.[10] About 2.1 million people were estimated to be living with HIV in India (prevalence of 0.26%) in 2015 making the country home to the third largest number of PLHIV globally. The HIV epidemic in India is heterogenous and concentrated among high risk groups, but it is showing a declining trend, probably due to prevention and treatment strategies by the National AIDS Control Programme (NACP). According to recent estimates, 86,000 new HIV infections occurred in 2015 in India, a decline of 66% compared to estimated numbers in 2000.[10] With an estimated HIV prevalence of 5% among people with TB,[11] India is home to the second largest number of HIV-infected TB patients in absolute terms (113,000), next only to South Africa (270,000), and accounts for about 10% of the global HIV-TB burden.[1] The number of deaths among HIV-TB patients was estimated at 37,000 in 2015.[1]

The evolution and progress of TB-HIV collaborative activities in India has been showcased as a success story globally, particularly for a country with a concentrated HIV epidemic.[12] As of now, India follows all the recommendations enshrined in the 2012 WHO global policy on TB-HIV collaborative activities,[13] though the extent of implementation varies across the components.[14] The basic mechanisms of collaboration between the national TB and HIV programmes in India are in place at all levels of the health service (national, state and district), and these include joint recording and reporting, joint monitoring and review. To quote a few performance indicators, the proportion of TB patients with a known HIV status was 67% which is higher than the global average of 55% while the proportion of HIV-TB patients receiving ART was 92% in India compared to 78% globally in 2015.[1] Despite this, the death rate among HIV-infected TB patients continues to be high at about 13%.[1]

SITUATIONAL ANALYSIS OF TUBERCULOSIS AND HIV IN INDIA IN 2010

Since this thesis consists of TB-HIV related operational research studies conducted in India during the period 2011-2015, we begin here by providing a brief overview of the evolution of TB-HIV care in India and analyse the situation in 2010 which stimulated and necessitated the conduct of these operational research studies.

Although the numbers of people living with HIV and TB were slightly different to what they are today, India in 2010 was the highest TB burden country in the world and was home to the second highest number of HIV-infected TB patients globally. In addition to these high absolute numbers, an important and unique challenge was the huge variation in TB-HIV burden across the states and districts of the country. This heterogenous distribution of HIV-associated TB continues to pose challenges in service delivery.

EVOLUTION OF JOINT TB–HIV COLLABORATION IN INDIA

The milestones in the evolution of joint TB-HIV collaboration in India are described below and depicted in **Figure 1**.

2001–2004

TB-HIV collaboration started in India in 2001, in six selected states of the country - Maharashtra, Manipur, Nagaland, Karnataka, Tamil Nadu and Andhra Pradesh (**Figure 1**). The early activities were primarily joint training of health staff in TB-HIV and cross-referrals (referral of people with presumptive TB among clients attending the HIV testing centres to the TB programme for diagnosis and treatment and vice versa).[12] These activities were then extended to eight additional states (Delhi, Gujarat, Himachal Pradesh, Kerala, Orissa, Punjab, Rajasthan and West Bengal) in the year 2004.

2005–2009

Several operational research studies conducted between 2005 and 2008 showed that i) it was feasible to implement intensified TB case finding in all HIV testing centres and ART centres, ii) it was feasible and acceptable to routinely offer HIV testing to TB patients under programmatic settings, and iii) it was feasible to provide cotrimoxazole preventive therapy to HIV-infected TB patients in a decentralised manner (at every peripheral health institution) and refer them to ART.[15–18] Based on this evidence and given the heterogeneity of the TB-HIV epidemic in the country, a decision was made at national level to implement a differential strategy in the country - a package of essential TB-HIV interventions to be implemented in all states, while an intensified package was to be implemented in selected states with a higher burden of HIV, improved availability of HIV testing, better treatment infrastructure and services and higher programme management capacity.

In 2007, the first National Framework for Joint TB-HIV Collaborative Activities was developed that endorsed a differential strategy, reflecting the heterogeneity of TB-HIV epidemic.[19] The components of the differential package were put together drawing on the WHO's 2004 interim policy of TB-HIV collaborative activities at the time.[20] These are summarized in **Table 1** and are described below.

THE ESSENTIAL TB–HIV PACKAGE INCLUDED:

1. Establishment of a formal mechanism for coordination, at the national, state and district levels. At the national level, a National Technical Working Group (NTWG) was established, comprising key officials from both TB and HIV programmes dealing with TB-HIV Collaborative activities and experts from the WHO. The purpose of the NTWG was to plan, review, optimize, monitor and evaluate TB-HIV coordination activities in the country. At the state level, State Coordination Committees (SCC) chaired by the Principal Health Secretary were established to ensure smooth implementation and regular review of TB-HIV Collaborative activities in the state. The State Working Group (SWG) was another body at state level, comprising key officials from State AIDS Control Societies (SACS) (Project Director and Additional Project Director) and the State TB Cell (State TB Officer), along with other officials and WHO consultants involved in TB-HIV collaborative activities. At the district level, District Coordination Committees (DCC), chaired by the District Magistrate, were formed in most districts of the country. In addition, monthly joint co-ordination meetings between the field staff of both TB and HIV programmes were started.
2. Training of programme officials and field staff on TB-HIV. Training manuals for the different cadres of staff were drafted at the national level and provided to states for training purposes. Budgets were allocated to conduct trainings at state and district level.
3. Intensified TB case finding at HIV counselling and testing centres, ART Centres, and other HIV care and support centres. Separate recording and reporting formats were designed to document and monitor this activity.
4. Risk-based, selective referral of TB patients for voluntary HIV counselling and testing.
5. Referral of HIV-infected TB patients to NACP settings for additional care and support, including ART.

THE INTENSIFIED TB–HIV PACKAGE INCLUDED IN ADDITION TO THE ABOVE:

1. Routine referral of all TB patients for HIV counselling and testing.
2. Provision of cotrimoxazole preventive therapy (CPT) to HIV-infected TB patients in a decentralized manner at every peripheral health institution.
3. Referral of HIV-infected TB patients to ART centres for initiation of ART. Initiation of ART followed CD4-cell count based guidelines, which at the time were based on WHO 2006 guidelines (ART for any HIV-infected extra-pulmonary TB patient or for HIV-infected pulmonary patients whose CD4 counts were less than 350 cells per µL).
4. Expanded recording and reporting, including recording HIV status, CPT and ART status in the TB treatment cards and TB registers and reporting of related indicators in quarterly reports of the TB programme.

2009–2012

The National Framework for joint TB-HIV collaborative activities was revised in 2009 and it was decided to scale-up the implementation of "Intensified TB-HIV activities" nationwide and the goal was reached in July 2012.[19] The scale-up of TB-HIV collaboration in India is summarized in **Figure 1**.

This expansion was accompanied by provision of additional dedicated human resources for coordinating TB-HIV activities, strengthening of joint monitoring and evaluation, with specified national TB-HIV programme indicators and performance targets. The additional human resources for supervision and monitoring included:

- A full-time regular government officer in-charge of TB-HIV collaborative activities in the programmes at the National and State level in both the NACP and Revised National TB Control Programme (RNTCP).
- National Consultants for TB-HIV provided to the NACP and RNTCP through the WHO technical assistance project.[21]
- Technical officers at SACS for basic services (including TB-HIV) (1-2 per state).
- State TB-HIV Coordinators initially sanctioned by the RNTCP in all states.
- District level supervisors for monitoring TB-HIV and drug resistant TB related activities who were sanctioned for all districts by the RNTCP.

In addition, joint planning, supervision, monitoring and review were started through joint TB-HIV visits to states and districts and joint programme reviews were conducted at national and state level. National targets for assessing TB-HIV collaborative activities were defined. The performance of TB-HIV collaborative activities was analysed and indicators were published by the RNTCP every quarter in their website http://tbcindia.nic.in/. However, despite the planning, there were important challenges for implementation.

CHALLENGES IN TB–HIV COLLABORATION

The challenges are described under three broad headings, in line with those present in the global policy document on TB/HIV collaboration : i) Overarching challenges in setting up mechanisms of collaboration ii) Challenges in reducing the burden of TB among PLHIV iii) Challenges in reducing the burden of HIV among TB patients.

OVERARCHING CHALLENGES IN SETTING UP COLLABORATION MECHANISMS

Setting up mechanisms of collaboration

- **Establishing a coordinating body** for TB-HIV collaborative activities at all levels of the health system was challenging. Some districts did not have a functional district co-ordination committee, especially those without a full-time nodal officer for HIV/AIDS. Only about 65% of the district level committees were reported to be functioning in 2010.
- **Administrative guidelines for organizing training** of staff were not uniform under the NACP and RNTCP and were frequently a source of conflict in programme implementation.

These needed to be aligned. There was no joint planning, joint implementation and joint monitoring between NACP and RNTCP, especially at state and district levels.

- **Lack of time and capacity to conduct policy-relevant operational research within the national programmes**

CHALLENGES IN REDUCING THE BURDEN OF TB AMONG PLHIV

- **Intensified TB case finding (ICF)** activities, though were established in all HIV testing and counselling centres and ART centres across the country, there were many challenges in implementation, especially from states with lower prevalence of HIV, perhaps reflecting the low perceived priority among decision makers. There were many recording and reporting errors. Changing the definition of presumptive TB patient in PLHIV from "any cough" to "any of the four symptoms of "cough, fever, weight loss and night sweats" needed to be disseminated. Sputum smear microscopy was still the mainstay of diagnosis at the time despite its known limitations among PLHIV (limited sensitivity, inability to identify drug resistance). The widely acclaimed newer and rapid diagnostic test such as the Xpert MTB/RIF assay (a cartridge based automated nucleic acid amplification test that uses a common platform to diagnose both TB and Rifampicin resistance) was still not widely available in India.
- **Isoniazid preventive therapy (IPT)** for PLHIV without TB was not a policy at the time. However, the NTWG for TB-HIV recognized the value of IPT and recommended operational research to assess the operational feasibility of adoption of the IPT strategy into programme settings. [22]
- **TB infection control in health care and congregate settings (IC):** The National Airborne Infection Control Committee (NAICC) was established and national guidelines were developed in 2008. Despite these, the TB infection control measures were not implemented or poorly practiced in many HIV settings. [22]

CHALLENGES IN REDUCING THE BURDEN OF HIV AMONG TB PATIENTS

- **HIV testing of TB patients:** On the basis of international recommendations and Indian operational research,[16] routine referral of all TB patients for HIV testing was incorporated into the national policy in 2008. This increased the number and proportion of TB patients with known HIV status from 34% in 2008 to 65% in 2010. However, there were several implementation challenges which included i) wide geographic variations ii) lack of HIV testing services at TB diagnostic centres iii) delays in trainings and procurement and iv) interrupted supply of HIV testing kits.[22]
- **HIV testing of presumptive TB patients** was not a national policy at the time, even though WHO recommended moving HIV testing upstream by testing all patients with presumptive TB (formerly referred to as TB suspects) as a way of early detection of HIV-infected TB patients.[13] Evidence from observational studies in sub-Saharan Africa[23–29] had shown that testing for HIV in patients with presumptive TB yielded a high number

of new diagnoses of HIV infection as the prevalence of HIV was higher than among the general adult population; these findings, however, could not be generalized to the Indian situation. HIV testing of contacts of HIV-infected TB patients was not a policy in India at the time, despite favourable evidence from other settings. [30]

- **Provision of CPT and ART to all HIV-infected TB patients:** At the time, while nearly 90% of HIV-infected TB patients received CPT, only about 50% HIV-infected TB patients were linked to ART care and support. One of the reasons ascribed to the low proportion of HIV-TB patients on ART was that not all HIV-infected TB patients were eligible for ART. India still followed the WHO 2006 guidelines and had concerns about adopting the WHO 2010 ART guidelines (these specified that all HIV-infected TB patients were eligible for ART irrespective of the CD4-cell count) since there were concerns about the resource implications and the increased workload that such a strategy would impose on the national ART programme. Other barriers to ART linkage were related to long travel times, distances and financial barriers as ART services were centralised and were provided in selected health facilities only.[22]

To address some of the challenges described above, several operational research studies were planned and carried out. The aims and objectives and their rationale are described below.

AIM AND OBJECTIVES AND THEIR RATIONALE

The aim of the operational research projects that constitute this thesis was to generate and use policy-relevant national evidence to improve the management of HIV-infected TB patients in India.

There were three key objectives namely:

1. To evaluate the additional number of patients that would be initiated on ART if India adopted the current 2010 WHO ART guidelines of placing all HIV-infected TB patients on ART regardless of CD4 cell count.
2. To assess the prevalence of HIV among patients with presumptive TB in different settings with different levels of HIV prevalence and the proportion eligible for starting ART according to 2015 WHO Guidelines.
3. To document the operational research capacity building initiatives undertaken in India, their evolution and impact on policy and practice.

The Sustainable Development Goals (SDGs) of the United Nations aim to end HIV and TB epidemics by 2030 and this is also endorsed by the WHO's END TB strategy. To achieve these goals, UNAIDS and the STOP TB partnership of the WHO have proposed 90-90-90 targets. All the studies included in this thesis were conducted in India, which harbours the highest number of TB patients and about 10% of all HIV-TB patients globally. Importantly, the studies

address the HIV-TB component of these international goals and efforts to achieve the set targets. A conceptual framework of the work in thesis and how they fit into the international communities' ambition to end the TB and HIV epidemics by 2030 is depicted in **Figure 2**.

OUTLINE OF THE THESIS

We describe six operational research studies (including two multicentre operational research projects) and their findings in this thesis and discuss their overall contribution to changes in policy, practice and the improvement of health outcomes among HIV-infected TB patients in India.[31–37] Most of these studies were carried out in collaboration with national TB and HIV programmes and other key stakeholders at international and local levels.

To catalyse the generation of evidence, we built capacity of several public health professionals in India using the SORT IT (Structured Operational Research Training Initiative) model of capacity building, developed by the International Union Against Tuberculosis and Lung Disease (The Union) and Médecins Sans Frontières in partnership with the WHO's Special Programme for Research and Training in Tropical Diseases (WHO-TDR).[38] In addition, the author of this thesis was mentored under a global OR fellowship programme run by The Union in 2012. The SORT IT model and its adaptations, the OR fellowship programme and the impact of these on policy and practice has been described in a series of viewpoint and original research articles.[39–42]

A brief outline of what is covered in each chapter is provided below structured as per the key objectives.

Objective 1: This is covered in Chapter 2. In 2010, WHO expanded previously-recommended indications for ART to include all HIV-infected TB patients irrespective of the CD4 count. India, however, still limited ART to TB patients with CD4-cell counts <350/mm3 or with extra-pulmonary TB. We sought to evaluate the additional number of patients that would be initiated on ART if India adopted the current 2010 WHO ART guidelines for HIV-infected TB patients. The findings of this research study are described in Chapter 2.

Objective 2: This is covered in Chapters 3-8. HIV testing of persons referred for tuberculosis diagnosis (patients with presumptive TB) is recommended by the WHO, but was not a policy in India where HIV prevalence among presumptive TB patients had never been studied. To fill this knowledge gap, a study was conducted in two districts of South India to assess the prevalence of HIV among patients with presumptive TB and the feasibility of provider initiated HIV testing under programmatic settings. The findings of these studies are reported in Chapters 3 and 4. Based on the findings of the studies described in Chapters 3 and 4, a national policy decision was taken to routinely offer HIV testing to patients with presumptive TB in high-burden HIV states of India. However, how this should best be implemented and

monitored in routine health care settings in India was not known. An operational research was conducted in Karnataka State (South India, population 64 million and accounting for 10% of India's national HIV burden), to test processes and learn the challenges of screening presumptive TB patients for HIV within routine health care settings. The findings of this operational research study are described in Chapter 5. An innovative process using open-access technologies like EpiData, Dropbox and TeamViewer was used to co-ordinate quality-assured data capture in the multicentre study described in Chapter 5. This model of data capture is described in detail in Chapter 6. While it became clear that HIV testing among presumptive TB patients was of value in high-HIV burden settings of India, it was not clear if it was of value in low-HIV burden settings. A study was undertaken in Puducherry to answer this question. The findings of this study are described in Chapter 7. Chapter 8 describes the results of an operational research study conducted in the state of Karnataka to assess the proportion of HIV-infected presumptive TB patients eligible for initiating ART according to the WHO guidelines at the point in time.

Objective 3: This is covered in chapters 9-12. As mentioned earlier, capacity building using the SORT IT model and the OR Fellowship programme was key to catalyse the generation of programme relevant operational research evidence. Most of the papers described in this thesis are a result and outcome of these two initiatives. We describe in chapters 9-12 the evolution of this model of capacity building and its impact on policy and practice.

REFERENCES

1 World Health Organization (WHO). Global Tuberculosis Report 2016. Geneva, 2016.

2 The Joint United Nations Programme on HIV/AIDS (UNAIDS). Global AIDS Update. 2016.

3 Harries AD, Lawn SD, Getahun H, Zachariah R, Havlir D V. HIV and tuberculosis - Science and implementation to turn the tide and reduce deaths. J Int AIDS Soc. 2012; 15: 17396.

4 Harries AD, Zachariah R, Corbett EL, et al. The HIV-associated tuberculosis epidemic-when will we act? Lancet. 2010; 375: 1906–19.

5 United Nations. Transforming Our World: The 2030 Agenda For Sustainable Development Transforming Our World: The 2030 Agenda For Sustainable Development. 2016.

6 Uplekar M, Weil D, Lonnroth K, et al. WHO's new end TB strategy. Lancet 2015; 385: 1799–801.

7 The Joint United Nations Programme on HIV/AIDS (UNAIDS). Press release: UNAIDS Board calls for ending the AIDS epidemic as a public health threat by 2030. 2014. http://www.unaids.org/en/resources/presscentre/pressreleaseandstatementarchive/2014/july/20140704prpcb34 (accessed April 23, 2017).

8 The Joint United Nations Programme on HIV/AIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. Geneva, 2014.

9 World Health Organization (WHO), Stop TB Partnership. The Paradigm Shift 2016-2020: Global Plan to End TB. Geneva, 2015.

10 National AIDS Control Organization, National Institute of Medical Statistics, ICMR, Ministry of Health and Family Welfare, Government of India. India HIV Estimations 2015 Technical Report. 2016.

11 Dewan PK, Gupta D, Williams BG, et al. National estimate of HIV seroprevalence among tuberculosis patients in India. Int J Tuberc Lung Dis 2010; 14: 247–9.

12 World Health Organization (WHO). Scaling up of collaborative TB/HIV activities in concentrated HIV epidemic settings: A case study from India. Geneva, 2015.

13 World Health Organization. WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. Geneva, 2012.

14 Central TB Division Directorate General Health Services, Ministry of Health and Family Welfare, Government of India. Revised National TB Control Programme Technical and Operational Guidelines for Tuberculosis Control in India 2016. New Delhi, 2016.

15 Thomas BE, Dewan PK, Vijay S, et al. Perceptions of tuberculosis patients on provider-initiated HIV testing and counseling--a study from south India. PLoS One 2009; 4: e8389.

16 Vijay S, Swaminathan S, Vaidyanathan P, et al. Feasibility of provider-initiated HIV testing and counselling of tuberculosis patients under the TB control programme in two districts of South India. PLoS One 2009; 4: e7899.

17 Raizada N, Chauhan LS, Babu BS, et al. Linking HIV-infected TB patients to cotrimoxazole prophylaxis and antiretroviral treatment in India. PLoS One 2009; 4: e5999.

18 Shetty PVD, Granich RM, Patil AB, et al. Cross-referral between voluntary HIV counselling and testing centres and TB services, Maharashtra, India, 2003-2004. Int J Tuberc Lung Dis 2008; 12: 26–31.

19 National AIDS Control Organization and Central TB Division, Ministry of Health and Family Welfare, Government of India. National Framework For Joint HIV/TB Collaborative Activities October 2009. New Delhi, India, 2009.

20 World Health Organization (WHO). Interim Policy on collaborative TB/HIV Activities. Geneva, 2004.

21 Singh RM, Castro KG. Rapid Assessment of the Technical Support Network Provided by the World Health Organization to the Revised National Tuberculosis Control Programme in India. Health Finance & Governance Project, Abt Associates Inc., Bethesda, MD. 2016.

22 Ministry of Health and Family Welfare, Government of India, World Health Organization. Joint Monitoring Mission Revised National Tuberculosis Control Programme (RNTCP), India 21-31 August 2012. New Delhi, India, 2012.

23 Porskrog A, Bjerregaard-Andersen M, Oliveira I, et al. Enhanced tuberculosis identification through 1-month follow-up of smear-negative tuberculosis suspects. Int J Tuberc Lung Dis 2011; 15: 459–64.

24 Deribew A, Negussu N, Kassahun W, Apers L, Colebunders R. Uptake of provider-initiated counselling and testing among tuberculosis suspects, Ethiopia. Int J Tuberc Lung Dis 2010; 14: 1442–6.

25 Srikantiah P, Lin R, Walusimbi M, et al. Elevated HIV seroprevalence and risk behavior among Ugandan TB suspects: implications for HIV testing and prevention. Int J Tuberc Lung Dis 2007; 11: 168–74.

26 Odhiambo J, Kizito W, Njoroge A, et al. Provider-initiated HIV testing and counselling for TB patients and suspects in Nairobi, Kenya. Int J Tuberc Lung Dis 2008; 12: 63–8.

27 Munthali L, Mwaungulu JN, Munthali K, Bowie C, Crampin AC. Using tuberculosis suspects to identify patients eligible for antiretroviral treatment. Int J Tuberc Lung Dis 2006; 10: 199–202.

28 Dimairo M, MacPherson P, Bandason T, et al. The risk and timing of tuberculosis diagnosed in smear-negative TB suspects: a 12 month cohort study in Harare, Zimbabwe. PLoS One 2010; 5: e11849.

29 Adjei AA, Adiku TK, Ayeh-Kumi PF, Hesse IF. Prevalence of human immunodeficiency virus infection among tuberculosis suspect patients in Accra, Ghana. West Afr J Med 2006; 25: 38–41.

30 Suggaravetsiri P, Yanai H, Chongsuvivatwong V, Naimpasan O, Akarasewi P. Integrated counseling and screening for tuberculosis and HIV among household contacts of tuberculosis patients in an endemic area of HIV infection: Chiang Rai, Thailand. Int J Tuberc Lung Dis 2003; 7: S424-31.

31 Kumar AM V, Gupta D, Rewari BB, et al. Will adoption of the 2010 WHO ART guidelines for HIV-infected TB patients increase the demand for ART services in India? PLoS One 2011; 6: e24297.

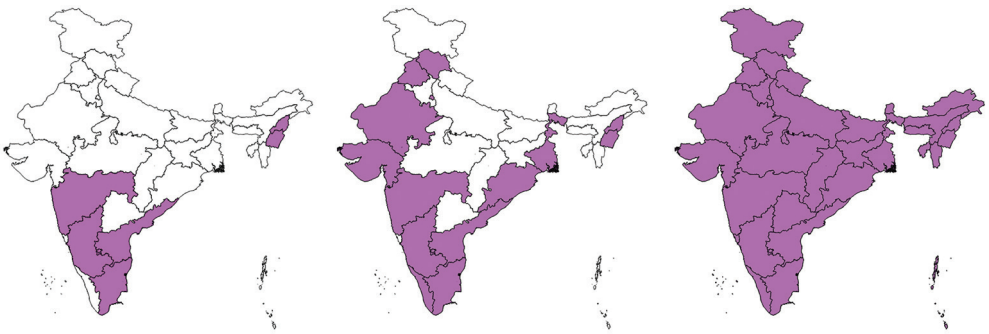
32 Palanivel C, Kumar AM V, Mahalakshmi T, et al. Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India. Public Health Action 2013; 3: 220–3.

33 Kumar AM V, Gupta D, Gupta RS, et al. HIV testing in people with presumptive tuberculosis: time for implementation. Lancet Respir Med 2013; 1: 7–9.

34 Kumar AM V, Singarajipura A, Naik B, et al. HIV-infected presumptive tuberculosis patients without tuberculosis: How many are eligible for antiretroviral therapy in Karnataka, India? J Epidemiol Glob Health 2017; 7: 11–9.

35 Kumar AM V, Naik B, Guddemane DK, et al. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. Public Health Action 2013; 3: 60–2.
36 Naik B, Kumar Mv A, Lal K, et al. HIV prevalence among persons suspected of tuberculosis: policy implications for India. J Acquir Immune Defic Syndr 2012; 59: e72-6.
37 Achanta S, Kumar AM V, Nagaraja SB, et al. Feasibility and effectiveness of provider initiated HIV testing and counseling of TB suspects in Vizianagaram district, South India. PLoS One 2012; 7: e41378.
38 Ramsay A, Harries AD, Zachariah R, et al. The Structured Operational Research and Training Initiative for public health programmes. Public Health Action 2014; 4: 79–84.
39 Kumar AM V, Satyanarayana S, Wilson N, Zachariah R, Harries AD. Operational research capacity building in Asia: innovations, successes and challenges of a training course. Public Health Action 2013; 3: 186–8.
40 Kumar AM V, Zachariah R, Satyanarayana S, et al. Operational research capacity building using 'The Union/MSF' model: adapting as we go along. BMC Res Notes 2014; 7: 819.
41 Kumar AM V, Satyanarayana S, Berger SD, et al. Promoting operational research through fellowships: a case study from the South-East Asia Union Office. Public Health Action 2015; 5: 6–16.
42 Kumar AM V, Shewade HD, Tripathy JP, et al. Does research through Structured Operational Research and Training (SORT IT) courses impact policy and practice? Public Health Action 2016; 6: 44–9.

Figure 1. Scale-up of TB-HIV collaborative activities in India 2001-12



2001 (Essential Package initiated)
2007 (Shift to intensified Package)

Coverage (in purple), of 6 states (Maharashtra, Manipur, Nagaland, Karnataka, Tamil Nadu and Andhra Pradesh)

2004 (Essential Package initiated)
2009 (Shift to intensified Package)

Coverage (in purple), extended to 8 more states (Delhi, Gujarat, Himachal Pradesh, Kerala, Orissa, Punjab, Rajasthan and West Bengal)

2007 (Essential Package initiated)
2012 (Shift to intensified Package)

Coverage (in purple) extended Nationwide

Essential Package: 1. Establishing mechanisms of coordination at national, state (sub-national) and district levels. 2. Joint Training of field staff on TB-HIV. 3. Intensified TB case finding at HIV testing and ART centres (documentation and reporting in dedicated formats). 4. Risk-based selective referral of TB patients for HIV testing 5. Referral of HIV-infected TB patients to HIV care, support and treatment centres

Intensified Package: 1. Provider-initiated, routine offer of HIV testing to all TB patients 2. Decentralized provision of CPT to all HIV-TB patients at peripheral health institution level 3. Referral of HIV-infected TB patients to ART centres for initiation of ART based on eligibility 4. Expanded recording and reporting system which includes documentation of HIV status, CPT and ART in TB treatment cards and TB registers
TB=Tuberculosis; HIV=Human Immunodeficiency Virus; ART=Antiretroviral therapy; CPT= Cotrimoxazole Preventive Therapy;

Figure 2: Conceptual Framework

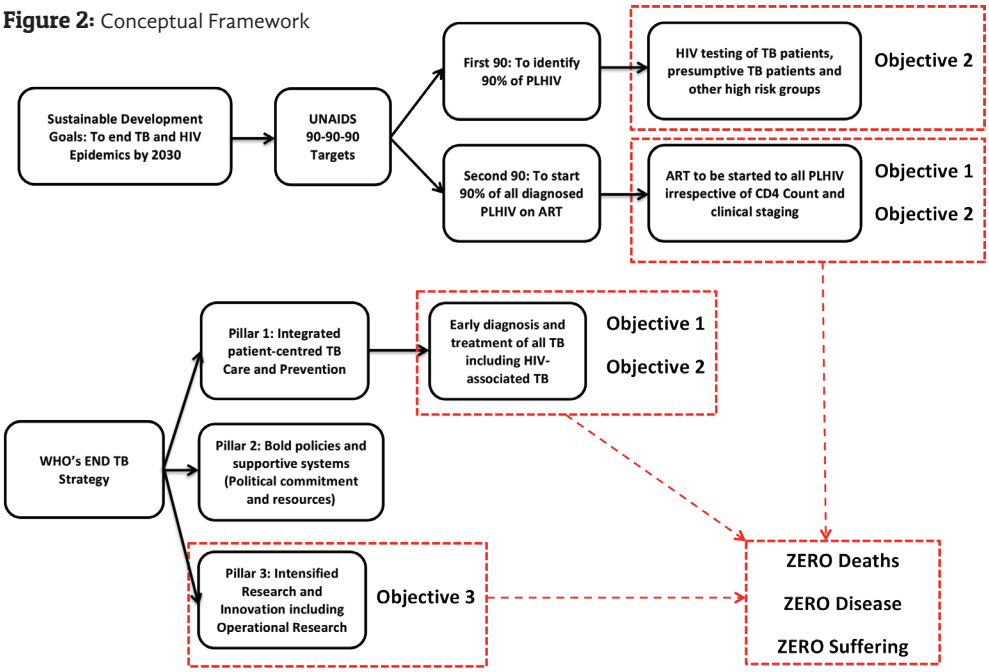


Table 1: Components of differential packages provided in the early years of TB-HIV collaboration in India, 2007-09.

Essential TB-HIV Package (all states)	Intensified TB-HIV Package (selected states with high burden of TB-HIV)
1. Establishing mechanisms of coordination at national, state (sub-national) and district levels	1. Provider-initiated, routine offer of HIV testing to all TB patients
2. Joint Training of field staff on TB-HIV	2. Decentralized provision of CPT to all HIV-TB patients at peripheral health institution level
3. Intensified TB case finding at HIV testing and ART centres (documentation and reporting in dedicated formats)	3. Referral of HIV-infected TB patients to ART centres for initiation of ART based on eligibility
4. Risk-based selective referral of TB patients for HIV testing	4. Expanded recording and reporting system which includes documentation of HIV status, CPT and ART in TB treatment cards and TB registers
5. Referral of HIV-infected TB patients to HIV care, support and treatment centres	

TB=Tuberculosis; HIV=Human Immunodeficiency Virus; ART=Antiretroviral therapy; CPT= Cotrimoxazole Preventive Therapy.

2.

Will Adoption of the 2010 WHO ART Guidelines for HIV–Infected TB Patients Increase the Demand for ART Services in India?

Kumar AMV, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, Lal K, Reddy HRR, Naik B, Prasad R, Yaqoob M, Deepak KG, Shastri S, Satyanarayana S, David Harries A, Chauhan LS, Dewan P. PLoS ONE. 2011;6(9):e24297.

Background

In 2010, WHO expanded previously-recommended indications for anti-retroviral treatment to include all HIV-infected TB patients irrespective of CD4 count. India, however, still limits ART to those TB patients with CD4 counts <350/mm^3 or with extrapulmonary TB manifestations. We sought to evaluate the additional number of patients that would be initiated on ART if India adopted the current 2010 WHO ART guidelines for HIV-infected TB patients.

Methods

We evaluated all TB patients recorded in treatment registers of the Revised National TB Control Programme in June 2010 in the high-HIV prevalence state of Karnataka, and cross-matched HIV-infected TB patients with ART programme records.

Results

Of 6182 TB patients registered, HIV status was ascertained for 5761(93%) and 710(12%) were HIV-infected. 146(21%) HIV-infected TB patients were on ART prior to TB diagnosis. Of the remaining 564, 497(88%) were assessed for ART eligibility; of these, 436(88%) were eligible for ART according to 2006 WHO ART guidelines. Altogether, 487(69%) HIV-infected TB patients received ART during TB treatment. About 80% started ART within 8 weeks of TB treatment and 95% received an efavirenz based regimen.

Conclusion

In Karnataka, India, about nine out of ten HIV-infected TB patients were eligible for ART according to 2006 WHO ART guidelines. The efficiency of HIV case finding, ART evaluation, and ART initiation was relatively high, with 78% of eligible HIV-infected patients actually initiated on ART, and 80% within 8 weeks of diagnosis. ART could be extended to all HIV-infected TB patients irrespective of CD4 count with relatively little additional burden on the national ART programme.

INTRODUCTION

HIV-infected TB patients experience a high case-fatality rate during anti-tuberculosis (TB) treatment[1]. Antiretroviral therapy (ART) reduces this risk of death, provided ART is started early enough during anti-TB treatment[2]. The efficient and timely initiation of ART in HIV-infected TB patients is crucial to reduce mortality among HIV-infected TB patients.

In India, the National AIDS Control Programme (NACP) ART guidelines are still in line with 2006 World Health Organization (WHO) Guidelines for ART[3,4]. As per 2006 guidelines, all HIV-infected persons with extra-pulmonary (EPTB) or disseminated TB and HIV-infected pulmonary tuberculosis (PTB) patients with a CD4-lymphocyte count <350/mm^3 are considered eligible for ART. In contrast, the 2010 WHO ART Guidelines recommend that ART be initiated in all HIV-infected TB patients (PTB and EPTB), irrespective of CD4 count, as soon as possible during the initial phase of anti-TB treatment[5].

India proposes to change over to the new 2010 WHO ART Guidelines, but there is concern that giving ART to all HIV-infected TB patients may have major resource implications for the national ART programme. There is little information available about what proportion of HIV-infected TB patients are eligible for ART according to the current NACP criteria and how this might change if the new 2010 WHO ART Guidelines were adopted and implemented in India. There was some information on ART eligibility from a previous study, but this was not representative as most of the HIV-infected TB patients could not be evaluated for ART eligibility because of poor information on CD4 counts [6]. Better knowledge of ART eligibility and the efficiency with which patients are initiated on ART is critical for policy makers to plan for increases in demand for drugs and services.

We conducted a cross-sectional survey in the state of Karnataka, one of the highest HIV prevalent states in India, to evaluate the additional number of patients that would be initiated on ART if India adopted current WHO ART guidelines for HIV-infected TB patients. The specific objectives were to assess:- i) number (proportion) of TB patients ascertained for HIV status with their results, ii) number (proportion) of HIV-infected TB patients eligible for ART and started on ART during anti-TB treatment and iii) when ART was started and the type of regimen used.

METHODS

DESIGN

This was a cross sectional study involving review of routinely collected data recorded in TB and HIV programme records.

SETTING

Karnataka, a south Indian state with a population of 61 million, has an estimated 0.25 million people living with HIV in 2009 and accounts for about 10% of country's HIV burden[7]. Hence,

the state has been classified as 'high priority' for HIV interventions by the Indian National AIDS Control Organization (NACO) on the basis of consistently high HIV seroprevalence rates of >1% during sentinel surveillance at antenatal clinics[8,9]. In the state, tuberculosis control programme services are available through a decentralized network of primary health care facilities which provide general health services including diagnosis and treatment for TB. All TB patients are treated with standardized fully intermittent thrice-weekly short-course regimens (6-9 months) administered under direct observation and are registered at one of the 125 sub-district level TB programme management units according to Indian programme guidelines[10].

There is a national policy of Provider-Initiated HIV Testing and Counseling (PITC) of all TB patients, and HIV-infected TB patients are provided cotrimoxazole preventive therapy (CPT) and referred to ART centres for assessment of ART eligibility and initiation on ART if found to be eligible[11]. TB patients are referred for free HIV counseling and testing to one of the 1000 integrated counseling and testing centre (ICTC) throughout the state, which are usually co-located with sputum microscopy services. Free ART is provided through a network of 40 ART centres (with at-least one ART centre in every district), where HIV-infected patients (including TB patients) are screened for ART eligibility and offered treatment and care. These service delivery sites under NACP follow the national guidelines for counseling, testing, care and treatment of HIV-infected patients[12]. In the year 2010, of 68,655 TB patients registered in Karnataka, 82% were tested for HIV and 8,485 HIV-infected TB patients were identified[13].

STUDY POPULATION

From a cohort of TB patients (except transfer-in cases) registered in Karnataka state, India, between 1st and 30th June 2010, all those identified as HIV-infected were consecutively included in the study.

DATA COLLECTION AND VALIDATION

Data on the number of TB patients registered, number with known HIV status and number HIV-infected were extracted from the TB registers. TB-HIV data were collected into a pre-tested structured data abstraction form by trained consultants between November and December 2010. Data collected included age, sex, type and category of TB, CD4 count, ART initiation, timing of ART initiation and ART regimen. These data were collected from the existing programme records of Revised National TB Control Programme (TB registers and TB treatment cards) and NACP (TB/HIV register, pre-ART registers, ART registers and the electronic patient database maintained at the ART centres). If HIV-infected TB patients were receiving ART from another district, the records of the respective ART centres were reviewed. If there were discrepancies between data in the different records, these were resolved by interviewing the medical officers of the respective health institution. Except where mentioned, standard definitions according to the national programme guidelines were used.

DATA ENTRY AND ANALYSIS

Data were double-entered into an EpiData database by two data entry operators independently[14]. Databases were compared and discrepancies resolved through referral to the original questionnaire. Proportions of TB patients with known HIV status and proportions of HIV-infected TB patients who were eligible for ART, initiated on ART with timing of ART initiation were calculated.

ETHICS APPROVAL

Ethics approval was obtained by the Ethics Advisory Group of the International Union against TB and lung disease (The Union). Approvals of Central TB Division, Ministry of Health and Family Welfare and National AIDS Control organization were also obtained for conducting this evaluation.

RESULTS

Of 6,182 TB patients registered in Karnataka in June 2010, HIV status was known for 5,761 (93%), and 710 (12%) were recorded as HIV-infected. The demographic, clinical and immunological characteristics of HIV-infected TB patients are shown in **Table 1**. Two thirds of the patients were men, with the majority being in the age group 25-54 years. Most of the patients had new TB and about three quarters of patients were classified as pulmonary tuberculosis with almost equal division between sputum-smear positive and sputum smear negative. CD4-counts were recorded for 621 (87%) patients, of whom 512 (82%) had a CD4 count less than or equal to 350 cells/mm^3.

Assessment for ART eligibility and initiation of ART is shown in **Figure 1**. Of all 710 HIV-infected TB patients identified, 146 (21%) were already on ART prior to TB diagnosis. Of the 564 patients who were not on ART at the time of TB diagnosis, 145 (25%) had extra-pulmonary TB and were immediately ART eligible. Of the 419 pulmonary TB patients not already on ART, 352 (84%) had available CD4 information, among whom 291 (83%) had a CD4 count <350 cells/mm^3 and were ART eligible. Altogether, 497/564 (88%) could be assessed for ART eligibility and among them, 436 (88%) were eligible for ART.

Overall, 487(67%) HIV-infected TB patients received ART during TB treatment, with ART started either before or after the diagnosis of TB.

For those patients who received ART either before or after TB diagnosis, the time of initiation of ART and the type of regimen are shown in **Table 2**. Of the 341 patients who started ART after TB diagnosis, 272 (80%) started within eight weeks of commencing anti-TB treatment. Almost 95% of patients received an efavirenz-based ART regimen.

DISCUSSION

This study in Karnataka state showed the majority of TB patients in a high HIV prevalence state in India were tested for HIV, and of those found to be HIV-positive nearly 90% were eligible for ART according to current NACP and 2006 WHO ART guidelines. As a public health approach to ART, this strongly justifies the adoption of the WHO 2010 ART Guidelines, recommending that all HIV-infected TB patients are started on ART regardless of CD4 count. As <10% of HIV-infected TB patients had CD4 counts > 350 cells/mm^3, the adoption of the WHO ART Guideline recommendation for HIV-infected TB patients is not likely to place a large additional burden on the national ART programme.

We also determined sub-optimal programme efficiency in the initiation of ART for patients eligible under current guidelines; 23% of HIV-infected TB patients should have got ART, but did not. To illustrate this point, we can apply these findings to the state of Karnataka. In the state of Karnataka in 2010, of 68,665 tuberculosis patients registered for treatment, 56,622 knew their HIV status and 8,485 were identified as HIV-infected[13]. Assuming existing operational efficiency, 67% (5,685) would be receiving ART and another 23% (1,951) would be eligible for ART as per current ART eligibility criteria, but not yet on ART due to operational challenges. Increasing the programme efficiency of ART initiation could place 1,951 additional people on ART. About 10% (849) would be eligible for ART if new guidelines are implemented. Given that there were about 55,102 people alive and on ART in the state of Karnataka at the end of 2010, the annual addition of 849 (1.5%) people to the ART programme from 'changed guidelines', and 1,951 (3.5%) people from 'improved programme efficiency' would be modest. Improvements in programme efficiency of ART initiation for HIV-infected TB patients offers another important opportunity to improve ART coverage in HIV-infected TB patients, and in the larger context of ART provision would pose little additional burden on existing HIV treatment services.

This was the first state-wide study in India assessing the management of HIV diagnosis and care in TB patients under programmatic settings. The only other study to examine this issue in India found similar results in 2 districts of South India, in which about 83% of HIV-infected TB patients were eligible for ART; but this finding suffered from very low completion of CD4 evaluation in that cohort[6]. Similar findings have been reported from sub-Saharan Africa, where 90% of HIV-infected TB patients had CD4 counts below 350 cells/mm^3 [15]. Our study covered the entire state of Karnataka and had very high rates of HIV case finding among TB patients and CD4 testing. Hence, these results are likely to be broadly generalizable. Given the similarity of results from various settings, we also believe that the results may be extrapolated to other high HIV prevalent states in the country, though more research is required to confirm this. The high rates of HIV testing among TB patients in this cohort could be attributed to the widespread availability of HIV testing services co-located with the TB microscopy centres in the state. Since TB patients can be a high-yield

source of HIV case finding, this calls for scale-up of co-located HIV testing and TB testing services across the country.

This study also emphasizes that in resource-poor settings, the majority of HIV-infected TB patients who are not already on ART present to health services late and with low CD4 counts. The reasons for late presentation are many and include late diagnosis of HIV and the low CD4 threshold currently used for initiating ART among all HIV-infected persons. Hence, the national programmes should explore other opportunities of improved and earlier diagnosis of HIV-infected TB patients like PITC of TB suspects and strengthening intensified TB case finding activities at HIV care settings by the use of WHO-endorsed, new, rapid molecular technologies to diagnose TB[16]. The 2010 WHO ART guidelines which recommends initiation of ART for all PLHIV with CD4 count of <350/mm^3 is a welcome change in this regard which may not only prevent TB cases from occurring but may also ensure that those who develop TB would have higher CD4 counts and consequently the likelihood of better clinical outcomes. NACP and RNTCP are considering all the above options in their next joint national strategic plan (2012-17) to achieve improved and earlier diagnosis of HIV-infected TB patients[17].

This study also revealed operational weaknesses in ART services. There were various reasons for poor ART uptake that included failure to reach the ART centre, not getting CD4 counts done, having a CD4 count > 350 cells/uL in the case of pulmonary tuberculosis and not returning to the ART centre after starting TB treatment. Some of these patients may have died or been too sick to reach the ART centre. Removal of the CD4 count hurdle as part of ART eligibility criteria may make it easier to start ART. More than one in five patients defined as ART eligible still failed to receive ART during TB treatment. As per NACP guidelines, patients were required to show proof of address and needed to make 2-3 visits for baseline investigations and adherence counseling before initiation of ART. Though this was important to ensure long term adherence to treatment, it might have contributed to losing track of even those who were eligible for ART. An assessment of reasons for the lack of ART initiation for eligible patients was beyond the scope of the current study and this needs further investigation. On a positive note, the majority of patients who started ART did so within 8 weeks of commencing TB treatment in accordance with the NACP and WHO recommendations, with efavirenz-based ART regimens being those most commonly used as per current NACP guidelines. Early ART initiation for HIV-infected TB patients has been convincingly shown to save lives, and the timeliness of ART initiation should be monitored to ensure continued effective implementation.

This study had some limitations mainly related to our reliance on data collected routinely by the national TB and HIV programmes, where high accuracy of recording is difficult to ensure. Although the 2010 WHO ART guidelines are justified as a public health approach, it is important to study the TB treatment outcomes among the subgroup of HIV-infected TB patients with CD4 count of >350/mm^3 and assess if they actually benefit by early initiation of ART. A previous study from Cote d'Ivoire indicated that although mortality was less among HIV-infected TB patients with CD4 count of >200/mm^3 when compared with those

whose CD4 count was <200/mm^3, it still remained many times higher than in HIV-negative TB patients[18]. Information on mortality in HIV-infected TB patients whose CD4 counts of >350/mm^3 is limited and this needs further study. Further, we did not extend our research to do a costing exercise, but this can and should be a subject of further analysis.

In conclusion, this study indicates that about 90% of HIV-infected TB patients are eligible for ART as per 2006 WHO ART guidelines. Hence as a public health approach, this strongly justifies the adoption of 2010 WHO ART guidelines which recommends that all HIV-infected TB patients should be initiated on ART irrespective of CD4 count; this policy change should have few additional resource implications for the national ART programme. However, systematic measures need to be taken by the national TB and HIV programmes to improve access of HIV-infected TB patients to ART and bridge the gap in ART uptake.

ACKNOWLEDGEMENTS

The authors are thankful to the staff of the State TB Cell and Karnataka State AIDS prevention and control society, District TB Officers and their staff and the staff of the ART centres of the state of Karnataka for enthusiastically assisting in the process of data collection. Finally the authors are grateful to the HIV-infected TB patients of Karnataka state who have indirectly contributed to this learning.

REFERENCES

1. Mukadi YD, Maher D, Harries A (2001) Tuberculosis case fatality rates in high HIV prevalence populations in sub-Saharan Africa. AIDS 15: 143-152.
2. Harries AD, Zachariah R, Corbett EL, Lawn SD, Santos-Filho ET, et al. (2010) The HIV-associated tuberculosis epidemic--when will we act? Lancet 375: 1906-1919.
3. World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach (2006 revision). Geneva: World Health Organization; 2006 updated 9th May; Available: http://www.who.int/hiv/pub/arv/adult/en/index.html. Accessed 9th May 2011.
4. National AIDS Control Organization. Antiretroviral Therapy Guidelines for HIV-Infected Adults and Adolescents Including Post-exposure Prophylaxis, 2007. New Delhi: Ministry of Health and Family Welfare, Government of India; 2007; Available: http://www.nacoonline.org/Quick_Links/Publication/Treatment_Care__Support/. Accessed 9th May 2011.
5. World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach: 2010 revision. Geneva: World Health Organization; 2010 updated 9th May; Available: http://www.who.int/hiv/pub/arv/adult2010/en/index.html. Accessed 9th May 2011.
6. Vijay S, Swaminathan S, Vaidyanathan P, Thomas A, Chauhan LS, et al. (2009) Feasibility of provider-initiated HIV testing and counselling of tuberculosis patients under the TB control programme in two districts of South India. PLoS One 4: e7899.
7. National AIDS Control Organization. HIV estimates for India 2009. New Delhi: Ministry of Health and Family Welfare, Government of India; 2010; Available: http://www.nacoonline.org/upload/HomePage/NACO%20Press%20Release%20on%20HIV%20Estimates.pdf. Accessed 13 June 2011.
8. Ofice of the Registrar General and Census Commissioner. Provisional Population Totals paper-1 : 2011 – Karnataka. New Delhi: Government of India; 2011; Available: http://censusindia.gov.in/2011-prov-results/prov_data_products_karnatka.html. Accessed 9th May 2011.
9. National AIDS Control Organization. HIV Sentinel Surveillance and HIV Estimation, 2007, A technical brief. New Delhi: Ministry of Health and Family Welfare, Government of India; 2008; Available: http://www.nacoonline.org/Quick_Links/Publication/ME_and_Research_Surveillance/. Accessed 9th May 2011.
10. Central TB Division. Technical and Operations Guidelines for Tuberculosis Control. New Delhi: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2005; Available: http://www.tbcindia.org/documents.asp. Accessed 9th May 2011.
11. National AIDS Control Organization and Central TB Division. National framework for Joint HIV/TB collaborative activities. Delhi: Ministry of Health and Family Welfare, Government of India; 2009; Available: http://www.tbcindia.org/pdfs/Final%20National%20Framework%20for%20TB%20HIV%20Collaboration%202009.pdf. Accessed 28th May 2011.

12. National AIDS Control Organization. Operational Guidelines for Integrated Counselling and Testing Centres. New Delhi: Ministry of Health and Family Welfare, Government of India; 2008; Available: http://www.nacoonline.org/Quick_Links/Publication/Basic_Services/. Accessed 9th May 2011.
13. Central TB Division. TB India 2011. Revised National TB Control Programme Annual Status Report. New Delhi: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2011; Available: http://www.tbcindia.org/pdfs/RNTCP%20TB%20India%202011.pdf. Accessed 9th May 2011.
14. EpiData Association. EpiData Entry version 3.1. EpiData Association, Odense, Denmark, Europe; Available: http://www.epidata.dk/. Accessed 9th May 2011.
15. Teck R, Ascurra O, Gomani P, Manzi M, Pasulani O, et al. (2005) WHO clinical staging of HIV infection and disease, tuberculosis and eligibility for antiretroviral treatment: relationship to CD4 lymphocyte counts. Int J Tuberc Lung Dis 9: 258-262.
16. World Health Organization (2010) Roadmap for rolling out Xpert MTB/RIF for rapid diagnosis of TB and MDR-TB. Geneva, Switzerland: World Health Organization
17. National AIDS Control Organization and Central TB Division. Minutes of National Technical Working Group on TBHIV collaborative activities on March 23, 2010. Delhi: Ministry of Health and Family Welfare, Government of India; 2009; Available: http://www.tbcindia.org/pdfs/10-NTWG%20minutes%20230310.pdf. Accessed 13th June 2011.
18. Ackah AN, Coulibaly D, Digbeu H, Diallo K, Vetter KM, et al. (1995) Response to treatment, mortality, and CD4 lymphocyte counts in HIV-infected persons with tuberculosis in Abidjan, Cote d'Ivoire. Lancet 345: 607-610.

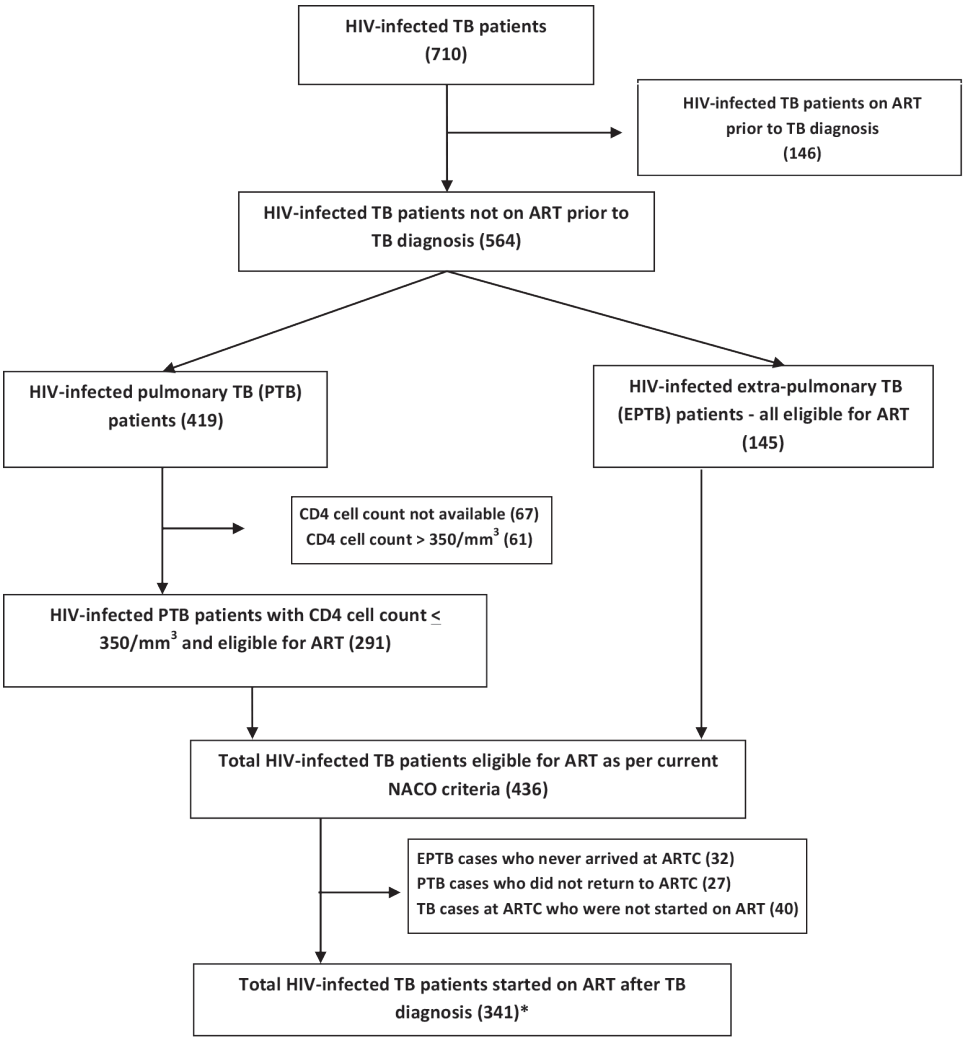


Figure 1. Eligibility for and initiation of antiretroviral treatment in HIV-infected TB patients registered in Karnataka state, India, in June 2010.

*4 PTB patients were started on ART even though not eligible as per guidelines TB-Tuberculosis; HIV-Human immunodeficiency virus; PTB-pulmonary tuberculosis; EPTB-extrapulmonary tuberculosis; NACO-National AIDS Control Organization; ART-antiretroviral treatment; ARTC-ART centre

Table 1: Characteristics of HIV-infected TB patients registered in Karnataka state, India, in June 2010.

Category	Sub-category	Number (%)
All patients		710 (100)*
Sex	Male	465 (66)
	Female	245 (34)
Age group	0-14 years	33 (5)
	15-24 years	23 (3)
	25-35 years	214 (30)
	35-44 years	283 (40)
	45-54 years	114 (16)
	55-64 years	38 (5)
	> 65 years	5 (1)
Type of TB**	Pulmonary TB	516 (73)
	Extra-pulmonary TB	194 (27)
Smear status of Pulmonary TB (N=516)	Smear Positive	285 (55)
	Smear Negative	216 (42)
	Smear Unknown	15 (3)
Site of Extra-pulmonary TB (N=194)	Lymph Node	62 (32)
	Pleura	39 (20)
	Meninges/CNS	33 (17)
	Abdomen	30 (16)
	Other	7 (3)
	Not recorded	23 (12)
TB registration type	New	593 (83)
	Relapse	30 (4)
	Treatment after Default	19 (3)
	Treatment after Failure	5 (1)
	Other	63 (9)
CD4 cell count	< 50/mm3	72 (10)
	50-200/mm3	291 (41)
	201-350/mm3	149 (21)
	> 350/mm3	109 (15)
	Not available	89 (13)

*Percentages may not always add up to 100 due to rounding errors
** There were 10 patients who had both pulmonary and extrapulmonary TB; they have been classified under extrapulmonary TB as they belong to HIV stage 4 and are ART eligible
TB-Tuberculosis; HIV-Human immunodeficiency virus; CNS-Central Nervous System

Table 2: Timing of ART initiation and ART regimen in HIV-infected TB patients registered in Karnataka state, India, in June 2010.

Category	Sub category	Number (%)
All patients on ART		487 (100)
Timing of ART initiation	Prior to TB diagnosis	146 (30)
	<2 weeks of TB treatment	67 (14)
	2-8 weeks of TB treatment	205 (42)
	>8 weeks of TB treatment	69 (14)
ART regimen	Zidovudine-Lamivudine-Efavirenz	224 (46)
	Stavudine-Lamivudine-Efavirenz	235 (48)
	Zidovudine-Lamivudine-Nevirapine	9 (2)
	Stavudine-Lamivudine-Nevirapine	13 (3)
	Other/Not recorded	6 (1)

TB-Tuberculosis; HIV-Human immunodeficiency virus; ART-antiretroviral treatment

3.

HIV prevalence among persons suspected of tuberculosis: policy implications for India

Naik B, **Kumar AM**, Lal K, Doddamani S, Krishnappa M, Inamdar V, Satyanarayana S, Gupta D, Dewan PK.
Journal of Acquired Immune Deficiency Syndromes. 2012;59(4):e72–6.

Background

HIV testing of persons referred for tuberculosis diagnosis (TB suspects) is recommended by World Health Organization but is not a policy in India, where HIV prevalence among TB suspects has never been reported. The current Indian policy of offering HIV testing only to TB cases may limit opportunities for early HIV diagnosis and treatment.

Methods

All adult TB suspects examined for diagnostic sputum microscopy in Mandya district (2 million population), in December 2010, were offered voluntary HIV counseling and testing. Participants were assessed for subsequent TB diagnosis.

Results

Of 1668 eligible TB suspects, HIV status was ascertained for 1539 (92%). Among these, 108 (7%) were HIV positive. Of the 108, 43 (40%) were newly diagnosed as HIV (ie, not previously known to have HIV infection). To detect a new case of HIV infection, the number needed to screen among TB patients was 13, as compared to a number needed to screen of 37 among "TB suspects not diagnosed as TB". Applied annually in 2010, HIV testing of TB suspects in 2010 could have identified approximately 534 newly diagnosed HIV cases, a 51% increase in district HIV case finding.

Conclusion

Routine HIV testing of TB suspects was feasible and yielded a large number of HIV cases in absolute terms and would increase district HIV case finding by 51%. The number of patients needed to be HIV tested to find a previously undetected HIV case among TB suspects was greater than for TB cases but was potentially acceptable. Given heterogeneity of HIV epidemic in India, broader surveillance is required before national policy decision.

INTRODUCTION

Globally and in India, tuberculosis (TB) is the most common opportunistic infection and the most common cause of death among HIV-infected individuals.[2-5] Unless HIV-infected TB patients are initiated on cotrimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) in addition to TB treatment, mortality may remain high.[5] The first step in this process is early identification of HIV-infected persons. Globally, less than half of those living with HIV know their HIV status[6]. To facilitate early HIV case-finding, World Health Organization (WHO) and International Standards for TB Care (ISTC) recommend provider initiated HIV testing and counseling (PITC) for people suspected and/or diagnosed to be having TB.[7-8] India has adopted the policy of PITC for TB patients.[9] The current policy of offering HIV testing only to TB cases may limit opportunities of early HIV diagnosis and treatment. Moving HIV testing upstream to include all persons suspected of having TB and referred for diagnostic evaluation (henceforth referred to as 'TB suspects'), though recommended internationally, is not a policy in India and HIV prevalence in this population has never been reported. Previous studies on this topic are mostly from African countries where HIV epidemic is generalized; the findings from these studies cannot be generalized to Indian situation with a concentrated HIV epidemic.[10-11] Indian policy makers seek evidence of the value of HIV testing of TB suspects for HIV case finding.[12]

We conducted this study in Mandya district of Karnataka, one of the highest HIV prevalent states in India, to assess the prevalence of HIV among persons referred to any microscopy center in the district for diagnostic evaluation. The specific objectives were, i) To determine the HIV prevalence among TB suspects examined for diagnostic smear microscopy, ii) To assess the number of HIV cases 'newly' diagnosed by testing all TB suspects, iii) To assess the number needed to screen (NNS) to find an additional case of HIV infected person among 'TB suspects' in comparison to 'TB patients', and iv) to assess the potential contribution of this activity to HIV case finding.

METHODS

DESIGN

This was a cross-sectional study done by offering HIV counseling and testing to TB suspects attending the microscopy centres for TB diagnosis.

SETTING

The study was done in Mandya district (population 2 million) of Karnataka state, India. In the district, tuberculosis control programme services are available through a decentralized network of primary health care facilities which provide general health services including diagnosis and treatment for TB. Any patient with a cough of 2 weeks or more is considered as

pulmonary TB suspect and referred to the microscopy centre for diagnostic evaluation. The sputum smear microscopy is done in 25 designated microscopy centres (DMC) of the district, which are RNTCP supported microscopy services embedded into the public health system clinics. Microscopy is supported by a district-wide system of external quality assurance. All TB patients diagnosed are treated with standardized fully intermittent thrice-weekly short-course regimens (6-9 months) administered under direct observation and are registered at 1 of the 4 sub-district level TB programme management units according to Indian TB programme guidelines.[13]

HIV counseling and testing services are offered through the National AIDS Control Programme-supported network of integrated counseling and testing centres (ICTC). There are about 24 ICTCs throughout the district, and these are co-located in the same health facilities as DMCs. These service delivery sites under National AIDS Control Programme follow the national guidelines for counseling, testing, care and treatment of HIV-infected patients.[14]

The current national policy is to offer routinely HIV counseling and testing to TB patients; those identified as HIV-infected are provided cotrimoxazole prophylaxis and referred to the nearest antiretroviral treatment (ART) centre for assessment of ART eligibility and initiation on ART—if found to be eligible. Free ART is provided through the district ART centre, where HIV-infected patients (including TB patients) are screened for ART eligibility and offered treatment and care. In the year 2010, 20,165 TB suspects were examined for sputum microscopy and 2,156 TB patients were registered in Mandya district. Of the TB patients registered, 74% were tested for HIV and 237 HIV-infected TB patients were identified.[15]

SAMPLE SIZE AND SAMPLING

Assuming 3% HIV seroprevalence (p) among TB suspects, an error margin (d) of 1%, 95% confidence limit (z=1.96) and a possible attrition rate of 10%, the sample size was calculated using the formula ((z2*p*(1-p))/d2) as 1280. Considering the TB suspect examination rate of 2010, it was decided to examine all the TB suspects attending the microscopy centres in one month.

STUDY POPULATION

The study population consisted of all the TB suspects attending the 25 microscopy centres for diagnostic sputum smear examination in the month of December 2010. TB suspects less than 18 years of age were excluded from the study.

DATA COLLECTION, STUDY VARIABLES AND STUDY INSTRUMENT

All the TB suspects aged older than 18 years were provided a patient information sheet by the laboratory technician (LT) at the microscopy centre and enrolled into the study. After obtaining a written informed consent, they were further referred to the ICTC for HIV testing located mostly in the same premises. From one microscopy centre which did not have a HIV testing centre in its premises, the patients were referred to the nearby ICTC. At the ICTC,

the prevailing national guidelines for HIV testing were followed which includes a pre-test counseling, post-test counseling and referral to ART centre in case the patient is found to be HIV positive. TB suspects with an already known HIV status were not tested again as per the national protocol. 'Known' HIV status referred to those who were HIV positive or with a HIV negative result within the past 6 months. Those TB suspects who had a negative sputum smear result were tracked for one month to assess if they were diagnosed as smear negative pulmonary TB or extra-pulmonary TB. The results of sputum smear microscopy and HIV testing were informed to the client and offered TB treatment and HIV care and support accordingly. The data were collected by the LT into a pre-tested, structured questionnaire for all the eligible TB suspects; data collected included laboratory number, age, sex, sputum smear result, HIV status and type of TB. The completed questionnaires were collected once a week by the trained laboratory supervisor of the national TB programme and were checked for completeness and validated by the principal investigator. In addition, the data on total clients tested and diagnosed as HIV was collected from the local programme division to assess the potential of this strategy to improve HIV case finding.

DATA ENTRY AND ANALYSIS

Data were double-entered into an EpiData software package16 by two data entry operators independently, databases were compared and discrepancies resolved through referral to the original questionnaire. Proportions of HIV positive patients among the TB suspects and TB patients with 95% confidence intervals were calculated. The proportion of all HIV-infected persons who were 'newly diagnosed' (after excluding previously known HIV cases) was calculated. To find one additional HIV case, the number needed to screen (NNS) among TB suspects and TB patients was determined. All variables have been described as proportions, and differences between groups were compared for statistical significance using the Chi-square test or Fisher's exact test, as applicable. A p-value less than 0.05 was considered statistically significant.

ETHICS APPROVAL

All study subjects provided written informed consent for study participation and HIV testing. The study protocol was reviewed and approved by the Ethics committee of National Tuberculosis Institute, India and the Ethics Advisory Group of the International union against TB and lung disease (The Union), France.

RESULTS

Of the 1,723 TB suspects who underwent diagnostic sputum smear microscopy, 1,668 TB suspects were eligible to participate in the study. Out of those eligible, 1,539 (92%) participated and had HIV status ascertained and recorded (**Figure 1**).

The demographic and clinical characteristics of the 1,539 who participated and had a HIV test result and the 129 who declined to ascertain HIV status are shown in **Table 1**. TB suspects who did not have a HIV test result were more likely to belong to older age groups. Among 1,539 TB suspects with a known HIV status, 100 (6.5%) were eventually diagnosed as TB. Of the TB cases, 87 were sputum smear positive, 8 were sputum smear negative and 5 were diagnosed as extra-pulmonary TB.

HIV prevalence among TB suspects disaggregated by age, sex and TB status is shown in **Table 2**. Overall, HIV prevalence among TB suspects was 7% with significantly higher prevalence noted among those aged 25-54 years, females and the subset of TB suspects who were subsequently diagnosed as TB patients.

To highlight the incremental effect of the policy change from 'HIV testing of TB patients' to 'HIV testing of the larger group of TB suspects', we calculated the difference in the number of instances of newly-detected HIV infections (i.e. excluding those persons with previously-known HIV infection) (**Table 3**). Of the 108 HIV positive patients, 65 (60%) knew their HIV status prior to the study. While the current policy of HIV testing of TB patients would have yielded 7 instances of newly-detected HIV infection, HIV testing of TB suspects added 36 instances of newly-detected HIV infection. To detect a new case of HIV infection, the number needed to screen (NNS) among TB patients was 13, compared to an NNS of 37 among 'TB suspects not diagnosed as TB' (**Table 4**). Among the subset of TB suspects aged 25-54 years who were not subsequently diagnosed as TB, the NNS to detect a new case of HIV infection was 21.

Application of the prevalence of new cases of HIV infection among TB suspects to the overall number of TB suspects examined in 2010 suggested that a policy change could yield markedly increased HIV case-finding. Overall in 2010 in Mandya, 23,909 general clients (including TB patients) and 18681 antenatal mothers were tested, and respectively 999 (4.2%) and 57 (0.3%) were HIV positive. If all 19,070 TB suspects were also tested, then approximately 534 cases of previously-undiagnosed HIV infection could be expected. This would represent a 51% increase in district HIV case-finding relative to current practice.

DISCUSSION

Routinely testing TB suspects for HIV infection in Mandya detected large numbers of new cases of HIV infection, and may represent a major opportunity for increased HIV-case-finding. Surveillance during our one-month study period found overall 15 cases of HIV infection among TB patients, including 8 (50%) with newly-diagnosed HIV infection; these would be detected by the existing policy. HIV testing among TB suspects, limited to those not subsequently diagnosed with TB, detected 93 cases of HIV infection, including 36 (39%) with newly-diagnosed HIV infection. In the overall district context, effective application of a policy of HIV testing of TB suspects in 2010 could have increased HIV case-finding by 51%.

TB suspects are an easily accessible group of population, already at health facilities with HIV testing. These findings suggest that HIV testing of TB suspects should be carefully explored in India, particularly in high HIV prevalence settings where HIV testing services are widely available and co-located with TB diagnostic services.

This is among the first studies to report HIV prevalence among TB suspects from India or any concentrated HIV epidemic setting globally. A similar study done during the same time period in Andhra Pradesh (India) showed HIV prevalence of 10.3% among TB suspects compared to 8.1% in TB patients (Shanta Achanta, MPH, Personal Communication, September 2011). Limited data from generalized HIV epidemics has also shown HIV prevalence in TB suspects to be similar to HIV prevalence among TB patients[10,17-21]. The World Health Organization has recommended that in generalized HIV epidemics, HIV testing be offered to all persons attending health care facilities, including TB suspects. While the magnitude of HIV prevalence among TB suspects and TB patients was substantially higher in those generalized HIV epidemic settings than found in our study, the principle of a comparable HIV case-finding yield remains.

With more than 90% of TB suspects accepting HIV testing, this study showed that it was feasible to routinely implement PITC among TB suspects in the general health system with the existing staff. Availability of decentralized HIV testing services with co-location in the same facility as the TB microscopy centres might have facilitated such high levels of acceptance.

While 'PITC among TB patients' was clearly a more efficient strategy of HIV case finding than 'PITC among TB suspects', HIV testing of TB suspects remained reasonably efficient, and yielded major improvements in HIV-case finding. While the NNS to detect a case of HIV in the general ICTC client pool was 23, the NNS for TB suspects not diagnosed with TB was 37, and was 20 among those aged 25–54 years. Given the feasibility of HIV testing clients already in health care facilities for TB diagnosis and the high yield in terms of absolute numbers of HIV infections diagnosed, we believe that the strategy of 'routine offer of HIV testing for TB suspects' in high-HIV settings may be recommended by the National programme. The effective implementation of this strategy is highly dependent on the presence of a co-located HIV testing service in the same facility as TB diagnostic centre; hence it should not be recommended in areas where HIV testing services are not sufficiently decentralized. Additionally, this strategy is likely to be beneficial by resulting in earlier diagnosis of HIV among TB patients, earlier initiation of CPT and ART and consequent reduction in mortality.

The study had a few limitations. Firstly, about 8% of the study population could not be assessed for HIV due to various reasons; however, if we conservatively assume all of the untested patients were HIV-negative, then the minimum HIV prevalence among TB suspects would be 6.5%. Hence our interpretation of the findings would not change. Secondly, the HIV prevalence reported in our study was mainly among pulmonary TB suspects who attended the government-run sputum microscopy centres. We were not able to assess HIV prevalence among isolate extra-pulmonary TB suspects who were not eligible for sputum examination,

or TB suspects evaluated at private laboratories outside national programme. Though this will remain a limitation in assessment of true HIV prevalence among all TB suspects, we feel that information is not required to inform the policy question facing national TB and AIDS programmes. Thirdly, our study did not assess whether the strategy of moving HIV testing upstream to test all TB suspects instead of TB patients actually resulted in increased linkage to HIV care and support and reduced mortality among HIV-infected TB patients. This needs further research. Fourthly, though indicative, results from a single district is not sufficient to inform national policy decision as the HIV epidemic is heterogenic with varied HIV prevalence across states and districts of India.[22] Hence, broader surveillance from across the country is required before national policy decision.

CONCLUSION

This study demonstrated that routine HIV testing of TB suspects was feasible in settings with decentralized availability of HIV testing services and yielded a large number of HIV cases in absolute terms. HIV testing of TB suspects was somewhat less efficient than current efforts for HIV case-finding among TB patients or then general ICTC population, but remained reasonably efficient in the context of a concentrated HIV epidemic. More importantly, in the context of overall district HIV case-finding efforts, a policy of HIV testing of TB suspects could substantially increase HIV case detection relative to existing practice. Though these findings are promising, given the heterogeneity of HIV in India broader surveillance of HIV among TB suspects is indicated to inform national policy decisions.

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CONFLICTS OF INTEREST

None declared

Author contributions: Study design BN AK KL DO MO VI SS PD Data collection BN AK Data entry and analysis BN AK Drafting of Manuscript BN AK Inputs on the draft manuscript KL DO MO VI SS PD

REFERENCES

1. Ghate M, Deshpande S, Tripathy S, et al. Incidence of common opportunistic infections in HIV-infected individuals in Pune, India: analysis by stages of immunosuppression represented by CD4 counts. *Int. J. Infect. Dis.* Jan 2009;13(1):e1-8.
2. Rajasekaran S, Raja K, Jeyaseelan L, et al. Post-HAART tuberculosis in adults and adolescents with HIV in India: incidence, clinical and immunological profile. *Indian J Tuberc.* Apr 2009;56(2):69-76.
3. Sharma SK, Kadhiravan T, Banga A, Goyal T, Bhatia I, Saha PK. Spectrum of clinical disease in a series of 135 hospitalised HIV-infected patients from north India. *BMC Infect Dis.* Nov 22 2004;4:52.
4. World Health Organization. Global Tuberculosis Control 2010. 2010; http://www.who.int/tb/publications/global_report/2010/en/index.html. Accessed 9th May, 2011.
5. Harries AD, Zachariah R, Corbett EL, et al. The HIV-associated tuberculosis epidemic--when will we act? *Lancet.* May 29 2010;375(9729):1906-1919.
6. UNAIDS. *Report on the Global AIDS epidemic.* Geneva2008.
7. World Health Organization. *Interim Policy on Collaborative TB/HIV Activities.* 1rst ed. Geneva, Switzerland: World Health Organization; 2004.
8. Tuberculosis Coalition for Technical Assistance. International Standards for Tuberculosis Care (ISTC), second edition. 2009. www.istcweb.org. Accessed 13th June.
9. National AIDS Control Organization and Central TB Division. National framework for Joint HIV/TB collaborative activities. 2009; http://www.tbcindia.org/pdfs/Final%20National%20Framework%20for%20TB%20HIV%20Collaboration%202009.pdf. Accessed 28th May, 2011.
10. Srikantiah P, Lin R, Walusimbi M, et al. Elevated HIV seroprevalence and risk behavior among Ugandan TB suspects: implications for HIV testing and prevention. *Int. J. Tuberc. Lung Dis.* Feb 2007;11(2):168-174.
11. Porskrog A, Bjerregaard-Andersen M, Oliveira I, et al. Enhanced tuberculosis identification through 1-month follow-up of smear-negative tuberculosis suspects. *Int. J. Tuberc. Lung Dis.* Apr 2011;15(4):459-464.
12. National AIDS Control Organization and Central TB Division. Minutes of National Technical Working Group on TBHIV collaborative activities on March 23, 2010. 2009; http://www.tbcindia.org/pdfs/10-NTWG%20minutes%20230310.pdf. Accessed 13th June, 2011.
13. Central TB Division. Technical and Operations Guidelines for Tuberculosis Control. 2005; http://www.tbcindia.org/documents.asp. Accessed 9th May, 2011.
14. National AIDS Control Organization. Operational Guidelines for Integrated Counselling and Testing Centres. 2008; http://www.nacoonline.org/Quick_Links/Publication/Basic_Services/. Accessed 9th May, 2011.
15. Central TB Division. TB India 2011. Revised National TB Control Programme Annual Status Report. 2011; http://www.tbcindia.org/pdfs/RNTCP%20TB%20India%202011.pdf. Accessed 9th May, 2011.
16. EpiData Association. EpiData Entry version 3.1. http://www.epidata.dk/. Accessed 9th May, 2011.

17. Munthali L, Mwaungulu JN, Munthali K, Bowie C, Crampin AC. Using tuberculosis suspects to identify patients eligible for antiretroviral treatment. *Int. J. Tuberc. Lung Dis.* Feb 2006;10(2):199-202.
18. Odhiambo J, Kizito W, Njoroge A, et al. Provider-initiated HIV testing and counselling for TB patients and suspects in Nairobi, Kenya. *Int. J. Tuberc. Lung Dis.* Mar 2008;12(3 Suppl 1):63-68.
19. Deribew A, Negussu N, Melaku Z, Deribe K. Investigation outcomes of tuberculosis suspects in the health centers of addis ababa, ethiopia. *PLoS One.* 2011;6(4):e18614.
20. Adjei AA, Adiku TK, Ayeh-Kumi PF, Hesse IF. Prevalence of human immunodeficiency virus infection among tuberculosis suspect patients in Accra, Ghana. *West Afr. J. Med.* Jan-Mar 2006;25(1):38-41.
21. Dimairo M, MacPherson P, Bandason T, et al. The risk and timing of tuberculosis diagnosed in smear-negative TB suspects: a 12 month cohort study in Harare, Zimbabwe. *PLoS ONE.* 2010;5(7):e11849.
22. National AIDS Control Organization. HIV estimates for India 2009. 2010; http://www.nacoonline.org/upload/HomePage/NACO%20Press%20Release%20on%20HIV%20Estimates.pdf. Accessed 13 June, 2011.

Table 1: Demographic and clinical characteristics of the study population, Mandya district, India, December 2010.

Characteristic	TB suspects who did not consent for ascertaining HIV status N (%)	TB suspects who consented for ascertaining HIV status N (%)	P value
Total	129 (100)	1539 (100)	
Age (years)			
<45	31 (24)	616 (40)	<0.001
>45	98 (76)	923 (60)	
Sex			
Male	91 (71)	1060 (69)	0.69
Female	38 (29)	479 (31)	
TB status			
TB patients	5 (4)	100 (6)	0.24
TB suspects without TB	124 (96)	1439 (94)	

Table 2: HIV prevalence among TB suspects examined for diagnostic smear microscopy, Mandya district, India, December 2010.

Characteristic	Number of TB suspects with HIV status ascertained	Number (%) HIV Positive
Total	1539	108 (7.0)
Age (years)		
18-24	117	4 (3.4)
25-34	247	38 (15.4)
35-44	252	41 (16.3)
45-54	260	11 (4.2)
55-64	283	11 (3.9)
>65	380	3 (0.8)
Sex		
Male	1060	57 (5.4)
Female	479	51 (10.6)
TB status		
TB patients	100	15 (15.0)
TB suspects without TB	1439	93 (6.5)

Table 3: Newly detected instances of HIV infections among TB patients and TB suspects, Mandya district, India, December 2010.

Category	Prior HIV status Known		Prior HIV status Unknown		Proportion of newly-detected instances of HIV infections
	HIV Positive [a]	HIV Positive [b]	HIV Positive [c]	HIV Positive [d]	[c]/[a+c]
TB patients (n=100)	8	2	7	83	47%
TB suspects without TB (n=1439)	57	51	36	1295	39%
Total	65	53	43	1378	40%

Table 4: Number needed to screen to find an additional case of HIV, by strategy, Mandya district, India, December 2010.

Strategy	Number with Prior HIV status Unknown	Number (%) HIV Positive	Number Needed to Screen (NNS)
HIV testing for all TB patients	90	7 (7.7)	13
HIV testing for TB suspects excluding TB patients	1331	36 (2.7)	37
HIV testing for all TB suspects including TB patients	1421	43 (3.2)	33
HIV testing of all TB suspects in the age group 25-54 years	664	31 (4.7)	21

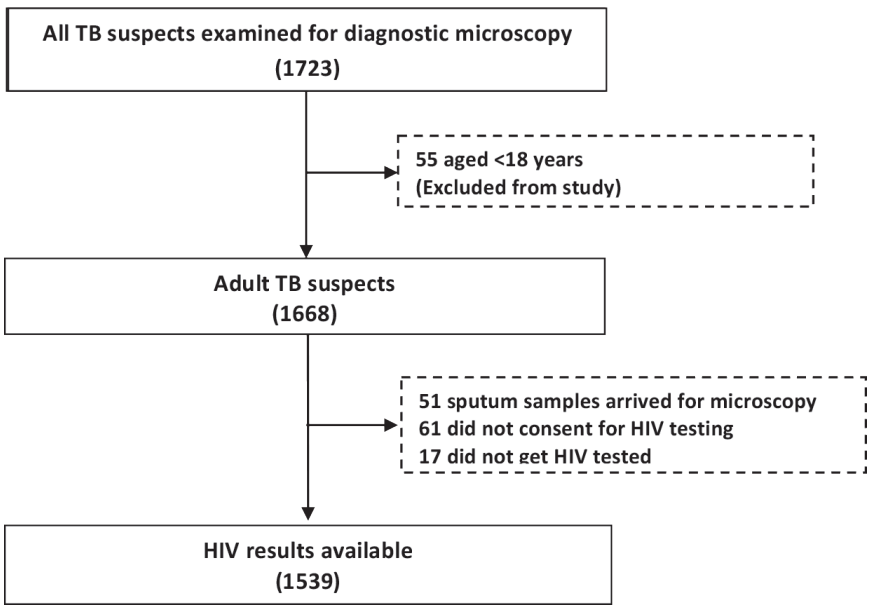

Figure 1. TB suspects examined for sputum smear microscopy, Mandya district, India, December 2010

4.

Feasibility and effectiveness of Provider initiated HIV testing and counseling of TB suspects in Vizianagaram district, South India

Achanta S, **Kumar AMV**, Nagaraja SB, Jaju J, Shamrao SRM, Uppaluri R, Tekumalla RR, Gupta D, Kumar AMVA, Satyanarayana S, Dewan PK.
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Background

Though internationally recommended, provider initiated HIV testing and counseling (PITC) of persons suspected of tuberculosis (TB) is not a policy in India; HIV seroprevalence among TB suspects has never been reported. The current policy of PITC for diagnosed TB cases may limit opportunities of early HIV diagnosis and treatment. We determined HIV seroprevalence among persons suspected of TB and assessed feasibility and effectiveness of PITC implementation at this earlier stage in the TB diagnostic pathway.

Methods

All adults examined for diagnostic sputum microscopy (TB suspects) in Vizianagaram district (population 2.5 million), in November-December 2010, were offered voluntary HIV counseling and testing (VCT) and assessed for TB diagnosis.

Results

Of 2918 eligible TB suspects, 2465(85%) consented to VCT. Among these, 246(10%) were HIV-positive. Of the 246, 84(34%) were newly diagnosed as HIV (HIV status not known previously). To detect a new case of HIV infection, the number needed to screen (NNS) was 26 among 'TB suspects', comparable to that among 'TB patients'. Among suspects aged 25-54 years, not diagnosed as TB, the NNS was 17.

Conclusion

The seroprevalence of HIV among 'TB suspects' was as high as that among 'TB patients'. Implementation of PITC among TB suspects was feasible and effective, detecting a large number of new HIV cases with minimal additional workload on staff of HIV testing centre. HIV testing of TB suspects aged 25-54 years demonstrated higher yield for a given effort, and should be considered by policy makers at-least in settings with high HIV prevalence.

INTRODUCTION

According to World Health Organization's (WHO) global TB report 2010, Tuberculosis (TB) accounted for 25% of all deaths among people living with HIV/AIDS (PLHIV) in 2009[1]. Unless HIV-infected TB patients are diagnosed early and linked to both TB and HIV treatment, mortality will remain high. To facilitate early and enhanced diagnosis of HIV-infected TB patients, WHO recommends intensified TB case finding at all HIV care settings and 'provider initiated HIV testing and counseling' (PITC) for patients with diagnosed and presumptive TB [2].

The recommendation of PITC for all TB suspects is based on study findings from sub-Saharan African countries, which have shown a very HIV prevalence among persons being evaluated for TB (TB suspects), sometimes even higher than HIV prevalence among TB patients [3,4]. These findings from HIV endemic settings cannot, however, be generalized to lower HIV burden settings such as India. With no previously published literature on this issue from India, it remains unclear if TB suspects indeed have a similar HIV prevalence as compared to diagnosed TB patients, or even if HIV prevalence among TB suspects is higher than that found in the general community. Hence, despite recommendations from WHO and International Standards of TB Care (ISTC) [5], in India routine HIV testing is offered only to 'TB patients' and not to all 'TB suspects'.

The strategy of routine HIV testing of all TB suspects offers the potential for early HIV diagnosis and treatment with consequent reduction of morbidity and mortality. Evidence showing that HIV prevalence among TB suspects is relatively high and PITC implementation among them is feasible might guide policy makers seeking to improve TB and HIV care [6].

We conducted this study to assess the feasibility and effectiveness of routinely offering HIV counseling and testing to all TB suspects in a relatively high-HIV prevalence district of South India. The four specific objectives were: (1) to assess the proportion of 'TB suspects' and 'TB patients' tested for HIV and found HIV positive, (2) to assess the number of newly-detected cases of HIV infection detected as a result of this strategy, (3) to assess the number needed to screen (NNS) to find one new case of HIV among 'TB patients' and 'TB suspects', and (4) to assess the additional workload at HIV testing centers due to this strategy.

METHODS

STUDY DESIGN

This was a cross sectional study conducted among TB suspects attending the designated microscopic centers (DMC) in the district for diagnosis of TB.

SETTING

The study was conducted in Vizianagaram, a coastal district in the state of Andhra Pradesh, India with a population of 2.5 million. This district has been prioritized for HIV services by

National AIDS Control Programme (NACP) as the HIV prevalence among antenatal clinic attendees has been consistently exceeding 1% over the past 5 years [7]. HIV diagnostic and treatment services are offered free of cost through a network of 70 HIV testing centers and one Anti Retro-viral Therapy(ART) centre as per national guidelines [8].

Under the ambit of Revised National TB Control Programme (RNTCP), TB diagnosis and treatment services are offered through the primary health care system of the district. TB suspects, defined as anybody with a cough of two weeks or more with or without other symptoms (For PLHIV, cough of any duration is considered as TB suspect) are examined at one of the 31 DMC for sputum smear microscopy. Those who are diagnosed as TB patients are treated with fully intermittent short course chemotherapy administered under direct observation (DOT) and registered in one of the six programme management units as per national guidelines [9].

As per the national framework of joint TB/HIV collaborative activities [10], HIV testing is offered routinely to all the TB patients treated under RNTCP and those who are found HIV-infected are provided cotrimoxazole prophylaxis and referred to ART centre for assessment of ART eligibility and initiation. During 2010, 18,799 TB suspects underwent sputum smear microscopy and 3,760 TB patients were registered for treatment [11]. Of the TB patients registered, 3,619 (96%) were ascertained for HIV status and 320 (9%) were found to be HIV-infected [11].

STUDY POPULATION AND STUDY PERIOD

The study was conducted during the period from October 2010 to January 2011. All the adult TB suspects (more than 18 years of age) examined for diagnostic smear microscopy at the DMCs of Vizianagaram district from November 1 to December 31, 2010 formed the study population.

SAMPLE SIZE AND SAMPLING

Assuming 7% HIV prevalence among TB suspects, an absolute precision of 1% with 95% confidence, a possible attrition rate of 10%, the sample size was calculated to be 2744. Considering the number of TB suspects examined per month in the district, it was decided to enroll all the eligible TB suspects for a period of two months.

DATA COLLECTION AND DATA VALIDATION

All the adult TB suspects attending the DMC were provided information on the study by the laboratory technician (LT) trained for the purpose. Those who consented to participate in the study were referred to the co-located HIV testing centre for HIV testing and counseling. Those with a prior known positive HIV status or with a HIV negative result within the previous six months were not tested again as per national guidelines. The study participants were tracked for a month by the TB treatment supervisors of the programme, to assess if they were diagnosed as smear negative pulmonary TB or extra-pulmonary TB. The information

on the following variables – name of DMC, age, sex, sputum smear result, whether diagnosed as TB, type of TB, HIV status - were extracted into a pre-tested structured data collection format by LT in co-ordination with the counselor at HIV testing centre. All the data collection formats were checked for completeness and consistency by the TB laboratory supervisors of the programme once a week and by the principal investigator once in a fortnight. All the staff involved in data collection, data validation and data entry were trained in carrying out the respective procedures, using the study protocol and data collection formats.

DEFINITIONS OF KEY OUTCOMES

We calculated the following key indicators – i) Proportions of 'TB suspects' and 'TB patients' with known HIV status, ii) Proportions of 'TB suspects' and 'TB patients' found HIV positive, iii) The number (proportion) of all HIV cases diagnosed newly as the result of the strategy of 'PITC of TB suspects', iv) Number needed to screen (NNS) to diagnose an additional case of HIV, separately among 'TB patients' and 'TB suspects not diagnosed as TB', v) The average increase in daily workload at the HIV testing centers calculated centre wise by dividing the total number of TB suspects who underwent HIV testing by the average number of working days.

DATA ENTRY AND ANALYSIS

The data were entered twice, independently by two data entry operators into a pre-designed data entry form with inbuilt checks to minimize data entry errors using EpiData entry software[12]. Both the data bases were compared and discrepancies were resolved by referring to the original data collection formats. All analysis was done using EpiData analysis softwares[13]. NNS is the reciprocal of the proportion of newly-detected HIV infection, i.e. excluding those persons with previously-known HIV status. Chi-square tests were used for comparing proportions and 'p' value of less than 0.05 was considered as statistically significant.

ETHICS CONSIDERATIONS

Ethics clearance was obtained from Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease (The Union) and National Tuberculosis Institute, Bangalore. Administrative approvals were obtained from state and central authorities for conducting this study. A written informed consent was taken from each patient and confidentiality was assured as data collection formats were maintained securely by programme staff and electronic databases contained no personal identifiers.

RESULTS

Of the 3,232 TB suspects examined for sputum smear microscopy, 314 were aged less than 18 years and excluded from the study. Of the remaining 2,918 adult TB suspects, 2,465 (85%) consented for HIV testing.

The demographic and clinical characteristics of study participants who consented for HIV testing as compared to those who did not are shown in Table 1. Those who did not consent for HIV testing were more likely to belong to older age groups and less likely to have HIV.

The proportions of TB suspects who were tested for HIV and found to be HIV infected are shown in Table 2. Of the 2465 (85%) of TB suspects tested for HIV, 246 (10%) were HIV infected. The HIV prevalence was found to be higher among the age-group 25-44, females and 'TB suspects without TB'.

The newly detected number of HIV patients is shown in Table 3. Among the 246 HIV-infected patients identified in the study population, 162 (67%) had their HIV status known prior to the study and 84 (34%) were diagnosed newly as part of the study. Of the 84 newly-detected cases of HIV among the population of TB suspects, 70 (83%) were among those not ultimately diagnosed with TB, and only 14 (17%) were subsequently diagnosed with TB. These are the additional number of HIV cases detected by the strategy of offering HIV testing to all TB suspects. Excluding those with prior known HIV status, the number needed to screen (NNS) to find an additional HIV case was found to be 25 among 'TB patients' and was comparable to that among 'TB suspects without TB' (Table 4).

The average increase in daily workload at the HIV testing centers due to the implementation of this strategy is shown in Table 5. Most of the centers (27/31) had minimal increase in workload with only 1-2 extra clients to be counseled and tested in a day.

DISCUSSION

PITC for TB suspects effectively detected a large number of additional HIV cases and could be feasibly implemented with the existing resources within the programme. About 33 % of the newly-diagnosed instances of HIV infection in the overall population of TB suspects would likely have been missed if HIV testing was applied after TB diagnosis, i.e. to TB cases only. We found that overall 10% of the TB suspects tested for HIV were HIV-infected, indicating that HIV prevalence among TB suspects is higher than that reported among general population in the state of Andhra Pradesh (0.96%) [14], comparable to HIV prevalence among TB patients (9%) [11].

This is one of the first studies from India examining the effectiveness and feasibility of implementing the strategy of PITC of TB suspects under programmatic settings. Another

study conducted in Mandya district of state of Karnataka in South India showed a HIV prevalence of 7% among TB suspects with nearly 40% of the HIV cases newly diagnosed as a result of the strategy of routine offer of HIV testing [15]. Similar studies from other parts of the world, mainly from African countries, indicate that HIV prevalence among TB suspects varied from 27% to 63% and was as high as or even higher than among TB patients [3,4,16,17,18,19]. However, the very high levels of HIV among TB suspects in African countries are reflective of the high levels of HIV in their general population.

Among the 246 HIV-infected patients identified in the study population, 84 (34%) were newly diagnosed during the study, but most of these (70) were among TB suspects not subsequently diagnosed as TB. These 70 newly-detected instances of HIV infection reflect the additional increase in detection of HIV-infected cases because of offering HIV testing to all TB suspects. Clearly, PITC among TB suspects is a very effective strategy of HIV case finding in an easily accessible population.

This study also demonstrated the feasibility of implementation of PITC among TB suspects. We found that a great majority of the TB suspects (about 85%) consented for HIV testing indicating very high acceptance levels for HIV testing among the TB suspects. Further, centre-wise workload analysis indicated that most of the HIV testing centers (27/31) had a minimal increase in additional workload with only 1-2 extra clients to be counseled and tested in a day. Hence this strategy can be implemented with the existing human resources and almost negligible additional burden on the health staff delivering services. If the resource investment were still felt to be too great, limiting HIV testing of TB suspects to adults could also be considered. A sub-analysis among TB suspects aged 25-54 years indicated that examining as few as 17 TB suspects in this age group would yield one additional case of HIV. Since, about 90% of all HIV-infected individuals were in this age group and could be detected by testing only 60% of TB suspects; selectively adopting the strategy of PITC among TB suspects aged 25-54 years would be highly resource-optimizing.

There are two key considerations and reasons for policy makers to exercise caution before implementing this strategy more widely. Firstly, the high HIV testing rates among TB suspects in our study was hugely facilitated by the widespread availability of HIV testing services co-located with the DMCs. The easy availability of HIV-testing services has been shown to be closely associated with HIV testing uptake [20]. Co-location of HIV testing services at all DMCs is seemingly a pre-requisite for successful implementation of this strategy. Secondly, the total number of HIV tests performed can increase substantially as a result of this strategy and national programme needs to plan for enhanced procurement and supply chain management of HIV testing kits before launching this strategy.

There are other positive implications of this strategy to consider. Firstly, the early diagnosis of HIV-infected TB patients and linkage to HIV care and support can potentially be life saving. Secondly, this strategy identifies HIV-infected individuals in whom TB has been ruled out and who are thus eligible for Isoniazid preventive therapy (IPT) as per WHO

guidelines; linking these individuals to early antiretroviral therapy (ART) and IPT can have a substantial impact in preventing TB in this vulnerable group.

There were some limitations to this study. Firstly, about 15% of the TB suspects did not consent for HIV testing. Non-consenting TB suspects were more likely to belong to older age group who are in general less likely to be HIV infected; hence this could have overestimated the overall HIV prevalence. However, if we assume all the untested patients were HIV negative, then the minimum HIV prevalence among TB suspects would still be 8.5%. Thus our enrollment rate did not change the interpretation of study findings. Secondly, the study captured only pulmonary TB suspects attending state-run designated microscopy centres. We were not able to assess HIV prevalence among isolate extra-pulmonary TB suspects who were not eligible for sputum examination, or TB suspects evaluated at private laboratories outside national programme. Furthermore, it was beyond the scope of this study to evaluate if offering an early opportunity for HIV testing among TB suspects actually translated into early initiation of HIV care and support and the expected morbidity and mortality benefits; longer term HIV care outcomes should be the subject of future operational research.

TRANSLATING RESEARCH FINDINGS INTO POLICY

Acknowledging the strong evidence found as part of this study and another study conducted simultaneously in another district of South India [15], the National Technical Working Group (NTWG) of TB/HIV collaborative activities took a policy decision to implement PITC among TB suspects in high HIV settings (states of Karnataka, Andhra Pradesh, Tamil Nadu, Maharashtra, Manipur and Nagaland) in India. It was further recommended that PITC among TB suspects be piloted in 1-2 high prevalence states (and select districts in other high prevalent states, at all microscopy centres with co-located HIV testing facility) for a period of 3-6 months with mechanisms for recording and reporting to finalize the operational guidance before scale-up to other high HIV settings.

Considering a high yield of HIV among TB suspects in high prevalent settings, which was hitherto unexpected in India, the national policy making body also opined that similar surveillance efforts should be conducted jointly by RNTCP and NACP in moderate and low HIV settings (states other than the ones mentioned above) of the country and findings presented before national policy decision. Given the heterogeneity of HIV epidemic in India across states/districts, it is not possible to define a cutoff value of HIV prevalence to decide if PITC among TB suspects is justified. Hence, it has been agreed that if the prevalence of HIV among TB suspects is as high as or greater than HIV positivity among the ICTC clients, then the strategy of PITC for TB suspects may be justified.

CONCLUSION

Our study found that the prevalence of HIV among TB suspects was as high as that among TB patients and could be an important source of HIV case finding. The strategy of PITC in TB suspects was highly effective in detecting a large number of additional HIV cases and could be feasibly implemented with minimal additional workload on existing health staff. HIV testing of TB suspects aged 25-54 years demonstrated higher yield for a given effort. This study contributed towards making routine offer of HIV testing among TB suspects a policy in settings with high HIV prevalence. However, programme managers must scale up decentralized availability of HIV testing services and ensure availability of HIV testing kits in adequate numbers before launching this strategy.

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CONFLICTS OF INTEREST

None. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of the World Health Organization.

AUTHOR CONTRIBUTIONS

Conceived and designed the experiments: SA BN AK JJ RK RR MS DG SS PKD Performed the experiments: SA BN RR Analyzed the data: AK Contributed reagents/materials/analysis tools: SA AK BN Wrote the manuscript: SA AK Provided comments and inputs to revise manuscript: BN JJ RK RR MS DG SS PKD.

REFERENCES

1. World Health Organization (2010) Global Tuberculosis Control 2010. Geneva: World Health Organization.
2. World Health Organization (2004) Interim Policy on Collaborative TB/HIV Activities. Geneva, Switzerland: World Health Organization.
3. Srikantiah P, Lin R, Walusimbi M, Okwera A, Luzze H, et al. (2007) Elevated HIV seroprevalence and risk behavior among Ugandan TB suspects: implications for HIV testing and prevention. Int J Tuberc Lung Dis 11: 168-174.
4. Deribew A, Negussu N, Melaku Z, Deribe K (2011) Investigation outcomes of tuberculosis suspects in the health centers of addis ababa, ethiopia. PLoS One 6: e18614.
5. Tuberculosis Coalition for Technical Assistance (2009) International Standards for Tuberculosis Care (ISTC), second edition. The Hague.
6. National AIDS Control Organization and Central TB Division (2009) Minutes of National Technical Working Group on TBHIV collaborative activities on March 23, 2010. Delhi: Ministry of Health and Family Welfare, Government of India.
7. National AIDS Control Organization (2008) HIV Sentinel Surveillance and HIV Estimation, 2007, A technical brief. New Delhi: Ministry of Health and Family Welfare, Government of India.
8. National AIDS Control Organization (2008) Operational Guidelines for Integrated Counselling and Testing Centres. New Delhi: Ministry of Health and Family Welfare, Government of India.
9. Central TB Division (2005) Technical and Operations Guidelines for Tuberculosis Control. New Delhi: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India.
10. National AIDS Control Organization and Central TB Division (2009) National framework for Joint HIV/TB collaborative activities. Delhi: Ministry of Health and Family Welfare, Government of India.
11. Central TB Division (2011) TB India 2011. Revised National TB Control Programme Annual Status Report. New Delhi: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India.
12. EpiData Association EpiData Entry version 3.1. EpiData Association, Odense, Denmark, Europe.
13. EpiData Association EpiData Analysis Version 2.2. EpiData Association, Odense, Denmark, Europe.
14. National AIDS Control Organization (2010) HIV estimates for India 2009. New Delhi: Ministry of Health and Family Welfare, Government of India.
15. Naik B, Kumar A, Lal K, Doddamani S, Krishnappa M, et al. (2011) HIV prevalence among persons suspected of tuberculosis: Policy implications for India. Journal of Acquired Immune Deficiency Syndromes.
16. Odhiambo J, Kizito W, Njoroge A, Wambua N, Nganga L, et al. (2008) Provider-initiated HIV testing and counselling for TB patients and suspects in Nairobi, Kenya. Int J Tuberc Lung Dis 12: 63-68.
17. Munthali L, Mwaungulu JN, Munthali K, Bowie C, Crampin AC (2006) Using tuberculosis suspects to identify patients eligible for antiretroviral treatment. Int J Tuberc Lung Dis 10: 199-202.

18. Dimairo M, MacPherson P, Bandason T, Zezai A, Munyati SS, et al. (2010) The risk and timing of tuberculosis diagnosed in smear-negative TB suspects: a 12 month cohort study in Harare, Zimbabwe. PLoS ONE 5: e11849.
19. Adjei AA, Adiku TK, Ayeh-Kumi PF, Hesse IF (2006) Prevalence of human immunodeficiency virus infection among tuberculosis suspect patients in Accra, Ghana. West Afr J Med 25: 38-41.
20. Bishnu B, Bhaduri S, Chowdhury DS, Srinath S, Dewan PK, et al. (2011 supplement 3) Factors associated with low level HIV testing among TB patients in one district, West Bengal, India. International Journal of Tuberculosis and Lung Disease 15: S214.

Table 1: Demographic and clinical characteristics of the study population, Vizianagaram district, India, November-December 2010.

Characteristic	TB suspects who did not consent for HIV testing N (%)	TB suspects who consented for HIV testing N (%)	P value
Total	453 (100)	2465 (100)	
Age (years)			
18-24	43 (10)	220 (9)	<0.01
25-34	71 (16)	417 (17)	
35-44	86 (19)	569 (23)	
45-54	79 (17)	561 (23)	
55-64	87 (19)	473 (19)	
>65	87 (19)	225 (9)	
Sex			
Male	317 (70)	1648 (67)	0.19
Female	136 (30)	817 (33)	
TB status			
TB patients	27 (6)	381 (16)	<0.01
TB suspects without TB	426 (94)	2084 (84)	

TB – Tuberculosis; HIV – Human immunodeficiency virus

Table 2: HIV prevalence among TB suspects examined for diagnostic smear microscopy, Vizianagaram district, India, November-December 2010.

Characteristic	Number of TB suspects examined for smear microscopy	Number (%) of TB suspects with known HIV status	Number (%) HIV Positive
Total	2918	2465 (84.5)	246 (10.0)
Age (years)			
18-24	263	220 (83.7)	15 (6.8)
25-34	488	417 (85.5)	86 (20.6)
35-44	655	569 (86.9)	105 (18.5)
45-54	640	561 (87.7)	31 (5.5)
55-64	560	473 (84.5)	8 (1.7)
>65	312	225 (72.1)	1 (0.4)
Sex			
Male	1965	1648 (83.9)	147 (8.9)
Female	953	817 (85.7)	99 (12.1)
TB status			
TB patients	408	381 (93.4)	31 (8.1)
TB suspects without TB	2510	2084 (83.0)	215 (10.3)

TB–Tuberculosis; HIV–Human immunodeficiency virus; CI-Confidence interval

Table 3: Newly detected HIV infections among TB patients and TB suspects, Vizianagaram district, India, November-December 2010.

Category	Prior HIV status Known		Prior HIV status Unknown		Proportionate increase in the number of new cases of HIV
	HIV Positive [a]	HIV Positive [b]	HIV Positive [c]	HIV Positive [d]	[c]/[a+c]
TB patients (n=381)	17	16	14	334	45%
TB suspects without TB (n=2084)	145	85	70	1784	33%
Total	162	101	84	2118	34%

TB – Tuberculosis; HIV – Human immunodeficiency virus

Table 4: Number needed to screen to find an additional case of HIV, by strategy, Vizianagaram district, India, November-December 2010.

Strategy	Number with Prior HIV status Unknown	Number (%) HIV Positive	Number Needed to Screen (NNS)
HIV testing for all TB patients	348	14 (4.0)	25
HIV testing for TB suspects excluding TB patients	1854	70 (3.7)	26
HIV testing for all TB suspects including TB patients	2202	84 (3.8)	26
HIV testing of all TB suspects in the age group 25-54 years	1331	75 (5.6)	17

TB –Tuberculosis; HIV –Human immunodeficiency virus; NNS-Number needed to screen

Table 5: Increase in workload at HIV testing centres due to strategy of 'routine HIV testing of TB suspects', Vizianagaram district, India, November-December 2010.

Average increase in number of clients tested for HIV per day	Number of ICTCs (N=31)
<3	27
3-5	3
6-10	1

HIV-Human immunodeficiency virus; ICTC-Integrated counseling and testing centre

5.

HIV Testing among Patients with Presumptive Tuberculosis: How do we implement in a Routine Programmatic Setting? Results of a large Operational Research from India

Kumar AM, Gupta D, Kumar A, Gupta RS, Kanchar A, Rao R, Shastri S, Suryakanth MD, Rangaraju C, Naik B, Guddemane DK, Bhat P, Nair AS, Harries AD, Dewan P. PLoS ONE. 2016;11(5):e0156487.

Background

In March 2012, World Health Organization recommended that HIV testing should be offered to all patients with presumptive TB (previously called TB suspects). How this is best implemented and monitored in routine health care settings in India was not known. An operational research was conducted in Karnataka State (South India, population 64 million, accounts for 10% of India's HIV burden), to test processes and learn results and challenges of screening presumptive TB patients for HIV within routine health care settings.

Methods

In this cross-sectional study conducted between January-March 2012, all presumptive TB patients attending public sector sputum microscopy centres state-wide were offered HIV testing by the laboratory technician, and referred to the nearest public sector HIV counselling and testing services, usually within the same facility. The HIV status of the patients was recorded in the routine TB laboratory form and TB laboratory register. The laboratory register was compiled to obtain the number of presumptive TB patients whose HIV status was ascertained, and the number found HIV positive. Aggregate data on reasons for non-testing were compiled at district level.

Results

Overall, 115,308 patients with presumptive TB were examined for sputum smear microscopy at 645 microscopy centres state-wide. Of these, HIV status was ascertained for 62,847(55%) among whom 7,559(12%) were HIV-positive, and of these, 3,034(40%) were newly diagnosed. Reasons for non-testing were reported for 37,700(72%) of the 52,461 patients without HIV testing; non-availability of testing services at site of sputum collection was cited by health staff in 54% of respondents. Only 4% of patients opted out of HIV testing.

Conclusion

Offering HIV testing routinely to presumptive TB patients detected large numbers of previously-undetected instances of HIV infection. Several operational challenges were noted which provide useful lessons for improving uptake of HIV testing in this important group.

INTRODUCTION

According to the World Health Organization (WHO) Global TB Report 2014, an estimated 1.1 million people globally had HIV-associated tuberculosis (TB), and 360,000 died from HIV-associated TB in 2013. [1] Three important reasons have been given for this unacceptably high death rate: i) in persons with HIV/AIDS, TB was not diagnosed and treated; ii) in patients with TB, HIV was not diagnosed and thus co-infected patients were not referred to HIV care and treatment; and iii) when the two diseases were diagnosed and treated, this often happened far too late to be effective.[2]

In March 2012, WHO launched its updated policy on collaborative TB/HIV activities to reduce the burden of TB and HIV. This policy uses the same framework as the 2004 WHO Policy of TB/HIV collaborative activities, but includes some important new recommendations, one of which is that routine HIV testing and counselling should be offered not only to patients diagnosed with TB, but also to those with presumptive TB (previously called TB suspects).[3] This recommendation was based on the findings from studies done predominantly in sub-Saharan African countries, which show a high HIV prevalence among patients with presumptive TB ranging from 27%-64%, sometimes even higher than HIV prevalence among TB patients.[4-10] However, these findings from HIV endemic settings were not generalizable to India, a country with a 'concentrated' HIV epidemic (meaning HIV prevalence in general population remains lower than 1%).[11] Hence, despite recommendations from WHO, routine HIV testing had been offered only to 'TB patients' and not to all 'patients with presumptive TB' in India. Operational research conducted in two districts of South India in 2010 showed that the HIV prevalence among presumptive TB patients can be as high as that among TB patients ranging from 7%-10%, and that 'Provider initiated HIV testing and counselling' (PITC, a term used when health care providers actively offer the HIV testing to certain patient groups) among presumptive TB patients can be feasibly implemented in settings with decentralized HIV testing facilities with potential for increased HIV case finding, early treatment initiation and reduction in mortality and morbidity.[12, 13]

The National Technical Working Group (NTWG) for joint TBHIV collaborative activities in India acknowledged the strong evidence and took a policy decision to implement PITC among presumptive TB patients in high HIV settings in India.[14] However, how this is best implemented and monitored in routine health care settings, especially when implemented at large scale, was not known, and this implementation-knowledge gap needed to be addressed. The roles and responsibilities of the different staff officers were unclear, and mechanisms for recording and reporting in routine settings had not been tested. So, NTWG recommended the pilot implementation of PITC in one State of India for a period of 3-6 months to finalize the operational guidance before scale-up to other high HIV settings.[14] Accordingly, a pilot study was implemented in the entire state of Karnataka (South India, population 64 million, high HIV prevalence). Karnataka State was chosen for two main reasons: 1) Large state enabling to test operational feasibility of the strategy when PITC is implemented to scale 2) relatively

high HIV prevalence and better TB-HIV related health infrastructure compared to other states in India. Duration of three months was chosen for the pilot so as to understand the operational challenges.

This paper describes the screening procedures deployed (including mechanisms for recording, reporting and monitoring), the experience of implementation, results and challenges of screening presumptive TB patients for HIV within routine health care settings of Karnataka State, India.

The specific objectives were to assess

1. the proportion of patients with presumptive TB whose HIV status was ascertained, disaggregated district-wise
2. the proportion HIV positive among those who had their HIV status ascertained, disaggregated district-wise
3. the reasons for not ascertaining the HIV status, from the perspective of the health care-provider
4. the number of HIV cases "newly" diagnosed and the number eligible for antiretroviral therapy (ART eligibility was assessed using WHO-2013 ART guidelines [all TB patients irrespective of CD4 count and for presumptive TB patients without TB, a CD4 count <500/mm^3 was considered ART eligible] in line with the recent decision of national AIDS control organisation in India)[15, 16]
5. The number needed to screen (NNS) to find an additional case of HIV-infection among "patients with presumptive TB " in comparison to "confirmed TB patients" and those in reproductive age group (25-54 years).
6. The average increase in daily workload at the HIV testing centers as a result of using this strategy (obtained by dividing the total number of Presumptive TB patients who underwent HIV testing by average number of working days in each centre)

MATERIALS AND METHODS

ETHICS APPROVAL

Approval of the competent national (Central TB Division and National AIDS Control Organization) and state authorities (State TB Cell and Karnataka State AIDS prevention and control society) was obtained for conducting this pilot. Ethics approval was obtained from Institutional Ethics Committee of the National Tuberculosis Institute, Bangalore, India. Individual written informed consent from each patient was not taken separately for the study as this was intended to be a pilot programme implementation and standard operating procedures of National AIDS Control Programme (NACP) were followed for counselling and HIV testing, which included obtaining written consent. The same was approved by the ethics committee including waiver of a separate informed consent. Given the programmatic nature of the study and availability of local ethics approval, the Ethics Advisory Group of International Union Against Tuberculosis and Lung Disease waived the need for ethics review. Data was

maintained securely by programme staff and electronic databases contained no personal identifiers.

DESIGN

This was a cross-sectional, implementation research study conducted among patients with presumptive TB examined for diagnostic smear microscopy within the routine health services of the state of Karnataka, India.

SETTING

Karnataka has an estimated 0.21 million people living with HIV in 2011 and accounts for about 10% of country's HIV burden.[11] Hence, the state has been classified as 'high priority' for HIV interventions by the National AIDS Control Organization (NACO) in India on the basis of consistently high HIV sero-prevalence rates of >1% among antenatal women and >5% in other high risk groups. [17,18] In the state, tuberculosis control programme services are available through a decentralized network of peripheral health institutions which provide general health services including diagnosis and treatment for TB.

Patients with presumptive TB (defined as people with cough for two weeks or more with or without other symptoms suggestive of TB) are identified at the peripheral health centres and referred for sputum smear microscopy to Designated Microscopy Centres (DMCs), which are geographically distributed, each covering a population of 0.05 to 0.1 million. In situations where the patient is unable to physically visit the DMC, the sputum is collected and transported by the health care workers in the general health system or non-governmental organizations. The diagnosis of TB is made in accordance with national guidelines, and all diagnosed TB patients are treated with standardized fully intermittent thrice-weekly short-course regimens (6-9 months) administered under direct observation. Such patients are registered at one of the 125 sub-district level TB programme management units (which are administrative and supervisory units for every 10-15 peripheral health institutions) according to Indian programme guidelines. [19]

As per national policy, HIV status is routinely ascertained for TB patients, and HIV-infected TB patients are provided Cotrimoxazole Preventive Therapy and referred to Anti-Retroviral Treatment (ART) centres for initiation on ART. [20] TB patients are referred for free HIV counselling and testing to one of the 1637 'integrated counselling and HIV testing centres' (ICTC, these are peripheral health institutions with HIV testing services) throughout the state. At the time of the study, about 90% of DMCs had co-located HIV testing services. Free ART is provided through a network of 44 ART centres (with at-least one ART centre in every district), where HIV-infected patients (including TB patients) are started on treatment and care. Once patients were clinically stable on ART, they were referred to one of 121 Link-ART centres in the state, closer to the patient's residence for continuing on ART. These service delivery sites under NACP follow the national guidelines for counselling, testing, care and treatment of

HIV-infected patients. [21] In line with the higher burden of HIV, there is a higher density of HIV testing and care centres in the northern parts of the state. [22]

STUDY POPULATION

All patients with presumptive TB examined for diagnostic smear microscopy at the DMCs of Karnataka state from January-March 2012 formed the study population.

SAMPLE SIZE AND SAMPLING

Since this was a pilot study intended to be implemented under programmatic conditions to answer questions of feasibility, it was decided to enrol all patients with presumptive TB (including children aged 0-14 years) examined for smear microscopy during the pilot period in all the 31 districts of the state. No patients were excluded. For this reason, sample size calculations were deemed not relevant for the study.

PLANNING AND IMPLEMENTATION

Following the decision of NTWG and based on the official government orders from the Revised National Tuberculosis Control Programme (RNTCP) and NACP, joint-meetings were organized between the state level programme managers for planning and rolling out the activities, training of the staff and ensuring supply chain management of HIV test kits.

All staff involved in data collection, data validation and data entry were trained in carrying out the respective procedures. The District TB Officers, District nodal officer of HIV/AIDS and WHO Consultants of the respective study district were trained at state level as master trainers who then trained the district level staff and oversaw the smooth implementation of study. The trainings were conducted jointly for the implementing staff (TB field supervisors, Laboratory technicians of DMCs and HIV testing centres, Counsellors of HIV testing centres) by programme managers of the state level with support from WHO consultants.

Regular supervisory visits were conducted by the state level programme managers (once a month), WHO Consultants (once a fortnight) and district programme managers (once a fortnight). Periodic review meetings were conducted to assess the progress of the pilot and address any implementation issues.

The screening procedures and the patient flow in the health system are shown in **Fig 1-3** and described in **Table 1**.

Since this was a pilot study and the objective was also to study the processes, separate data collection forms were used to capture individual patient information which included information on presence or absence of a co-located ICTC, age, sex, sputum smear result, HIV status, prior HIV status and CD4 count. These variables were extracted into a pre-tested structured data collection format by the Senior TB laboratory supervisor (STLS) in co-ordination with the LT and the counsellor at the HIV testing centre. STLS then coordinated with the district TB/HIV supervisor and referred to the HIV patient records maintained at the ART centre to obtain information on the baseline CD4 count. Aggregate data on reasons for

non-testing were extracted from the remarks column of the laboratory register and compiled at district and state level. Once the pilot period (January-March 2012) was over, the separate data collection formats were discontinued.

DATA VALIDATION

The STLSs were trained in extracting data from the laboratory register accurately and expected to visit the DMCs under their purview once a week to ensure that activities were implemented as per protocol including recording of HIV status in the laboratory register. This was in turn monitored by District TB Officer and the WHO field consultant once in a fortnight.

DATA ENTRY & ANALYSIS

In this multi-centre study, we used a method of coordinating data capture by utilizing a combination of three open access sources (EpiData for data entry, Dropbox for sharing data and TeamViewer for trouble-shooting remotely).[23] All data entry was done by the district-level data entry operators working for RNTCP. The technique has been detailed elsewhere.[23] Double data entry, validation and analysis were done using EpiData software (version 3.1 for entry and version 2.2.2.182 for analysis, EpiData Association, Odense, Denmark). Given the large numbers in the study, it is expected to find statistical significance even when the actual differences between groups are small. Hence, we have refrained from showing results of any statistical tests and make all the interpretations from programmatic point of view.

RESULTS

Data was obtained from all the 31 districts in the state. This included 645 microscopy centres, among which 573(89%) had HIV testing services available in the same facility. A total of 115,308 patients with presumptive TB [40% female, mean age of 44 years] were examined for sputum smear microscopy. HIV status was ascertained for 62,847 (55%) among whom 7,559 (12%) were found to be HIV positive.

The proportion whose HIV status was ascertained along with HIV positive results, disaggregated by age, sex and smear-positivity, is shown in **Table 2**. HIV testing varied little [ranged between 50% and 57%] across age groups and sexes. HIV testing rates were two times higher among patients visiting microscopy centres with co-located HIV testing facilities as compared to those without. Patients with confirmed smear-positive TB were more likely to be tested for HIV as compared to those with other types of TB. HIV testing rates varied between 15% and 95% across districts with districts in the northern part of the state performing better as compared to southern part (**Table 3, Fig 4**).

HIV positivity tended to be lower among elderly age groups, marginally higher among females as compared to males and varied between 3% and 28% across districts –

with a higher positivity in districts located in the northern part of the state. HIV positivity was similar among smear-positive and smear-negative patients (**Table 3, Fig 5**).

Of all presumptive TB patients in the study, 4525 were already diagnosed as HIV positive prior to the study. Of the remaining 110783 patients with unknown status prior to the study, HIV status could be ascertained for 53627 (48%) patients, in whom an additional 3034 HIV positive patients were identified. Thus, of a total of 7,559 HIV-positive patients identified, 3,034 (40%) were newly diagnosed with HIV infection as a result of this screening effort. Among 3,034 newly diagnosed HIV cases, ART eligibility could be assessed for 2,244 (74%) of whom 1,992 (89%) had CD4 count <500 and were found to be eligible for ART initiation. (**Table 4**)

When hypothetically comparing potential policies for HIV testing, the option of limiting HIV testing to adults in 25-54 years was most efficient. In this analysis, we excluded patients with previously known HIV status and examined the yield of HIV among those with a previously unknown HIV status. (**Table 5**)

The reasons for non-ascertainment of HIV status, collected from 37,300 (72%) of the 52,461 patients without HIV testing, is shown in **Table 6**. The key reason for non-testing was related to the fact that sputum samples were collected at peripheral health institutions and transported to microscopy centres instead of referring patients.

A workload assessment indicated that the median [inter quartile range] increase in the number of clients to be tested for HIV per day as a result of this intervention was 2 [1-2]. About 90% of the HIV testing centres had an increase of less than or equal to five clients per day (**Table 7**).

DISCUSSION

The study showed that the strategy of HIV testing among patients with presumptive TB could be feasibly and effectively implemented within the routine health system. We consider the intervention was feasible for the following reasons:

1. All the interventions including recording and reporting were implemented in a large state by the existing staff and resources. One of the major strengths of this study is that it was done with complete engagement of the national programmes from the stage of planning to execution, monitoring, recording and reporting. The existing programme resources were used for implementing all the activities without the need for any extra budget. There was a total increase in the need for HIV test kits which in turn needed optimisation of supply chain management and we need to factor-in this aspect in future procurement cycles.
2. There was minimal additional workload in the HIV testing centres. Barring a small proportion of tertiary care institutes with high patient load, the average daily increase in number of patients requiring to be tested was low at more than 95% of HIV testing centres. In centres which had an increase of more than 10 clients tested per day, additional staff may need to be deployed.

3. Only 4% of the patients opted out of HIV testing indicating high acceptability of this intervention among the patient population.

We consider the strategy to be effective as it led to finding thousands of new HIV-positive patients who were ART eligible. Nearly 40% of the 7559 HIV-positive cases were 'newly diagnosed' as a result of this strategy with almost 90% of them eligible for ART as per the existing criteria for starting ART. Nearly half of all presumptive TB patients were tested for HIV, although district-wise analysis indicated large variability. This is probably due to variation in availability of HIV testing facilities and their co-location at the sputum microscopy centres.

There are several important points that merit discussion. First, while WHO now recommends routine HIV testing of all presumptive TB patients, the operational guidance as to how to do this is lacking. This is among the first studies to fill that gap and addresses an area of global priority. This was also a national priority and addressed a specific request from the NTWG of Government of India.[14] Previous studies on this issue have focussed on assessing prevalence of HIV among presumptive TB patients rather than testing implementation models in routine programme settings. [4-10] These findings were presented back to NTWG and a decision to nationally scale up this intervention across all high HIV settings was made. Changes in recording and reporting have already been adopted by the national TB and HIV programmes in India. While we cannot attribute it directly, we note that some of these changes are now reflected in global guidance. [24]

Second, this is one of the largest studies on the issue of HIV testing among presumptive TB patients with more than 0.1 million patients screened in a period of three months across one of the HIV priority states of India. Being carried out in the routine health care setting, this study gives valuable information of the ground realities and challenges in implementing a new strategy within the general health system.

Third, we found that nearly 90% of HIV-infected presumptive TB patients (without TB) were eligible for ART. This is similar to the findings of two recent studies from Zimbabwe and India.[25, 26] As a public health approach, this is another subset of patients (similar to HIV-infected persons having active TB disease, hepatitis B virus infection with severe chronic liver disease, being pregnant or breast feeding, being aged under five years, and living in a sero-discordant relationship) in whom ART should be recommended irrespective of CD4 count. This strengthens the argument about moving towards a HIV 'test and treat' strategy for presumptive TB patients. This is in line with the recent guidance from WHO which calls for starting all HIV patients on ART irrespective of CD4 count.[27]

Fourth, about half of the presumptive TB patients were not tested for HIV. Not surprisingly, HIV testing was more likely in DMCs with co-located HIV testing facilities. This justifies the ongoing efforts of the national programmes to prioritise setting up of new HIV testing facilities at hospitals having sputum microscopy facilities. This, however, will not address the major reason for non-testing in a substantial proportion of presumptive TB patients in whom sputum samples were collected and transported from peripheral health

institutions to DMCs – such patients will miss the opportunity to get HIV tested at DMC. This calls for further decentralization of the HIV testing services to all the peripheral health institutions and sputum collection centres and national programmes should seriously consider this strategy to improve the uptake of HIV testing. We suggest scaling-up the use of rapid HIV screening tests at all the PHIs and those who are screened positive may be referred for further testing and confirmation at the ICTCs. The other programmatic challenge is to improve the procurement and supply chain management of HIV test kits to enhance HIV test uptake. Unavailability of laboratory technician or counsellors at DMC and/or ICTC was another reason for lack of HIV testing. This can be addressed by training the other staff within the general health system and motivating them to perform HIV testing in line with the overall approach to integrate NACP into the general health system and this would be sustainable in the long term.

Fifth, we captured data in an innovative manner using the freely available resources for data entry, storage, sharing and trouble shooting. This approach to ensuring quality of data capture in multicentre operational research in resource-constrained settings has been a great lesson.[23]

There were some limitations to our study given the operational nature of the study and reliance on routinely collected data. In this pilot, we could not capture the data among smear negative presumptive TB patients as to how many were eventually diagnosed with smear negative pulmonary TB and extrapulmonary TB. In assessing ART eligibility, information on whether the person was living in a sero-discordant relationship would have been useful, but was not captured. Including these criteria would have increased the number of people eligible for ART and hence the numbers obtained in this study are an underestimate. Furthermore, CD4 cell count data were missing in 30% of the HIV positive patients. Information on how many newly diagnosed HIV infected presumptive TB patients were put on ART and Cotrimoxazole Prophylactic Therapy later was also not documented. Information such as this would be very useful to assess if this strategy indeed increased the overall number of HIV-infected persons placed on ART and if it reduced the delay in initiating ART. Further studies are required to assess this and the impact on reducing overall HIV-TB associated mortality. While there could be multiple reasons in an individual for non-testing of HIV, only one predominant reason was captured and that too from the provider's perspective. In about one-third of patients, reason for non-testing was not mentioned and this is a serious limitation. Further, we do not have any information if this sub-group is similar to the rest in whom we know the reason for non-testing. Future research involving qualitative methods should be undertaken to understand patients' perspectives for not getting tested for HIV.

WHO and Joint United Nations Programme on HIV/AIDS (UNAIDS) have both embraced a bold new vision of "90-90-90" strategy which emphasizes the need to detect 90% of all HIV infected patients in the community, treat 90% of those detected with antiretroviral therapy (ART) and achieve viral suppression in 90% of those treated, and this has been reinforced by a similar 90-90-90 vision for TB control from the global STOP TB partnership.[28, 29]

Achieving these ambitious targets will require innovative efforts to find previously undetected HIV cases in the community. Testing presumptive TB patients in Karnataka proved to be an efficient means of HIV case-finding, and may complement that effort.

In conclusion, this operational research demonstrated a feasible way to make HIV testing among presumptive TB patients a reality in routine health settings. Several operational challenges were noted which provide useful lessons for moving forward.

ACKNOWLEDGEMENTS

The authors are thankful to the staff of the State TB Cell and Karnataka State AIDS prevention and control society, District TB Officers and their staff and the staff of the HIV testing centres of the state of Karnataka for enthusiastically assisting in the process of data collection. Further the authors are grateful to the presumptive TB patients of Karnataka state who have indirectly contributed to this learning.

REFERENCES

1. World Health Organization. Global tuberculosis report 2014. World Health Organization Document. 2014;WHO/HTM/TB/2014.08:1-149.
2. UNAIDS. How AIDS changed everything. MDG6: 15 Years, 15 lessons of hope from the AIDS response.: Joint United Nations Programme on HIV/AIDS, Geneva, Switzerland; 2015 [cited 2015 19th September]. Available from: http://www.unaids.org/sites/default/files/media_asset/MDG6Report_en.pdf.
3. World Health Organization. WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. World Health Organization Document. 2012;WHO/HTM/TB/2012.1:1-34.
4. Srikantiah P, Lin R, Walusimbi M, Okwera A, Luzze H, Whalen CC, et al. Elevated HIV seroprevalence and risk behavious among Ugandan TB suspects: implications for HIV testing and prevention. Int J Tuberc Lung Dis. 2007;11:168-74.
5. Deribew A, Negussu N, Kassahun W, Apers L, Colebunders R. Uptake of provider-initiated counselling and testing among tuberculosis suspects, Ethiopia. Int J Tuberc Lung Dis. 2010;14:1442-6.
6. Porskrog A, Bjerregaard-Andersen M, Oliveira I, Joaquím LC, Camara C, Andersen PL, et al. Enhanced tuberculosis identification through 1-month follow-up of smear-negative tuberculosis suspects. Int J Tuberc Lung Dis. 2011;15:459-64.
7. Odhiambo J, Kizito W, Njoroge A, Wambua N, Nganga L, Mburu M, et al. Provider-initiated HIV testing and counselling for TB patients and suspects in Nairobi, Kenya. Int J Tuberc Lung Dis. 2008;12(suppl 1):S63-S8.
8. Munthali L, Mwaungulu JN, Munthali K, Bowie C, Crampin AC. Using tuberculosis suspects to identify patients eligible for antiretroviral treatment. Int J Tuberc Lung Dis. 2006;10:199-202.
9. Dimairo M, Macpherson P, Bandason T, Zezai A, Munyati SS, Butterworth AE, et al. The risk and timing of tuberculosis diagnosed in smear-negative TB suspects: a 12 month cohort study in Harare, Zimbabwe. PLoS ONE. 2010;5(7): e11849:doi:10.1371/journal.pone.0011849.
10. Adjei AA, Adiku TK, Ayeh-Kumi PF, Hesse IFA. Prevalence of human immunodeficiency virus infection among tuberculosis suspect patients in Accra, Ghana. West Afr J Med. 2006;25:38-41.
11. National AIDS Control Organization, National Institute of Medical Statistics. Technical Report India HIV Estimates-2012: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2013 [cited 2015 23rd September]. Available from: http://www.naco.gov.in/upload/Surveillance/Reports%20&%20Publication/Technical%20Report%20-%20India%20HIV%20Estimates%202012.pdf.
12. Naik B, Kumar AMV, Lal K, Doddamani S, Krishnappa M, Inamdar V, et al. HIV prevalence among persons suspected of tuberculosis: policy implications for India. J Acquir Immune Defic Syndr. 2012;59:e72-e6.
13. Achanta S, Kumar AMV, Burugina Nagaraja S, Jaju J, Motta Shamrao SR, Uappaluri R, et al. Feasibility and effectiveness of provider initiated HIV testing and counseling of TB suspects in Vizianagaram district, South India. PLoS ONE. 2012;7(7): e41378:doi:10.1371/journal.pone.0041378.

14. National Aids Control Organization, Central TB Division. Minutes of National Technical Working Group on TBHIV collaborative activities on March 23, 2010: Ministry of Health and Family Welfare, Government of India; 2009 [cited 2011 13th June]. Available from: http://www.tbcindia.nic.in/pdfs/10-NTWG%20minutes%20230310.pdf.
15. World Health Organization. Consolidated guidelines for the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. June 2013: World Health Organization, Geneva, Switzerland; 2013 [updated 2013/07/03/]. Available from: http://www.who.int/hiv/pub/guidelines/arv2013/download/en/index.html.
16. National AIDS Control Organization. Shri Ghulam Nabi Azad launches National AIDS Control Programme-Phase IV: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2014 [cited 2015 23rd September]. Available from: http://pib.nic.in/newsite/PrintRelease.aspx?relid=103593.
17. Ofice of the Registrar General and Census Commissioner. Provisional Population Totals paper-1 : 2011 – Karnataka New Delhi: Government of India; 2011 [cited 2011 9th May]. Available from: http://censusindia.gov.in/2011-prov-results/prov_data_products_karnatka.html.
18. National AIDS Control Organization. HIV Sentinel Surveillance and HIV Estimation, 2007, A technical brief: Ministry of Health and Family Welfare, Government of India; 2008 [cited 2015 23rd September]. Available from: http://naco.gov.in/upload/Surveillance/Reports%20&%20Publication/HIV%20Sentinel%20Surveillance%20and%20HIV%20Estimation%202007_A%20Technical%20Brief.pdf.
19. Central TB Division. Technical and Operations Guidelines for Tuberculosis Control. New Delhi: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2005 [cited 2011 9th May]. Available from: http://www.tbcindia.nic.in/documents.asp.
20. National AIDS Control Organization and Central TB Division. National framework for Joint HIV/TB collaborative activities Delhi: Ministry of Health and Family Welfare, Government of India; 2009 [cited 2011 28th May]. Available from: http://www.tbcindia.nic.in/pdfs/Final%20National%20Framework%20for%20TB%20HIV%20Collaboration%202009.pdf.
21. National AIDS Control Organization. Operational Guidelines for Integrated Counselling and Testing Centres: Ministry of Health and Family Welfare, Government of India; 2008 [cited 2015 23rd September]. Available from: http://www.naco.gov.in/NACO/Quick_Links/Publication/Basic_Services/Operational__Technical_guidelines_and_policies/Operational_Guidelines_for_Integrated_Counseling_and_Testing_Centres/.
22. Central TB Division. TB India 2011. Revised National TB Control Programme Annual Status Report New Delhi: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2011 [cited 2011 9th May]. Available from: http://www.tbcindia.nic.in/pdfs/RNTCP%20TB%20India%202011.pdf.
23. Kumar AMV, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, et al. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. Public Health Action. 2013;3:60-2.
24. World Health Organization. Definitions and reporting framework for tuberculosis - 2013 revision. World Health Organization Document. 2013;WHO/HTM/TB/2013.2:1-40.

25. Dlodlo RA, Hwalima ZE, Sithole S, Takarinda KC, Tayler-Smith K, Harries AD. Are HIV-positive presumptive tuberculosis patients without tuberculosis getting the care they need in Zimbabwe? Public health action. 2015;5(4):217-21. doi: 10.5588/pha.15.0036. PubMed PMID: 26767174; PubMed Central PMCID: PMC4682612.
26. Kumar AM, Singarajipura A, Naik B, Guddemane DK, Patel Y, Shastri S, et al. HIV-infected presumptive tuberculosis patients without tuberculosis: How many are eligible for antiretroviral therapy in Karnataka, India? Journal of epidemiology and global health. 2016. doi: 10.1016/j.jegh.2015.12.002. PubMed PMID: 26821235.
27. World Health Organization. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV: World Health Organization; 2015 [cited 2016 10th February]. Available from: http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/.
28. Joint United Nations Programme on HIV/AIDS. An ambitious treatment target to help end the AIDS epidemic Geneva, Switzerland 2014. Available from: http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf.
29. STOP TB Partnership. Global Plan to STOP TB 2016/2020: Impact Modelling of the 90-(90)-90 Targets 2015 [Accessed on 10-02-2016]. Available from: http://stoptbplan2020.org/wp-content/uploads/2015/05/CH2.pdf.

Table 1: Operational procedures in provider-initiated HIV counselling and testing among patients with presumptive TB in Karnataka state, India, January-March 2012.

Operational Procedure	Steps
Procedure at Designated Microscopy Centre (DMC)	1. All Presumptive TB patients (including those coming for a repeat sputum examination) attending the designated microscopy centre (DMC) for diagnosis of TB were offered HIV counselling and testing by the DMC laboratory technician (DMC LT). 2. DMC LT after receiving the first sputum sample, referred the patient to the nearest, preferably the co-located HIV testing facility. a. If the patient was known to be HIV positive (in case of referral from ART centres, ICTCs or blood banks), the information regarding the HIV status was recorded in the laboratory register and the patient was not referred any further. The date of HIV testing was extracted from the ART patient booklet; if not available, the approximate date of HIV testing was documented as per patient's history. The information regarding **'HIV status' and 'date of HIV testing'** was documented in the **RNTCP laboratory register** (in a new column added for the purpose). b. In the case of presumptive TB patients whose HIV status was not known or HIV negative, LT referred them to the nearest or co-located HIV testing facility. 3. In cases where only the sputum samples reached the DMC (in the absence of the patient), it was recorded in the remarks column of the laboratory register. No active effort to track and offer an HIV test to such patients was undertaken. However, if there was a HIV testing facility at the peripheral health facilities (as in some districts like Bagalkot and Belgaum), HIV testing was offered to all presumptive TB patients whose sputum was collected at the collection points. The information regarding HIV status and date of HIV testing was then collected by DMC LT from the collection centres and this was updated in the laboratory register. 4. The counsellor at the HIV testing centre provided the feedback regarding HIV status (Positive/Negative/Indeterminate/Opted out) and date of HIV testing in the RNTCP laboratory form for sputum examination. A new field to capture HIV status and date of HIV testing was created in the RNTCP laboratory form for sputum examination. DMC LT updated the laboratory register based on the feedback on the laboratory form. Alternatively, the DMC LT discussed with the counsellor at the end of the day and updated the HIV status in the laboratory register – this is as per the national guidelines of shared confidentiality among health care providers for providing optimum care for the patient. 5. The predominant reason for not ascertaining the HIV status, wherever known, was recorded in the remarks column.
Procedure at the Integrated Counselling and HIV Testing Centre (ICTC)	1. Presumptive TB patients coming to the ICTCs were offered counselling and testing as per the norms and standard operating procedures of the NACP. 2. All referrals were recorded in the ICTC counselling register as referrals from RNTCP. 3. Presumptive TB patients who were known to be HIV positive and patients who had tested HIV negative within last 6 months were not re-tested. Patients who had an indeterminate result were re-offered the HIV test. 4. For patients with HIV positive results, the counsellor linked these patients to the nearest ART centre available in the district/state. This was done by giving a referral form and explaining to the patient about how to access the centre. The patient was given the contact details of the district programme managers for any assistance. 5. The counsellor then documented the HIV status in the RNTCP laboratory form as feedback to DMC LT. The counsellor also assisted the DMC LT to update the laboratory register with information on HIV status.

Recording	1. RNTCP laboratory form for sputum examination (Fig 2): A new field was created to capture the HIV status and date of HIV testing which was completed by the counsellor/LT at the HIV testing centre wherein one of the following options was noted – Positive, Negative, Indeterminate, Opted out. 2. RNTCP laboratory register (Fig 3): A column to capture HIV status was added in the laboratory register (Positive, Negative, Unknown)
Reporting	The following indicators were added in the monthly report submitted by each DMC to RNTCP 1. Of Presumptive TB patients examined for diagnosis, number with known HIV status 2. Of above, number HIV positive This information was then compiled quarterly in the district and State level programme management reports and reported in routine RNTCP surveillance.

Table 2: Ascertainment of HIV status and HIV positivity among patients with presumptive TB in Karnataka state, India, January-March 2012.

Parameter	Number examined for sputum smear microscopy	Number (%) with HIV status ascertained	Number (%) HIV Positive
Total	115308	62847 (55)	7559 (12)
Age (years)			
00-14	3808	1887 (50)	252 (13)
15-24	12804	7326 (57)	514 (7)
25-34	19595	11276 (57)	2157 (19)
35-44	20707	11738 (57)	2580 (22)
45-54	20336	11080 (55)	1333 (12)
55-64	18808	10022 (53)	510 (5)
>65	18857	9448 (50)	205 (2)
Unknown	393	70 (18)	8 (11)
Sex			
Male	69189	37498 (54)	4088 (11)
Female	46068	25335 (55)	3465 (14)
Transgender	7	6 (86)	5 (83)
Unknown	44	8 (18)	1 (13)
Sputum Smear status			
Smear Positive	9789	7071 (72)	802 (11)
Smear Negative	105519	55776 (53)	6757 (12)
HIV testing facility			
Not co-located	6248	1784 (29)	114 (6)
Co-located	109060	61063 (56)	7445 (12)

TB–Tuberculosis; HIV–Human immunodeficiency virus

Table 3: Ascertainment of HIV status and HIV positivity among patients with presumptive TB, district-wise, in Karnataka state, India, January-March 2012.

Parameter	Number examined for sputum smear microscopy	Number (%) with HIV status ascertained	Number (%) HIV Positive
Bagalkot	3351	3021 (90)	812 (27)
Bangalore City	9524	2330 (25)	251 (11)
Bangalore Rural	2054	591 (29)	39 (7)
Bangalore Urban	5311	816 (15)	61 (8)
Belgaum	8569	8122 (95)	959 (12)
Bellary	3533	2827 (80)	380 (13)
Bidar	2987	2540 (85)	137 (5)
Bijapur	2801	1873 (67)	530 (28)
Chamarajanagar	2735	899 (33)	117 (13)
Chikkaballapur	2523	1307 (52)	91 (7)
Chikmagalur	2928	1169 (40)	84 (7)
Chitradurga	2365	1613 (68)	71 (4)
Dakshina Kannada	4116	2761 (67)	170 (6)
Davanagere	3156	1070 (34)	250 (23)
Dharwad	3899	3261 (84)	451 (14)
Gadag	2237	1321 (59)	216 (16)
Gulbarga	4348	1835 (42)	193 (11)
Hassan	4938	2374 (48)	156 (7)
Haveri	2223	877 (40)	113 (13)
Kodagu	1317	661 (50)	33 (5)
Kolar	2733	1841 (67)	283 (15)
Koppal	2435	2032 (83)	446 (22)
Mandya	5026	2327 (46)	187 (8)
Mysore	6962	2407 (35)	180 (8)
Raichur	3201	2595 (81)	444 (17)
Ramanagara	3052	1463 (48)	38 (3)
Shimoga	3576	1788 (50)	209 (12)
Tumkur	5955	3391 (57)	405 (12)
Udupi	2455	1187 (48)	84 (7)
Uttara Kannada	3783	1573 (42)	97 (6)
Yadgiri	1215	975 (80)	72 (7)

Table 4: Antiretroviral therapy (ART) eligibility in newly diagnosed HIV among patients with presumptive TB, Karnataka state, India, January-March 2012.

Characteristic	TB patients	Presumptive TB patients without TB	Total
Number of newly diagnosed HIV cases	395	2639	3034
Number (%) assessed for ART eligibility	395 (100)	1849 (70)	2244 (74)
Number (%) ART eligible	395 (100)	1597 (87)	1992 (89)
Median (IQR) CD4 count	149 (74-290)	195 (89-361)	189 (87-355)

Table 5: Number needed to screen (NNS) to find one new (previously undiagnosed) case of HIV, by hypothetical strategy, Karnataka state, India, January-March 2012.

Strategy	Number with previously unknown HIV status tested for HIV	Number (%) HIV Positive	NNS
HIV testing for all smear-positive TB patients	6035	395 (6.5)	15
HIV testing for all presumptive TB patients	53627	3034 (5.7)	18
HIV testing of all presumptive TB patients in the age group 25-54 years	27769	2408 (8.7)	11

Table 6: Reasons for non-ascertainment of HIV status among presumptive TB patients, Karnataka state, India, January-March 2012.

Reasons for non-ascertainment of HIV status	Number	Percentage
Sputum specimens reaching microscopy centre instead of presumptive TB patients	20,454	54%
Non-availability of HIV test kits	7,179	19%
Non-availability of staff (Laboratory Technician, Counsellor) at the time of referral (due to leave, outreach duty, travel to attend meetings)	3,681	10%
HIV testing facility not co-located at microscopy centres	2,332	6%
Opted out of HIV testing	1,659	4%
Other reasons (lack of awareness among staff, gaps in recording, refusal to test due to workload, non-referral due to misconceptions of the staffs, death)	2,395	7%
Total	37,700*	100%

* Data about reasons for non-testing was available from 37,300 (72%) of the 52,461 patients

Table 7: Increase in workload at HIV testing centres due to strategy of 'routine HIV testing of presumptive TB patients', Karnataka state, India, January-March 2012.

Average increase in number of clients tested for HIV	Number (%) (based on actual numbers tested for HIV)	Number (%) (assuming all TB suspects will be tested for HIV)
1-2 clients per day	396 (69.5)	252 (44.2)
3-5 clients per day	141 (24.7)	224 (39.3)
6-10 clients per day	31 (5.4)	79 (13.9)
>10 clients per day	2 (0.4)	15 (2.6)

HIV-Human immunodeficiency virus;

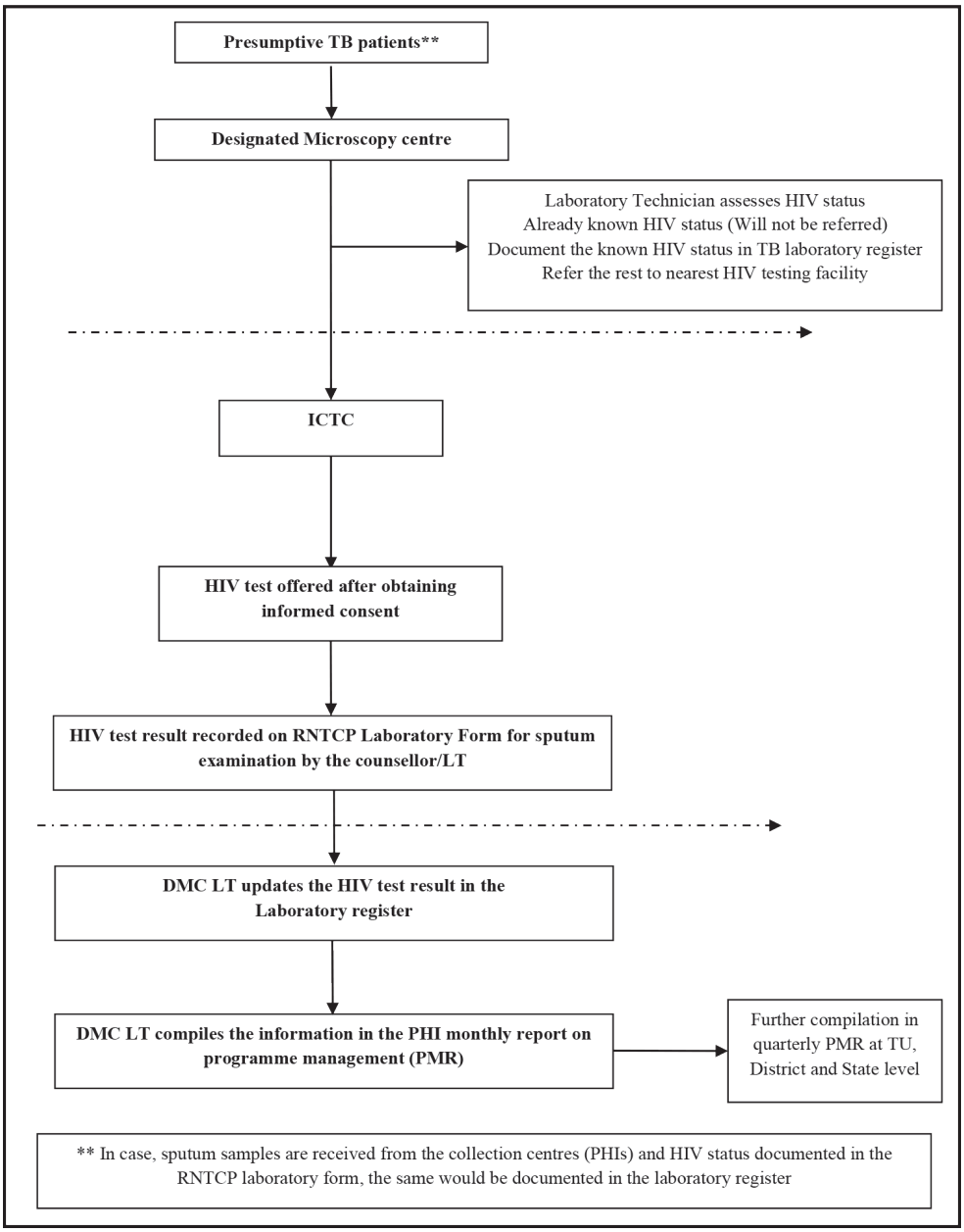

Figure 1. Flow Chart depicting the patient flow and the recording and reporting mechanism, PITC among presumptive TB patients, Karnataka, India, 2012

PITC-Provider initiated HIV testing and counselling; HIV-Human immunodeficiency virus; TB-tuberculosis; RNTCP-Revised National Tuberculosis Control Programme; PHI-Peripheral Health Institutions; TU-Tuberculosis Unit; LT-Laboratory Technician; DMC-Designated Microscopy Centre; PMR-Programme Management Report

REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME
Laboratory Form for Sputum Examination

Name of Referring Health Facility: _____ Date: _____

Name of patient: _____ Age: ____ Sex: M □ F □

Complete address: _____

_____

Contact Phone number / Mobile No.: _____

Type of suspect / disease: □ Pulmonary

□ Extra-pulmonary **Site**: _____

Reason for examination:

□ Diagnosis

□ Repeat Examination for Diagnosis

□ Follow-up examinations

□ For new and previously treated cases - Month of follow-up ……

□ For MDR-TB cases – Month of follow-up ……

Treatment Regimens (tick ✓ appropriate box):

□ New cases □ previously treated □ MDR-TB

Patient's TB No. _____

(Name and signature of referring person/ official)

If sputum samples are being transported:

Specimen identification No.: _____ Date of sputum collection: _____

Specimen Collector's name and signature _____

Sputum microscopy results (To be completed in the laboratory of DMC)

Name of DMC: _____

Lab. Serial No.: _____

Date of examination	Specimen	Visual appearance (M, B, S)*	Results (Neg or Pos)	Positive (grading)			
				3+	2+	1+	Scanty**
	A						
	B						

* M = Mucopurulent, B = Blood stained, S = Saliva

** Write actual count of AFB seen in 100 oil immersion fields

Date: _____ Signature of Lab. Technician

HIV test results (To be completed by counselor / LT at HIV testing centre)

HIV Test result: □ Negative □ Positive □ Indeterminate □ Opted out

Date of HIV testing: **PID Number:**

Figure 2. Modified format of laboratory form for sputum examination, PITC among presumptive TB patients, Karnataka, India, 2012.

REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAMME

LABORATORY REGISTER

Lab. Serial No.	Date	Name in Full	Age	Sex M/F	Complete address (for new patients) Phone No.	Name of referring Health Facility	Reasons for Examination*				Results		HIV status (P,N,U)	Sign	Remarks
							Diagnosis	Follow-up			A	B			
								TB No.	Regimen NT/PT	Month					

- *If sputum is examined for diagnosis, put a tick (✓) mark in the space under "Diagnosis" sputum is examined for repeat diagnosis, put 'RE' in the space under" Diagnosis"*
- *If sputum is for follow-up of patients on treatment, write the patient's TB No. in the space under "Follow up", treatment regimen and month of follow up*
- *Points to be mentioned in the remarks column: date of starting treatment, treatment regimen, TB No, Referral details, MDR-TB suspect identified and remarks on unblinded rechecking of slides during OSE visits by the STLS, etc.*
- *HIV status: P-Positive; N-Negative; U-Unknown*

Figure 3. Modified format of laboratory register, PITC among presumptive TB patients, Karnataka, India, 2012.

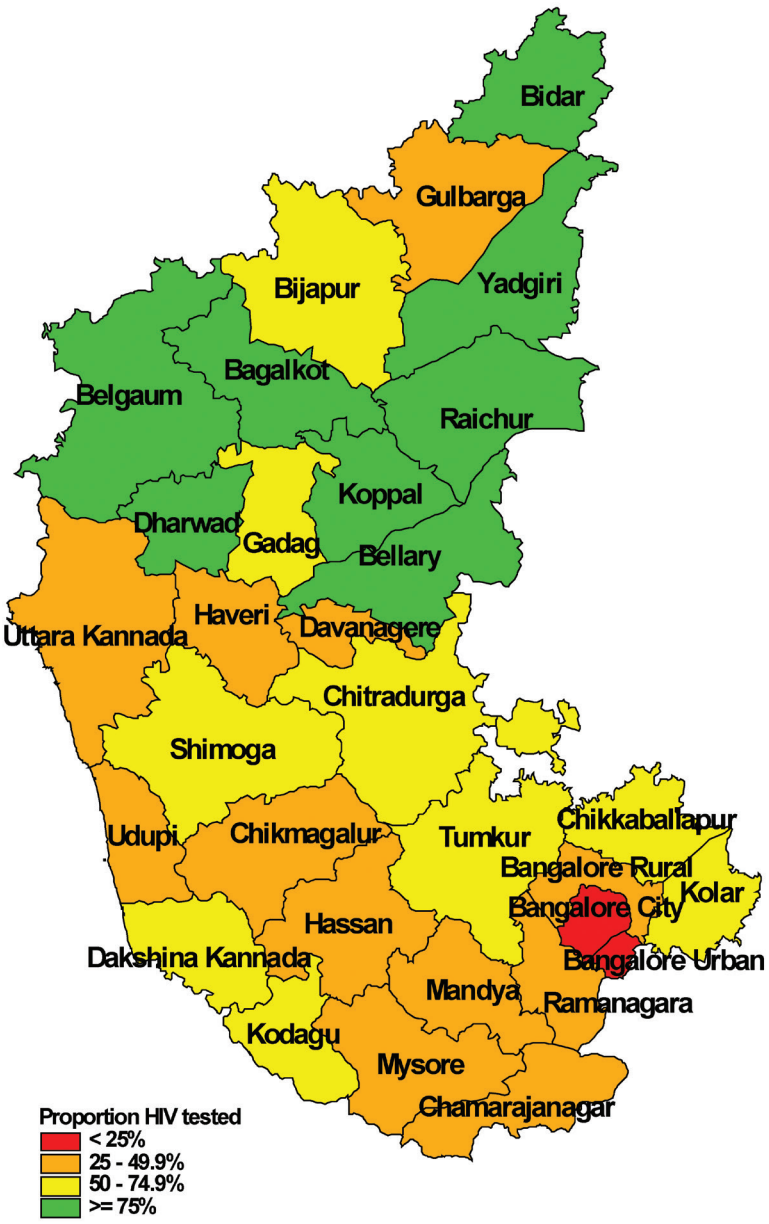

Figure 4. Ascertainment of HIV status among patients with presumptive TB, district-wise, in Karnataka state, India, January-March 2012.

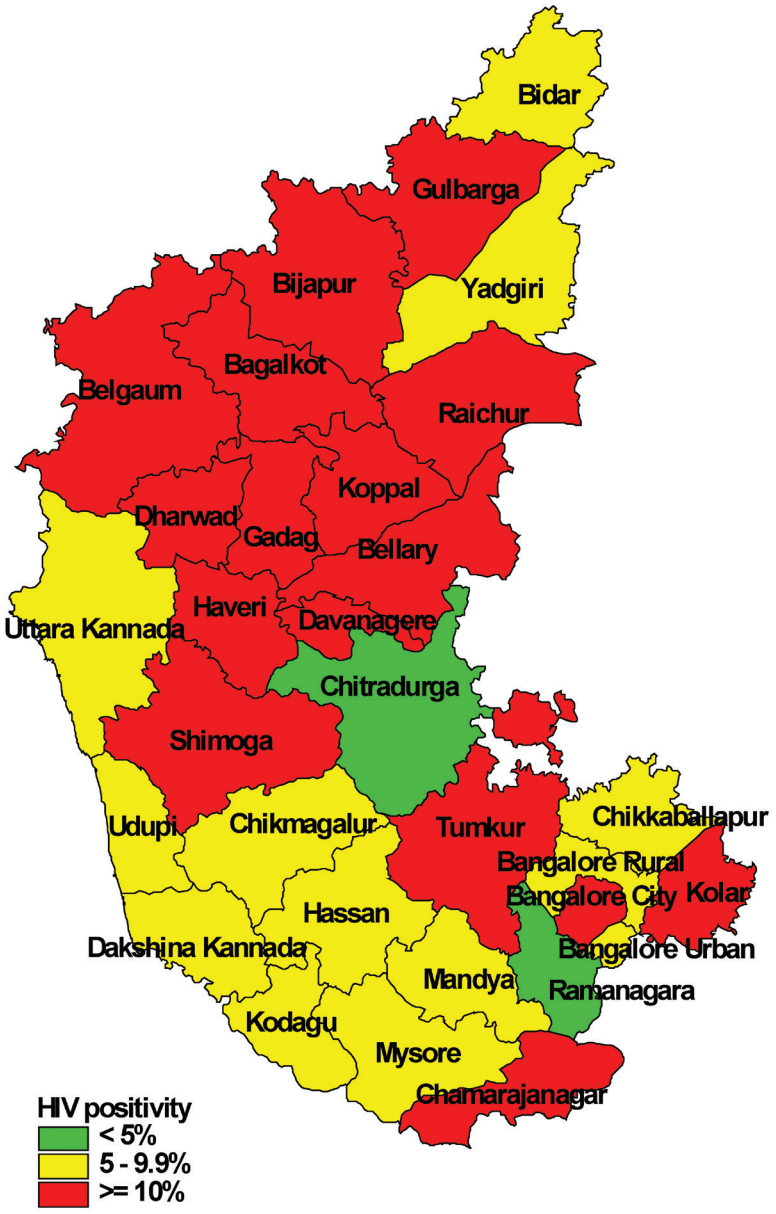

Figure 5. HIV positivity among patients with presumptive TB, district-wise, in Karnataka state, India, January-March 2012.

6.

Efficient quality–assured data capture in operational research through innovative use of open–access technology

Kumar AMV, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, Lauritsen JM, Rieder HL.

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Summary

Ensuring quality of data during electronic data capture has been one of the most neglected components of operational research. Multicentre studies are additionally challenged with issues about logistics of travel, training, supervision, monitoring and troubleshooting support. Allocating resources to these issues can pose a significant bottleneck for operational research in resource-limited settings. In this paper, we describe an innovative and efficient way of coordinating data capture in multicentre operational research using a combination of three open access technologies – EpiData for data capture, Dropbox for sharing files and TeamViewer for providing remote support.

INTRODUCTION

'Quality-assured data entry' has been aptly described as the 'Cinderella' of medical research, the most neglected one.[1] Though there are several ways of reducing data entry errors, 'double data entry and validation' has been considered the definitive gold standard[2] – where data are entered independently twice and value pairs compared for discordances, followed by resolution of discordances by referral to the original data source.[3] However, a review of all publications in the *International Journal of Tuberculosis and Lung Disease* in the year 2008 indicated that only 2/43 published articles related to tuberculosis (TB) epidemiology actually mentioned achieving this standard while more than half did not even mention anything about data quality.[4] This tendency to unquestioningly presume data quality in published research is highly questionable! Despite the easy availability of high-quality open-access tools for quality-assured data capture, the concept has seemingly been grossly neglected from academic curricula in medical and public health schools. The challenge to assure data quality gets compounded if the context is a multi-centric research study involving multiple study sites and personnel; costs of travel for training, supervision, monitoring and troubleshooting support are often substantial. These costs can become a significant barrier to assuring data quality while conducting high-quality operational research, especially in resource-limited settings. In this paper, we describe a model that innovatively used multiple open-access tools in a multi-centric operational research project with efficient use of resources.

CONTEXT

The subject of this operational research project was the implementation of provider-initiated HIV counselling and testing for patients with presumptive TB under routine programmatic conditions in the State of Karnataka, India. This State has a population of about 62 million and is divided into 31 districts spread across ~192,000 km^2 and extends to about 750 km from north to south and about 400 km from east to west. The study took place between January and March 2012. As part of this intervention, every patient with presumptive TB attending the microscopy centre was assessed for HIV status by the laboratory technician. Those with unknown HIV status were referred to the nearest HIV testing facility. HIV test results were captured by trained staff in a structured paper-based data collection form with measures built in to ensure data validity. Once the data were on paper, the forms were brought to the district TB centre for compilation and electronic capture. This meant that data entry would occur at 31 sites across the state and the responsibility was assigned to the data entry operator of the district under National Tuberculosis Programme.

INNOVATION: SETTING UP THE DATA CAPTURE SYSTEM FOR EACH SITE

We used three tools to set up the system for data entry.

First, we used EpiData Entry version 3.1 (EpiData Association, Odense, Denmark, http://www.epidata.dk) to design the data capture instrument. In addition to being open-access, this tool offers several advantages: small size of the software and the data files, non-interference of the software with the operating system of the user's computer during installation, excellent capabilities for inbuilt checks during data entry to reduce the frequency of data entry errors and a simple option that allows double data entry and validation. Most importantly, it is user-friendly, making it easy to teach and learn.

Second, we used Dropbox (http://www.dropbox.com) to share the folders with each other over the web (See Box). The principal investigator (PI) designed the data capture formats in EpiData and placed them in a district-specific Dropbox folder (thus 31 folders, one for each district) and an invitation was sent by email to each district data entry operator to join the shared folder. Once the user accepted the invitation and had installed Dropbox, the software created the shared folder on their local computer. This provided the powerful, simultaneous option of both offline data entry and online file synchronization. The option of offline data entry ensured that continuous internet connectivity is not required during data entry. Online synchronization meant near real-time sharing of data with the PI and data safety through online backup. Any need to change the structure of data capture instrument to suit needs of an individual site could be achieved very easily by manipulating the files in the shared folder by the PI. Without this instrument, a physical visit would have been required or considerable time expended in back-and-forth emailing of files.

Third, we used TeamViewer (http://teamviewer.com) to provide support remotely to the individual sites for initial set-up and troubleshooting (See Box). We used this software to connect to the district computers and set up the data capture system including software installation. This was also utilised as a training opportunity. After establishing telephone contact, the PI explained and demonstrated the use of the data capture system. The user was then allowed to enter data of a few records under PI supervision, allowing resolution of any early problems. Thereafter, if the user encountered any problem during data entry, he or she would connect with the PI on TeamViewer to actually show the error and get it resolved almost immediately. A problem that required an in-person visit to resolve hitherto could now be solved very easily and efficiently over a TeamViewer session!

DATA ENTRY

Once the system for data capture was set up, the data entry operators entered the data twice in files designated for the purpose already placed in the shared Dropbox folder. Once they finished data entry, this was communicated to the PI over email. Then the PI performed a 'data validation' ('data compare') between the two databases and generated a validation report listing discrepancies between the two databases, placing the report in the Dropbox folder. The data entry operator was informed and requested to refer to the original data for corrections and finalization.

WHAT WAS ACHIEVED? WHAT RESOURCES WERE REQUIRED?

In a span of three months, data on nearly 115,000 study participants were electronically captured while ensuring the highest standards of data quality coordinated across 31 sites. The PI was assisted by three colleagues working for the TB control programme in the state in ensuring that the data capture system was set up in their respective districts. These three colleagues also had access to the shared folders on Dropbox. They together co-ordinated data capture in a period of three months beyond and above their routine job responsibilities.

DISCUSSION

This is an innovative use of open-access technology to coordinate data capture in a multi-centric operational research project across 31 sites. While internet connection is decisive for success, the system does not require a large bandwidth nor 'always-on' capability: since EpiData file sizes are small (1000 records required 216 kilobytes only!), bandwidth is of minor importance; since Dropbox has the option of offline access to shared folders, uninterrupted internet connection is not required for data entry, a major pre-requisite in web-based data capture systems. Telephone costs can be circumvented, if required, by using Skype™ (http://www.skype.com), which was used for periodic video conference calls among the PI and co-investigators for monitoring the project. A recent study[5] has shown that an alternative to double entry could be 'Automatic Forms Processing' (a method by which one can 'automatically' capture information entered into data fields by scanning, and converting it into an electronic format through techniques like 'Optical Mark Recognition' or 'Intelligent Character Recognition'), but this is applicable only in highly structured questionnaires with only check boxes, numbers and no dates.[5] Further this would also require relatively expensive equipment and computer expertise, often not available in resource-limited settings.

Overall, this model for data capture proved highly efficient in terms of optimum utilization of resources including time and we feel that it can be easily replicated in any resource-limited setting for operational research.

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AUTHOR CONTRIBUTIONS

Ajay Kumar wrote the first draft. All the other co-authors reviewed the draft and provided critical inputs and helped in revision of the manuscript. All authors approve the final version.

CONFLICTS OF INTEREST

None declared.

BOX

WHAT IS DROPBOX?

Dropbox is a file hosting service operated by Dropbox Inc. that offers cloud storage and file synchronization. Dropbox uses a 'Freemium' business model, where users are offered a free account with a set storage size (2 Giga Bytes in this case) and paid subscriptions for accounts with more capacity. Dropbox allows users to create a special folder on each of their computers, which Dropbox then synchronises so that it appears to be the same folder (with the same contents) regardless of the computer it is viewed on. Files placed in this folder are also accessible through a website and mobile phone applications. Such folders can be shared with others for mutual access.
More information at www.dropbox.com

WHAT IS TEAMVIEWER?

Team Viewer is a secure software package for remote control, desktop sharing, online meetings, web conferencing and file transfer between computers. TeamViewer is a tool that makes it incredibly easy to set up and use a Virtual Private Network connection that lets you take complete control of another computer from your own computer via internet. It enables two-way connections in which users can flip control back and forth. While TeamViewer is proprietary, it is free to non-commercial purposes.
More information at www.teamviewer.com

REFERENCES

1. Cartwright A, Seale C. The Natural History of a Survey: Account of the Methodological Issues Encountered in a Study of Life Before Death. King Edward's Hospital Fund. London (ISBN: 1-85551-056-1): 1990.
2. Ohmann C, Kuchinke W, Canham S, Lauritsen J, Salas N, Schade-Brittinger C, et al. Standard requirements for GCP-compliant data management in multinational clinical trials. Trials 2011;12:85.
3. Rieder H L, Lauritsen J M. Quality assurance of data: ensuring that numbers reflect operational definitions and contain real measurements. [State of the Art Series. Operational Research. Number 3 in the series]. Int J Tuberc Lung Dis 2011;15:296-304.
4. Rieder H L. What knowledge did we gain through The International Journal of Tuberculosis and Lung Disease in 2008 on the epidemiology of tuberculosis? Int J Tuberc Lung Dis 2009;13:1219-23.
5. Paulsen A, Overgaard S, Lauritsen J M. Quality of data entry using single entry, double entry and automated forms processing--an example based on a study of patient-reported outcomes. PLoS One 2012;7:e35087.

7.

Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India

Palanivel C, **Kumar AMV**, Mahalakshmi T, Govindarajan S, Claassens M, Satyanarayana S, Gurumurthy D, Vasudevan K, Purty A, Paulraj AK, Raman K V.
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Setting
Puducherry, a low HIV prevalence (<1% among antenatal women) district in South India.

Objectives
(1) Among presumptive TB patients, to (i) estimate the proportion whose HIV status was ascertained and found HIV positive (ii) describe the demographic and clinical characteristics of those whose HIV status was not ascertained; (2) To assess the additional workload at HIV testing centers.

Design
Cross-sectional study – consecutive presumptive TB patients attending microscopy centers for diagnosis during March-May 2013 were asked if they knew their HIV status. Patients with an unknown HIV status were offered voluntary counseling and HIV testing.

Results
Of 1886 presumptive TB patients, HIV status was ascertained for 842 patients (44.6%) and 28(3.3%) were HIV positive. The uptake of HIV testing was significantly higher in younger age groups, males, residents of Puducherry and smear positive TB patients. The median (range) increase in number of clients tested for HIV per day per testing center was 1 (0-6).

Conclusion
The uptake of HIV testing was low. HIV prevalence was higher among presumptive TB patients than antenatal women and as high as in TB patients. With minimal increase in workload at HIV testing centers, HIV testing could be feasibly implemented using existing resources.

INTRODUCTION

Globally, in the year 2011, there were an estimated 0.43 million deaths from tuberculosis (TB) among people who were human immunodeficiency virus (HIV)-positive.[1] This high number of deaths is unacceptable given that HIV is manageable, though with life-long anti-retroviral therapy, and drug-sensitive TB is curable.

The World Health Organization (WHO) in the year 2012, updated its policy on TB/HIV collaborative activities recommending provider initiated HIV testing and counseling (PITC) of not only TB patients but also 'patients with presumptive tuberculosis' (erstwhile referred to as TB suspects) to enable early diagnosis of HIV and linkage to structured HIV care.[2, 3] The strategy of routinely offering HIV testing to patients with presumptive TB offers the potential for early HIV diagnosis and treatment which may reduce morbidity and mortality. Studies in sub-Saharan Africa and India have shown that the HIV prevalence among persons with presumptive TB is as high as among those with diagnosed TB, with prevalence rates varying according to the epidemiological context. [4-7]

Acknowledging the strong evidence, [6, 7] the National TB and HIV programs in India took a joint policy decision to implement PITC among patients with presumptive TB in high HIV settings (HIV prevalence >1% among pregnant women and >5% among High risk groups), namely the states of Karnataka, Andhra Pradesh, Tamil Nadu, Maharashtra, Manipur and Nagaland, and further recommended that similar surveillance efforts should be conducted in moderate and low HIV settings (HIV prevalence <1% among pregnant women and/or <5% among High risk groups) to inform national policy decision.[8]

To address this knowledge gap, we undertook a study with the aim of assessing HIV test uptake and HIV positivity among presumptive TB patients in Puducherry, a district with low HIV prevalence in South India. The specific objectives were (1) to estimate the proportion of presumptive TB patients whose HIV status was ascertained and found HIV positive (2) to describe the demographic and clinical characteristics of presumptive TB patients whose HIV status was not ascertained (3) to assess the additional workload at HIV testing centers due to PITC strategy.

METHODS

STUDY DESIGN

This was a health facility based cross-sectional study.

STUDY SETTING

The study was conducted in the Puducherry district, one of the four districts in the Union Territory of Puducherry with a population of ~1 million. Puducherry district is bordering a high HIV prevalence district (Cuddalore and Villupuram districts in Tamil Nadu state) and health facilities in Puducherry, including its eight medical colleges, have attracted

patients from neighboring districts for TB diagnostic services. Under the Revised National Tuberculosis Control Programme (RNTCP), TB diagnosis and treatment services are offered through the existing primary health care system. 'Patients with presumptive TB', defined as anybody with a cough of two weeks or more with or without other symptoms are examined at Designated Microscopy Centers (DMCs) in the district. All diagnosed TB patients are treated free of charge with fully intermittent, thrice weekly short course chemotherapy administered under direct supervision (DOTS) as per the national guidelines. HIV diagnostic and treatment services are offered free of charge as per the national guidelines through a network of eight stand-alone HIV testing centers and one anti-retroviral therapy (ART) center.[9] Of 18 DMCs in the district, 13 DMCs have HIV testing facility located in the same facility. As part of TB/HIV collaborative activities, HIV testing is routinely offered to all TB patients treated in the RNTCP. Those who are found to be HIV positive are referred to the ART center for further evaluation and management, including initiation of ART. During 2012, 96% of TB patients were ascertained for HIV and 2% were found to be HIV-infected in Puducherry district. The corresponding figure for the neighboring districts of Cuddalore and Villupuram was 5% in both districts. [10]

STUDY POPULATION AND STUDY PERIOD

Adult patients (aged 18 years and above) with presumptive TB attending designated microscopy centers (DMC) for diagnostic sputum smear microscopy between 15th March, 2013 and 10th May, 2013 constituted the study population. Of a total of 18 DMCs in the district, 7 DMCs were excluded. Of 7 DMCs, 5 DMCs didn't provide HIV testing services and 2 DMCs didn't give administrative permission to conduct the study. Presumptive TB patients who didn't come to the DMC but had their sputum collected and transported were excluded.

DATA COLLECTION PROCEDURE

Patients were asked if they already knew their HIV status by the RNTCP laboratory technician (LT) trained for the purpose. Those with unknown HIV status were referred to HIV testing center and offered voluntary counseling and HIV testing as per national guidelines.[9] RNTCP laboratory technicians and staff of HIV testing centres received training on HIV testing and counseling six months before the study as part of their routine in-service training.

STUDY VARIABLES AND SOURCE OF DATA

The data variables related to the study objectives were captured in a structured data collection proforma. The original sources of data were RNTCP laboratory registers and the records at the HIV testing centers. To assess the workload of each HIV testing center, the total number of clients counseled during the study period was collected and compared with the increase in the number of clients counseled due to the PITC strategy.

DEFINITIONS OF KEY OUTCOMES

We calculated the following key indicators – i) Proportions of 'presumptive TB patients' ascertained for HIV status, ii) Proportions of 'presumptive TB patients' found HIV positive, iii) The number (proportion) of all HIV cases diagnosed newly as the result of the strategy of 'PITC of presumptive TB patients', iv) Number needed to screen (NNS) to find an additional case of HIV, v) The average increase in daily workload at the HIV testing centers calculated center wise by dividing the total number of presumptive TB patients who underwent HIV testing by the average number of working days during the study period.

DATA ENTRY AND ANALYSIS

Dual data entry, validation and analysis was done using EpiData entry software (Version 3.1 for entry and 2.2.2.180 for analysis, EpiData Association, Odense, Denmark).[11] We used chi-square tests for comparing proportions and a p-value of < 0.05 was considered as statistically significant.

ETHICS CONSIDERATIONS

We obtained informed consent from study participants and standard operating procedures (SOPs) of the National AIDS Control Programme (NACP) were followed for counseling and HIV testing.9 Ethics approval was obtained from the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France and the Institutional Ethics Committee (IEC) of Indira Gandhi Medical College, Puducherry.

RESULTS

Of 2135 patients who underwent diagnostic sputum smear microscopy, 67 were excluded because sputum samples were transported instead of patients. Of the remaining 2068, 1886 (91.2%) were ≥ 18 years and eligible for the study. Of these, the HIV status was ascertained for 842 patients (44.6%) and 28 (3.3%) were HIV positive (**Table 1**). Of the 28 HIV cases, 13 (46%) knew their HIV status and 15 (54%) were newly identified due to the PITC strategy. The number needed to screen (NNS) to find one new HIV positive patient was 56. The NNS was relatively lower among patients in the 35-44 year age group, males and those with a positive smear.

The demographic and clinical characteristics of study participants according to the uptake of HIV testing are shown in **Table 2**. The uptake of HIV testing was significantly lower in older age groups, females, patients residing outside Puducherry (study area) and smear negative TB patients.

Due to the implementation of the PITC strategy, in most (8/11) of the HIV testing centers 1–2 extra clients per day were counseled and tested. In the remaining three centers, the increase in workload was 3-5 clients per day. The median (range) increase in the number of clients tested for HIV per center per day was 1 (0-6).

DISCUSSION

This is one of the first studies from India examining the effectiveness and feasibility of implementing the PITC strategy for presumptive TB patients in a low HIV prevalence setting under routine programmatic conditions. Overall, the HIV testing uptake was low with less than half of presumptive TB patients getting their HIV status ascertained. The uptake was higher among smear positive TB patients which could be attributed to the existing national policy of PITC among TB patients. The uptake was lower in older age groups, females and those who were smear negative. As smear negative patients form a larger group with a higher contribution to overall number of new HIV cases detected and given higher likelihood of HIV positive individuals being smear negative, this group should not be missed. Reasons for the low uptake are unknown but possible reasons could be a low self-perceived risk of HIV in older age groups, hesitation among providers in offering an HIV test, losses in the referral process and deficiencies of recording and reporting. In comparison to our findings, the uptake of HIV testing was higher in the states of Karnataka and Andhra Pradesh at 92% and 85% respectively.[6,7] These states have a high HIV prevalence and the high uptake could be due to greater awareness among the patients and providers about the need for HIV testing.

The other important finding was a relatively high HIV prevalence (3.3%) among presumptive TB patients who got tested as compared to antenatal clinic attendees (<1%), TB patients (2%) and clients attending HIV testing centres excluding pregnant women (1.6%).[10, 12] Nearly 60% of HIV cases identified were newly diagnosed as a result of PITC. This confirms the findings from other studies that 'presumptive TB patients' could be a target group for PITC. [6,7] Failing to test for HIV in this group represents a missed opportunity in diagnosing HIV infection. The number needed to screen (NNS) to find one new HIV positive patient was 56 overall and 81 among presumptive TB patients whose sputum smear was negative. The NNS was lower among the age group 25-54 years and nearly 80% of all new HIV patients diagnosed were in this age group. To optimize the use of existing resources, the national programme may selectively offer HIV testing to patients in the age group 25-54 years. As expected, the HIV positivity was higher among patients of neighbouring states, with a relatively higher HIV prevalence. This is another group that could be targeted for HIV testing.

The implementation of the PITC strategy did not pose a burden to the staff of the HIV testing centres according to our study findings. The additional workload at most of the HIV testing centres increased by two extra clients per day, even after assuming a 100% uptake. Hence HIV testing for presumptive TB patients is feasible and could be implemented using existing human resources. However, the overall requirement for HIV test kits would increase substantially and the HIV programme should properly plan procurement and supply chain management to ensure the uninterrupted supply of HIV test kits.

The study had a few limitations. First, the study could not be implemented in five DMCs due to the absence of HIV testing services, a pre-requisite for the implementation of PITC. Second, nearly 50% of patients were not tested for HIV with higher proportions among older age groups who were likely to have a lower HIV prevalence. This could have led to an

overestimation of HIV prevalence in our study. Third, we could not ascertain the reasons for non-testing; well-designed qualitative studies are required for a better understanding. Fourth, we could not assess CD4 counts of HIV positive patients and linkage to care services. This would be essential to assess if the PITC strategy actually impacts on mortality and morbidity of HIV-positive patients and could be a topic of future research.

CONCLUSION

Though the uptake of HIV testing was low, the HIV prevalence was higher compared to antenatal clinic attendees and as high as in TB patients. The PITC strategy could be implemented with existing resources with a minimal increase in workload at HIV testing centers. We recommend that HIV testing should be routinely offered to presumptive TB patients, especially those in age-group 25-54 years and the reasons for non-testing needs detailed evaluation. Further studies in similar settings across India are required to confirm these findings before wider scale-up decisions.

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AUTHOR CONTRIBUTIONS

Conceived and designed the experiments: AMVK PC MC SS. Performed the experiments: PC MT KV GS GD AKP. Analyzed the data: PC AMVK. Wrote the paper: PC AMVK MC. Provided comments and input to revise manuscript: SS MT AP RKV GD GS KV

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CONFLICTS OF INTEREST

None declared

REFERENCES

1. World Health Organization. Global Tuberculosis Control 2012. Geneva: World Health Organization, 2012. WHO/HTM/TB/2012.6: 1-272.
2. WHO policy on collaborative TB/HIV activities: Guidelines for national programmes and other stakeholders 2012. Geneva: World Health Organization, 2012. WHO/HTM/TB/2012.1: 1-34.
3. World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision. Geneva: World Health Organization, 2013. WHO/HTM/TB/2013.2: 1-40.
4. Macpherson P, Dimairo M, Bandason T et al, . Risk factors for mortality in smear-negative tuberculosis suspects: a cohort study in Harare, Zimbabwe. Int J Tuberc Lung Dis 2011; 15: 1390-1396.
5. Srikantiah P, Lin R, Walusimbi M, et al. Elevated HIV seroprevalence and risk behavious among Ugandan TB suspects: implications for HIV testing and prevention. Int J Tuberc Lung Dis 2007; 11: 168-174.
6. Achanta S, Kumar AM, Nagaraja SB et al). Feasibility and Effectiveness of Provider Initiated HIV Testing and Counseling of TB Suspects in Vizianagaram District, South India. PLoS One 2012; 7: e41378.
7. Naik B, Kumar AMV, Lal K et al. HIV prevalence among persons suspected of tuberculosis: policy implications for India. J Acquir Immune Defic Syndr 2012; 59: e72-e76.
8. Minutes of meeting of National Technical Working Group on HIV/TB Collaborative Activities at National AIDS Control Organization, New Delhi, on 19/07/2012. Available at http://tbcindia.nic.in/TBHIV.html. Last accessed on 12th September 2012.
9. Ministry of Health & Family Welfare. Guidelines for HIV Testing, March 2007. National AIDS Control Organization, Ministry of Health & Family Welfare, Government of India, 2007.
10. Ministry of Health and Family Welfare. TB India 2012. Annual status report. Revised National Tuberculosis Control Program. Ministry of Health and Family Welfare. Government of India, 2013.
11. Lauritsen JM. (Editor) EpiData Data Entry, Data Management and basic Statistical Analysis System. Odense, Denmark, EpiData Association, 2000-2008. Available from http://www.epidata.dk.
12. Ministry of Health and Family Welfare. Annual report 2010-2011. Department of AIDS control, National AIDS Control Organisation. Ministry of Health & Family Welfare, Government of India, 2012.

Table 1: HIV test uptake, HIV positivity and number needed to screen among presumptive TB patients, Puducherry, South India, March – May 2013.

Characteristic	Total Number	Number (%) HIV status ascertained	Number (%) HIV Positive	Number (%) New cases of HIV Positive	NNS
Total	1886	842 (44.6)	28 (3.3)	15 (1.8)	56
Age (years)*					
18-24	215	118 (54.9)	1 (0.8)	0 (0.0)	NA
25-34	332	187 (56.3)	7 (3.7)	3 (1.6)	62
35-44	336	149 (44.3)	10 (6.7)	6 (4.0)	25
45-54	378	175 (46.3)	5 (2.9)	3 (1.7)	58
55-64	335	129 (38.5)	4 (3.1)	3 (2.3)	43
>65	277	82 (29.6)	1 (1.2)	0 (0.0)	NA
Sex					
Male	1138	534 (46.9)	20 (3.7)	12 (2.2)	45
Female	748	308 (41.2)	8 (2.6)	3 (1.0)	103
Residence					
Puducherry	1327	617 (46.5)	16 (2.6)	6 (1.0)	103
Other states	559	225 (40.3)	12 (5.3)	9 (4.0)	25
Sputum Smear					
Positive	192	114 (59.4)	7 (6.1)	6 (5.3)	19
Negative	1694	728 (43.0)	21 (2.9)	9 (1.2)	81

HIV–Human immunodeficiency virus; NNS-Number needed to screen; NA-Not applicable;
*Age missing for 13 study participants.

Table 2: Factors associated with HIV test uptake among presumptive TB patients, Puducherry, South India, March - May 2013.

Characteristic	Number (%) HIV status ascertained	Number (%) HIV status not ascertained	P value
Total	842	1044	
Age (years)*			
18-24	118 (14.0)	97 (9.4)	<0.001
25-34	187 (22.3)	145 (14.0)	
35-44	149 (17.7)	187 (18.1)	
45-54	175 (20.8)	203 (19.7)	
55-64	129 (15.4)	206 (19.9)	
>65	82 (9.8)	195 (18.9)	
Sex			
Male	534 (63.4)	604 (57.9)	0.01
Female	308 (36.6)	440 (42.1)	
Residence			
Puducherry	617 (73.3)	710 (68.0)	0.01
Other states	225 (26.7)	334 (32.0)	
Sputum Smear result			
Positive	114 (13.5)	78 (7.5)	<0.001
Negative	728 (86.5)	966 (92.5)	

HIV–Human immunodeficiency virus
*Age missing for 13 study participants.

8.

HIV–infected presumptive TB patients without TB: How many are eligible for antiretroviral therapy in Karnataka, India?

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Summary

For certain subgroups within people living with HIV (active tuberculosis, pregnant women, under-five children and sero-discordant couples), the World Health Organization recommends antiretroviral therapy (ART) irrespective of CD4 count. Another subgroup which has received increased attention is 'HIV-infected presumptive TB patients without TB'. In this study, we assess the proportion of HIV-infected presumptive TB patients eligible for ART in Karnataka State (population 60 million), India. This was a cross-sectional analysis of data of HIV-infected presumptive TB patients diagnosed in May 2015 abstracted from national TB and HIV programme records. Of 42,585 presumptive TB patients, 28,964(68%) were tested for HIV and 2262(8%) were HIV positive. Of the latter, 377(17%) had active TB. Of 1885 'presumptive TB patients without active TB', 1100(58%) were already receiving ART. Of the remaining 789 who were not receiving ART, 617(79%) were assessed for ART eligibility and of those, 548(89%) were eligible for ART. About 90% of 'HIV-infected presumptive TB patients without TB' were eligible for ART. This evidence supports a public health approach of starting all 'HIV-infected presumptive TB patients without TB' on ART irrespective of CD4 count in line with global thinking about 'test and treat'.

INTRODUCTION

With an estimated 36.9 million people living with HIV (PLHIV), 2.0 million new HIV infections and 1.2 million deaths in 2014, HIV continues to be the most common infectious cause of mortality in the world and has claimed more than 34 million lives so far.[1] Anti-retroviral treatment (ART) is life-saving for PLHIV and, by the end of March 2015, about 15 million PLHIV were receiving ART. HIV is the only infectious disease where treatment is initiated only after it becomes clinically severe (assessed using CD4 counts). There have been various reasons for this strategy which include prioritizing toxic drugs for those with highest risk of progressing to AIDS, concerns about non-adherence and risk of drug resistance if treatment is started too early. However, this situation is fast changing with the availability of newer and safer antiretroviral medicines and the evidence that early ART is beneficial even in asymptomatic PLHIV.[2, 3]

WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS) have both embarked on an ambitious vision of "90-90-90": to detect 90% of all HIV infected patients in the community, treat 90% of those detected with antiretroviral therapy (ART) and achieve viral suppression in 90% of those treated.[4] Given this, there is an increased demand from civil society organizations and patient groups to move towards a 'test and treat' strategy. WHO in 2013 raised the threshold for ART initiation to a CD4 count ≤ 500 cells/uL in adults, adolescents and children aged five years and above. For certain patient groups like PLHIV having active TB disease, hepatitis B virus infection with severe chronic liver disease, pregnant and breast feeding women, children aged under five years, and those living in a sero-discordant relationship, ART is recommended irrespective of CD4 count (akin to a 'test and treat' strategy) (**Table 1**).[5] Another such subgroup which has caught global attention is 'presumptive TB patients' (previously called TB suspects and defined as people with cough for two weeks or more with or without other symptoms suggestive of TB), but without TB.

Several studies from sub-Saharan African countries and Asia, show a high HIV prevalence among patients with presumptive TB ranging from 10%-64%, sometimes even higher than the HIV prevalence among TB patients prompting WHO to recommend routine HIV testing in such patients.[6-14] A prospective study from Zimbabwe showed that HIV-infected presumptive TB patients are a neglected group with only 15% getting ART, while about 85% had CD4 cell counts < 350 cells/uL and were eligible for ART at the time.[4] However, no study has systematically assessed this aspect in India.

Hence, in this study, we aim to determine the number of HIV-infected presumptive TB patients eligible for ART in a large south Indian state of Karnataka. The specific objectives were to determine among a cohort of presumptive TB patients (stratified by whether they have TB or not) attending the microscopy centres of Karnataka in May 2015,

1. Number (proportion) ascertained for HIV status and found HIV positive
2. Among HIV-infected patients,
    a. number assessed for ART eligibility and found ART eligible
    b. number (proportion) initiated on ART

MATERIALS AND METHODS

STUDY DESIGN

This was a cross-sectional study involving secondary analysis of data routinely recorded under the Revised National TB Control Programme (RNTCP) and National AIDS Control Programme (NACP).

SETTING

India is considered a country with a concentrated HIV epidemic and contributes to about 10% of the global burden in absolute terms.[1] The HIV epidemic in India is showing a declining trend and in 2011, about 2.1 million people were living with HIV in India with an estimated 0.12 million new infections and 0.15 million deaths.[15]

Karnataka state has an estimated 0.21 million people living with HIV in 2011 and accounts for about 10% of country's HIV burden.[15] Hence, the state has been classified as 'high priority' for HIV interventions by the National AIDS Control Organization (NACO) in India on the basis of consistently high HIV sero-prevalence rates of >1% during sentinel surveillance at antenatal clinics.[16, 17] In the state, tuberculosis control programme services are available through a decentralized network of peripheral health institutions which provide general health services including diagnosis and treatment for TB.

Patients with presumptive TB are identified at the peripheral health institutions and referred for sputum smear microscopy to Designated Microscopy Centres (DMCs), which are geographically distributed, each covering a population of 0.05 to 0.1 million. In situations where the patient is unable to physically visit the DMC, the sputum is collected and transported using existing systems and health care workers in the general health system or non-governmental organizations. The diagnosis of TB is made in accordance with national guidelines. Presumptive TB patients are first tested using sputum smear microscopy and if found to be positive for acid-fast bacilli, patients are diagnosed as 'smear-positive pulmonary TB' and initiated on treatment. Patient with negative smears are given antibiotics for a 7-10 days and are tested for smear microscopy again if symptoms persist. If smears are negative in repeat sputum microscopy, patient undergoes chest radiography. A diagnosis of smear-negative pulmonary TB is made if lesions consistent with TB are found on chest radiograph. Patients with a normal chest x-ray and/or whose symptoms were subsided by the trial of antibiotics were categorized as 'presumptive TB without TB'. All diagnosed TB patients are treated with standardized fully intermittent thrice-weekly short-course regimens (6-9 months) administered under direct observation. Such patients are registered at one of the 177 sub-district level TB programme management units according to Indian programme guidelines. [18]

As per national policy, HIV status is routinely ascertained for all presumptive TB patients, and HIV-infected TB patients are referred to Anti-Retroviral Treatment (ART) centres for initiation on ART and Cotrimoxazole Preventive Therapy (CPT).[19] HIV status is ascertained

at 'integrated counselling and HIV testing centres' (ICTC) spread throughout the state, which are usually co-located with sputum microscopy services. HIV is diagnosed based on three positive rapid tests as per national guidelines.[20] Free ART is provided through a network of 64 ART centres (with at-least one ART centre in every district), where HIV-infected patients (including TB patients) are offered treatment and care. There are 194 Link-ART centres in the state which offer follow-up services at decentralized locations for HIV patients who are clinically stable on ART. These service delivery sites under NACP follow the national guidelines for counselling, testing, care and treatment of HIV-infected patients. [21] In line with the higher burden of HIV, there is a higher density of HIV testing and care centres in the northern parts of the state.[22]

STUDY POPULATION AND STUDY PERIOD

All patients with presumptive TB examined for diagnostic smear microscopy at the DMCs of Karnataka state in May 2015 constituted the study population. Patients attending for 'Re-examination' and follow-up examination were not included.

DATA COLLECTION PROCEDURE AND DATA VARIABLES

For objective 1, we collected aggregate data on number of presumptive TB patients examined for smear microscopy, number tested for HIV and number HIV positive. For the HIV-infected presumptive TB patients, individual patient data was collected using a structured, pre-tested data collection proforma. The data variables included laboratory number, age, sex, TB diagnosis (smear positive TB / smear negative TB / extra-pulmonary / No TB), TB treatment (Yes/No), WHO clinical staging, latest CD4 lymphocyte count (at the time of registration for newly detected HIV patients or latest available count for patients already receiving ART), ART status (Already on ART before visiting DMC/started on ART after DMC visit/Not started on ART). These variables were extracted from the TB laboratory register and TB treatment register of RNTCP and pre-ART patient register, patient ART card and HIV-TB register of NACP. Information on whether the patient is diagnosed as smear-negative TB or extra-pulmonary TB was extracted by referring to the TB register.

Data was collected by the 'district PMDT/TBHIV co-ordinators' working for RNTCP and trained in the study protocol under the supervision of WHO consultants and state-level government programme officers working for the TB and HIV programmes.

DATA ENTRY AND ANALYSIS

Aggregate information from each district was collected using an Excel format. For capture of patient-wise data, we used a combination of three open access sources (EpiData for data entry, Dropbox for sharing data and TeamViewer for trouble-shooting remotely). The technique has been detailed elsewhere.[23] Data entry was done by the data entry operators of the respective districts, trained for the purpose. Double data entry, validation and analysis was done using EpiData software (version 3.1 for entry and version 2.2.2.182 for analysis, EpiData Association,

Odense, Denmark). ART eligibility was assessed using WHO-2013 ART guidelines (CD4 count of <500, WHO clinical staging 3 and 4, children under the age of 5, all HIV-TB patients) as the NACP in India has agreed in principle to adopt the recommendations.[24, 25] In addition, if a patient was documented as 'ART eligible' in the records and started on ART (even though there was no full documentation of CD4 counts and/or WHO clinical staging), we considered such patients to be eligible for ART for this analysis.

ETHICS

Administrative approval to conduct the study and access the data was obtained from the State Tuberculosis Cell of Government of Karnataka. Ethics approval was obtained by the Ethics Advisory Group of International Union Against Tuberculosis and Lung Disease, Paris, France. Since the study involved a secondary analysis of routine programme records, the need for individual patient consent was waived by the ethics committee.

RESULTS

A total of 42,585 presumptive TB patients underwent sputum smear microscopy in 680 DMCs of 31 districts of Karnataka State, of whom 28,964 (68%) were ascertained for HIV status and 2262(8%) were found to be HIV positive. (**Figure 1**) The median (interquartile range, IQR) age of HIV-infected patients was 38 (30-45) years and about half of them were males.

TB DIAGNOSIS, TB TREATMENT AND ART

Of 2262 HIV-infected presumptive TB patients, 377(17%) were diagnosed to have active TB and of them, 370(98%) were initiated on TB treatment. Of 377 TB patients, 194(52%) had smear positive pulmonary TB, 122(32%) had smear negative pulmonary TB and 61(16%) had extra-pulmonary TB. Of the TB patients, 210 (57%) were receiving ART prior to TB diagnosis. Of the remaining 167, 122(73%) were started on ART after TB diagnosis. Thus, a total of 332 (88%) were receiving ART during TB treatment.

PRESUMPTIVE TB PATIENTS WITHOUT ACTIVE TB: ART ELIGIBILITY AND ART INITIATION

Among the 1885 'presumptive TB patients without active TB', 1100(58%) were already receiving ART prior to the current visit. Among the remaining 789 who were not receiving ART, 617 (79%) were assessed for ART eligibility and among them, 548 (89%) were found to be ART eligible as per WHO 2013 ART guidelines. Patients who were assessed for ART eligibility were similar to those not assessed by age (median age 39 and 40 years respectively, p=0.95) and sex (proportion male 49% and 51% respectively, p=0.54). The CD4 distribution and WHO clinical staging information of 548 patients who were found to be eligible for ART is shown in **Table 2**. Of those found to be ART eligible, 405 (74%) were initiated on ART. (**Figure 1**)

MEDIAN CD4 COUNTS

Of 2262 patients, 1998 (88%) had information on CD4 counts. The median (IQR) CD4 count among patients with active TB was 194 (100-333) as compared to 264 (123-438) among 'presumptive TB patients without active TB' (p <0.001). Among those without active TB, median (IQR) CD4 count was significantly higher (p<0.001) among those receiving ART at 281 (147-450) cells / uL as compared to those not on ART at 226 (92-399) cells / uL.

DISCUSSION

These findings confirm our hypothesis and showed that nine out of ten HIV-infected presumptive TB patients (without TB) are eligible for ART as per current WHO guidelines. This too is an underestimate as we did not assess all the criteria of ART eligibility in our study. For example, we did not have any information about whether the patients in our study had co-existing Hepatitis-B infection with severe liver disease or if they were pregnant or if they were living in a sero-discordant relationship. Some studies have indicated that nearly 75% of PLHIV in India are sero-discordant.[26, 27] If we apply this figure to our cohort, then nearly all HIV-infected presumptive TB patients would be eligible for ART. Hence, as a public health approach to ART initiation, there is a strong case to be made for recommending that all HIV-infected presumptive TB patients should be initiated on ART irrespective of CD4 count.

There are a number of advantages with adoption of this recommendation. First, this is likely to improve uptake of ART (possibly by removing barriers associated with CD4 testing) in this vulnerable group. We have observed this in the past with HIV-infected TB patients when after adopting a 'test and treat' strategy for TB patients, there was a significant increase in uptake of ART. The proportion of HIV-infected TB patients receiving ART in India increased from 41% in 2008 to 91% in 2014.[22] This is observed in our study sample too – nearly 90% of HIV-infected TB patients received ART as compared to only 74% among those without TB. Despite high uptake of ART among HIV-TB patients in India, mortality remains high at 13% emphasizing the need for early diagnosis and ART initiation.[22]

Second, this is likely to lead to early diagnosis and treatment of HIV, thus preventing avoidable mortality, morbidity and improving the quality of life in the long term. HIV testing among presumptive TB patients implies moving the HIV testing intervention to an upstream level in the TB diagnostic pathway and hence, patients are diagnosed earlier on in the natural course of disease. This is substantiated by higher median CD4 counts in our study, among presumptive TB patients (without TB) as compared to those with active TB. If active TB can be confidently ruled out using more sensitive diagnostic tools such as Xpert MTB/RIF or mycobacterial culture, such patients could be potentially eligible for isoniazid preventive therapy, which is known to act synergistically with ART in preventing TB. A recent randomized controlled trial has shown that early ART along with IPT is likely to provide maximum benefit to PLHIV in terms of preventing mortality and morbidity including TB.[2] It is essential to rule out active TB confidently before starting ART as not doing so might pose a higher risk of developing immune reconstitution inflammatory syndrome.

Third, starting these patients earlier on ART is likely to improve their immune status. As observed in our study, the median CD4 counts were higher among 'HIV-infected presumptive TB patients without active TB' already receiving ART prior to the current visit as compared to those who were not on ART. A previous study from Zimbabwe showed that not starting these patients on ART led to high mortality and morbidity.[4] In addition to individual benefits, early ART is also likely to have public health benefits – ART reduces the risk of transmission of HIV to partners[28] and avoids the operational problem of poor retention in pre-ART care.[29, 30]

Fourth, as only about 10% of presumptive TB patients were not eligible as per current guidelines, adopting this strategy is not likely to place a large additional burden on the national ART programme in India. From a public health perspective, this is a step towards 'immediate and universal ART' for every person with HIV in line with the vision of NACP phase-IV for the period 2012-17. [24]

Our study had several strengths. This is the first study from India examining the issue of ART eligibility among HIV-infected presumptive TB patients. Since the data come from a large and comprehensive sample of patients in a large state in India, the results are likely to reflect ground realities and are generalizable to similar high-HIV settings in India. However, we need more evidence, especially from low-HIV settings in India before a national policy decision can be considered. We used an innovative method of quality-assured data capture and this model is likely to be useful in co-ordinating data collection in multicentre research studies in resource-constrained settings.

There were a few limitations mainly related to our reliance on data collected routinely by the national TB and HIV programmes. However, we think this is not a major limitation as both TB and HIV programmes in the state of Karnataka are well supervised and monitored and hence the quality of data is likely to be high. Information on ART eligibility (CD4 counts and/or WHO clinical staging) was missing in about one-fifth of the patients. Since those assessed for ART eligibility were similar to those not assessed by age and sex, we think the results can be extrapolated to those not assessed for ART eligibility. We did not have any information on presumptive extra-pulmonary TB patients in our study and this should be a topic of future research. Although our recommendations are justified as a public health approach, it is important to study the long-term outcomes among the subgroup of patients with CD4 count of >500/mm^3 and assess if they actually benefit by early initiation of ART. We however think early ART will be beneficial based on the evidence of two randomized controlled trials which have confirmed the benefit of early ART in preventing death and/or AIDS related events.[2, 3] These trials have also confirmed that there was no or minimal increase in adverse events due to early ART initiation, thus allaying any fears that early ART initiation could be detrimental.

Finally, as the adage goes, 'what gets monitored gets done'. Hence we need to think about ways of monitoring the ART uptake among HIV-infected presumptive TB patients. We propose the addition of an extra column in the existing TB laboratory register to capture ART

initiation status. From this, two indicators can be calculated: 1) Proportion of presumptive TB patients ascertained for HIV 2) Proportion of HIV-infected presumptive TB patients receiving ART. These indicators could then be compiled and reported in the quarterly reports of the TB programme from the peripheral level to district to state to national levels, finally finding a place in global TB and HIV reports. Future operational research should test this and/or other models of recording and reporting to find out the most optimal way forward.

CONCLUSION

In conclusion, about 90% of 'HIV-infected presumptive TB patients without active TB' were eligible for ART as per WHO-2013 guidelines. As a public health approach, 'HIV-infected presumptive TB patients without TB' is a vulnerable subgroup qualifying for 'test and treat' strategy akin to HIV-infected TB patients.

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CONFLICTS OF INTEREST:

None declared

REFERENCES

1. UNAIDS. How AIDS changed everything. MDG6: 15 Years, 15 lessons of hope from the AIDS response.: Joint United Nations Programme on HIV/AIDS, Geneva, Switzerland; 2015 [cited 2015 19th September]. Available from: http://www.unaids.org/sites/default/files/media_asset/MDG6Report_en.pdf.
2. Group TAS, Danel C, Moh R, Gabillard D, Badje A, Le Carrou J, et al. A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa. N Engl J Med. 2015;373(9):808-22.
3. Group ISS, Lundgren JD, Babiker AG, Gordin F, Emery S, Grund B, et al. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. N Engl J Med. 2015;373(9):795-807.
4. Joint United Nations Programme on HIV/AIDS. An ambitious treatment target to help end the AIDS epidemic Geneva, Switzerland 2014. Available from: http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf.
5. World Health Organization. Consolidated guidelines for the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. June 2013: World Health Organization, Geneva, Switzerland; 2013 [updated 2013/07/03/]. Available from: http://www.who.int/hiv/pub/guidelines/arv2013/download/en/index.html.
6. Srikantiah P, Lin R, Walusimbi M, Okwera A, Luzze H, Whalen CC, et al. Elevated HIV seroprevalence and risk behavious among Ugandan TB suspects: implications for HIV testing and prevention. Int J Tuberc Lung Dis. 2007;11:168-74.
7. Deribew A, Negussu N, Kassahun W, Apers L, Colebunders R. Uptake of provider-initiated counselling and testing among tuberculosis suspects, Ethiopia. Int J Tuberc Lung Dis. 2010;14:1442-6.
8. Porskrog A, Bjerregaard-Andersen M, Oliveira I, Joaquím LC, Camara C, Andersen PL, et al. Enhanced tuberculosis identification through 1-month follow-up of smear-negative tuberculosis suspects. Int J Tuberc Lung Dis. 2011;15:459-64.
9. Odhiambo J, Kizito W, Njoroge A, Wambua N, Nganga L, Mburu M, et al. Provider-initiated HIV testing and counselling for TB patients and suspects in Nairobi, Kenya. Int J Tuberc Lung Dis. 2008;12(suppl 1):S63-S8.
10. Munthali L, Mwaungulu JN, Munthali K, Bowie C, Crampin AC. Using tuberculosis suspects to identify patients eligible for antiretroviral treatment. Int J Tuberc Lung Dis. 2006;10:199-202.
11. Dimairo M, Macpherson P, Bandason T, Zezai A, Munyati SS, Butterworth AE, et al. The risk and timing of tuberculosis diagnosed in smear-negative TB suspects: a 12 month cohort study in Harare, Zimbabwe. PLoS ONE. 2010;5(7): e11849:doi:10.1371/journal.pone.0011849.
12. Adjei AA, Adiku TK, Ayeh-Kumi PF, Hesse IFA. Prevalence of human immunodeficiency virus infection among tuberculosis suspect patients in Accra, Ghana. West Afr J Med. 2006;25:38-41.
13. Naik B, Kumar AMV, Lal K, Doddamani S, Krishnappa M, Inamdar V, et al. HIV prevalence among persons suspected of tuberculosis: policy implications for India. J Acquir Immune Defic Syndr. 2012;59:e72-e6.

14. Achanta S, Kumar AMV, Burugina Nagaraja S, Jaju J, Motta Shamrao SR, Uappaluri R, et al. Feasibility and effectiveness of provider initiated HIV testing and counseling of TB suspects in Vizianagaram district, South India. PLoS ONE. 2012;7(7): e41378:doi:10.1371/journal.pone.0041378.
15. National AIDS Control Organization, National Institute of Medical Statistics. Technical Report India HIV Estimates-2012: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2013 [cited 2015 23rd September]. Available from: http://www.naco.gov.in/upload/Surveillance/Reports%20&%20Publication/Technical%20Report%20-%20India%20HIV%20Estimates%202012.pdf.
16. Ofice of the Registrar General and Census Commissioner. Provisional Population Totals paper-1 : 2011 – Karnataka New Delhi: Government of India; 2011 [cited 2011 9th May]. Available from: http://censusindia.gov.in/2011-prov-results/prov_data_products_karnatka.html.
17. National AIDS Control Organization. HIV Sentinel Surveillance and HIV Estimation, 2007, A technical brief: Ministry of Health and Family Welfare, Government of India; 2008 [cited 2015 23rd September]. Available from: http://naco.gov.in/upload/Surveillance/Reports%20&%20Publication/HIV%20Sentinel%20Surveillance%20and%20HIV%20Estimation%202007_A%20Technical%20Brief.pdf.
18. Central TB Division. Managing the RNTCP in your area - A Training course (module1-4): Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2005 [updated 2012/08/12/; cited 2015 17th September]. Available from: http://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4262&lid=2906.
19. National AIDS Control Organization, Central TB Division. National framework for Joint HIV/TB collaborative activities: Ministry of Health and Family Welfare, Government of India; 2009 [cited 2015 23rd September]. Available from: http://tbcindia.gov.in/showfile.php?lid=2857.
20. National AIDS Control Organization. Guidelines for HIV Testing: Ministry of Health and Family Welfare, Government of India; 2007 [cited 2015 23rd September]. Available from: http://www.naco.gov.in/NACO/Quick_Links/Publication/Blood_Safety__Lab_Services/Operational__Technical_guidelines_and_policies/Guidelines_for_HIV_test/.
21. National AIDS Control Organization. Operational Guidelines for Integrated Counselling and Testing Centres: Ministry of Health and Family Welfare, Government of India; 2008 [cited 2015 23rd September]. Available from: http://www.naco.gov.in/NACO/Quick_Links/Publication/Basic_Services/Operational__Technical_guidelines_and_policies/Operational_Guidelines_for_Integrated_Counseling_and_Testing_Centres/.
22. Central TB Division. TB India 2015. Revised National TB Control Programme Annual Status Report: Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2015 [updated 2015/09/17/; cited 2015 17th September]. Available from: http://tbcindia.gov.in/showfile.php?lid=3166.
23. Kumar AMV, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, et al. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. Public Health Action. 2013;3:60-2.
24. National AIDS Control Organization. Shri Ghulam Nabi Azad launches National AIDS Control Programme-Phase IV: Directorate General of Health Services, Ministry of Health and Family Welfare,

Government of India; 2014 [cited 2015 23rd September]. Available from: http://pib.nic.in/newsite/PrintRelease.aspx?relid=103593.

25. Dodderi SK, Kumar AM, Naik BR, Kanchar A, B BR, Harries AD. How many people living with HIV will be additionally eligible for antiretroviral treatment in Karnataka State, India as per the World Health Organization 2013 guidelines? PLoS One. 2014;9(9):e107136.
26. Saggurti N, Schensul SL, Verma RK. Migration, mobility and sexual risk behavior in Mumbai, India: mobile men with non-residential wife show increased risk. AIDS and behavior. 2009;13(5):921-7.
27. Arora P, Nagelkerke N, Sgaier SK, Kumar R, Dhingra N, Jha P. HIV, HSV-2 and syphilis among married couples in India: patterns of discordance and concordance. Sexually transmitted infections. 2011;87(6):516-20.
28. Grinsztejn B, Hosseinipour MC, Ribaudo HJ, Swindells S, Eron J, Chen YQ, et al. Effects of early versus delayed initiation of antiretroviral treatment on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. Lancet Infect Dis. 2014;14(4):281-90.
29. Geng EH, Bwana MB, Muyindike W, Glidden DV, Bangsberg DR, Neilands TB, et al. Failure to initiate antiretroviral therapy, loss to follow-up and mortality among HIV-infected patients during the pre-ART period in Uganda. J Acquir Immune Defic Syndr. 2013;63(2):e64-71.
30. Ganga Devi NP, Ajay KM, Palanivel C, Sahu S, Selvaraj M, Valan A, et al. Implementation and Operational Research: High Loss to Follow-up Among Children on Pre-ART Care Under National AIDS Program in Madurai, South India. J Acquir Immune Defic Syndr. 2015;69(3):e109-14.

Table 1: Comparison of WHO guidelines for ART initiation among people living with HIV in the year 2010 and 2013.

Population	Target Population	2010 ART guidelines	2013 ART guidelines
Adults and adolescents	HIV infected individuals	CD4 count ≤350 cells/mm³ or WHO clinical stage 3 or 4 regardless of CD4 cell count	CD4 count ≤ 500 cells/mm³ or WHO clinical stage 3 or 4 regardless of CD4 cell count
	HIV infected pregnant and breastfeeding women	CD4 count ≤350 cells/mm³ regardless of clinical symptoms or WHO clinical stage 3 or 4 regardless of CD4 cell count	Regardless of CD4 cell count or WHO clinical stage
	HIV infected partners in serodiscordant couple relationship(s)	No recommendation established	
	HIV/TB co-infection HIV/HBV co-infection	Presence of active TB disease, regardless of CD4 cell count Evidence of chronic active HBV disease, regardless of CD4 cell count	No change Evidence of chronic HBV disease with advanced stage liver disease (e.g. cirrhosis), regardless of CD4 cell count
Children	HIV infected children ≥5 years old	CD4 ≤350 cells/mm³ or WHO clinical stage 3 or 4 regardless of CD4 cell count	CD4 count ≤500 cells/mm³ or WHO clinical stage 3 or 4 regardless of CD4 cell count
	HIV infected children 1–5 years old	1. Between 12 and 24 months of age, regardless of CD4 count or WHO clinical stage. 2. Between 24 and 59 months of age with CD4 count of ≤750 cells/ mm3 or CD4% ≤25, or whichever is lower, regardless of WHO clinical stage.	Regardless of CD4 cell count and clinical stage
	HIV infected infants <1 year old	All infants, regardless of CD4 cell count and clinical stage	No change

WHO-World Health Organization; ART-antiretroviral therapy; HIV-Human immunodeficiency virus; TB – Tuberculosis; HBV – Hepatitis B Virus.

Table 2: CD4 counts and WHO clinical staging of 'HIV-infected presumptive TB patients without TB' eligible for ART in May 2015, Karnataka State, India.

	WHO Clinical staging					
Baseline CD4 count [cells / uL]	**Stage 1** N (%)	**Stage 2** N (%)	**Stage 3** N (%)	**Stage 4** N (%)	**Unknown** N (%)	**Total** N (%)
<50	15 (7)	19 (10)	17 (22)	9 (60)	24 (50)	84 (15)
50-200	68 (32)	86 (44)	34 (45)	5 (33)	8 (17)	201 (37)
201-350	67 (31)	52 (27)	13 (17)	1 (7)	7 (15)	140 (26)
351-500	47 (22)	24 (12)	7 (9)	0 (0)	8 (17)	86 (16)
501 and above	14 (7)*	13 (7)*	3 (4)	0 (0)	0 (0)	30 (5)
Unknown	3 (1)*	1 (1)*	2 (3)	0 (0)	1 (2)*	7 (1)
Total	214	195	76	15	48	548

* These patients (n=32) were documented as 'ART eligible' in the programme records and started on ART even though the CD4/WHO staging criteria were either not documented or did not match eligibility criteria. They were considered 'ART eligible' for the purpose of this analysis.

WHO-World Health Organization; ART-antiretroviral therapy; HIV-Human immunodeficiency virus;

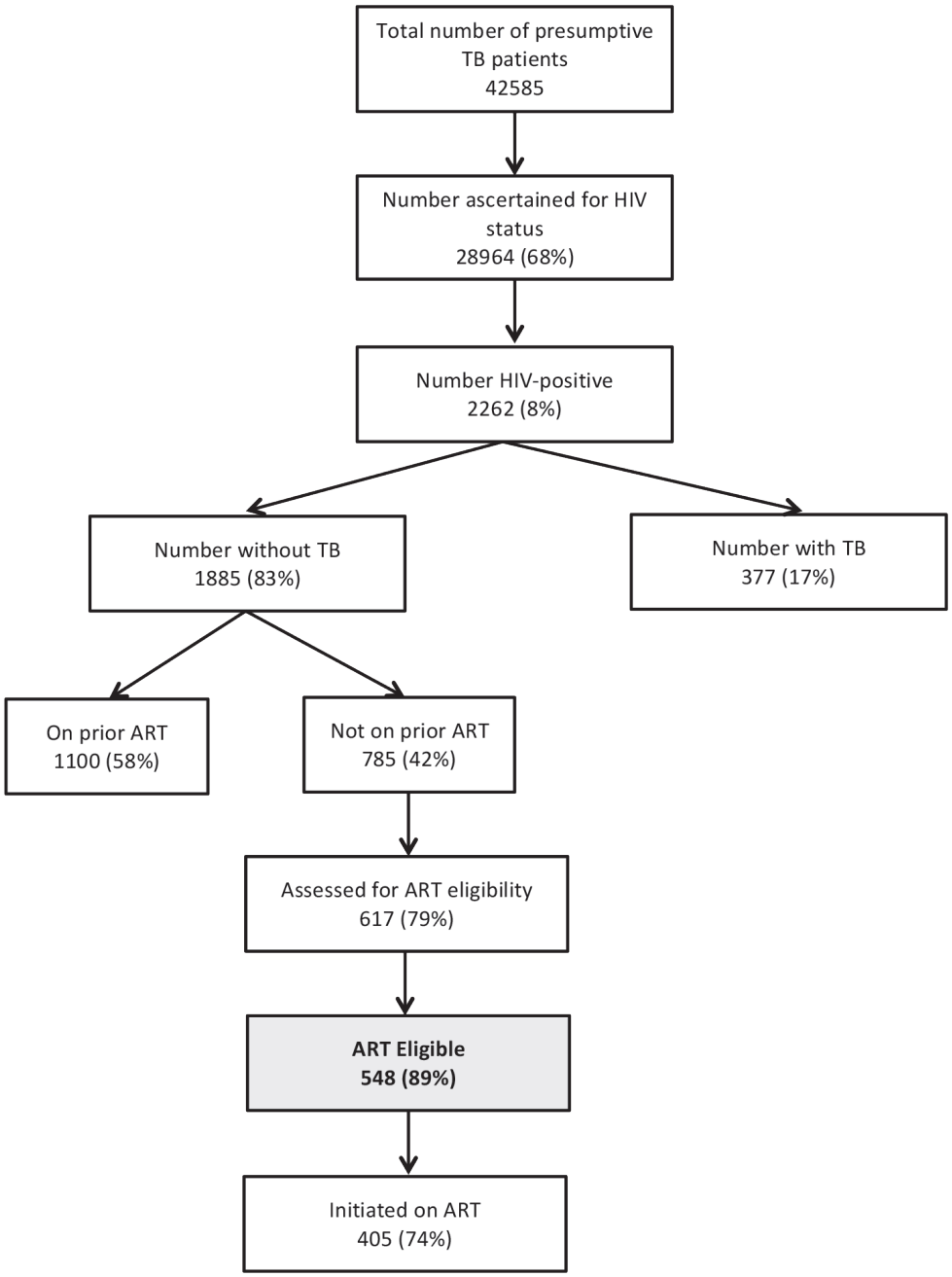

Figure 1. ART eligibility among HIV-infected presumptive TB patients in Karnataka, India, 2015
TB-Tuberculosis; ART-Antiretroviral therapy; HIV-Human Immunodeficiency Virus; On prior ART-Person who was receiving ART prior to the current visit to sputum microscopy centre (TB Clinic);

9.

Does research through Structured Operational Research and Training (SORT IT) Courses impact policy and practice?

Kumar AMV, Shewade HD, Tripathy JP, Guillerm N, Tayler-Smith K, Berger SD, Bissell K, Reid AJ, Zachariah R, Harries AD.
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Setting

'Structured Operational Research and Training Initiative'(SORT IT) courses are well-known for their outputs – nearly 90% participants complete the course and publish in scientific journals.

Objective

We assessed the impact of research papers on policy/practice that resulted from six SORT IT courses initiated between July 2012 and March 2013.

Design

A cross-sectional study involving email-based, self-administered questionnaires and telephone/skype/in-person responses from first and/or senior co-authors of course papers; a descriptive content analysis of responses was performed and categorized into themes.

Results

Of 72 participants, 63(88%) completed the course and course outputs included 81 submitted papers, of which 76(94%) were published. Of the 81 papers assessed, 45(55%) contributed to a change in policy and/or practice: these included 29 contributing to government policy/practice change (20 at national, four at sub-national and five at hospital level), 11 to non-government organizational policy change and five reinforcing existing policy. The changes ranged from modifications to monitoring and evaluation tools to redrafting of national guidelines to scaling-up existing policies.

Conclusion

Over half of SORT IT course papers contributed to a change in policy and/or practice. Future assessments should include more robust and independent verification of the reported change(s) with all stakeholders to improve their rigour/richness.

INTRODUCTION

A vital element to assess the success of operational research (OR) is to measure its impact on policy and/or practice.[1] The International Union Against Tuberculosis and Lung Disease (The Union) and Médecins sans Frontières (MSF) have developed a training model in operational research that is well-known for its outputs – nearly 90% of participants successfully complete the course and publish in peer-reviewed journals.[2] Both The Union and MSF are members of the 'Structured Operational Research and Training Initiative' (SORT IT), a global partnership led by the Special Programme for Research and Training in Tropical Diseases (TDR) at the World Health Organization (WHO). The Union/MSF courses are accredited as SORT IT courses.

Two follow-up studies published in 2014 assessed the impact of SORT IT - 74% of course papers contributed to changes in policy and practice and participants from the first eight SORT IT courses continued to conduct and publish OR after the course.[3, 4] A limitation of the studies was that the follow-up period was variable, ranging from nine months to three years after course completion.[3] Since then, we have been more systematic and now contact participants eighteen months after course completion to assess the impact of their OR on policy and/or practice. In this paper, we describe the self-reported impact of SORT IT course papers on policy/practice.

METHODS

This was a cross-sectional mixed-methods study design with both quantitative and qualitative components. This involved email-based, self-administered questionnaires and telephone/ Skype/in-person responses from first and/or senior co-authors. The study population included all participants of six SORT IT courses started between July 2012 and March 2013 and first author and/or senior co-authors of viewpoints that were written in conjunction with the courses. These courses were run in Chennai-India (1), Paris-France (1), Luxembourg-Luxembourg (1), Addis Ababa-Ethiopia (1), Nadi-Fiji (1) and Kathmandu-Nepal (1).

The questionnaire was sent to course participants as part of routine follow-up, about 18 months after the course completion, between December 2014 and March 2015 with three months' time to respond as previously described.(3) A specific question asked whether their course-related research contributed to change in policy/practice. If the answer was 'Yes', participants were asked to provide the details and similarly, if the answer was 'No', participants were asked to provide the reasons. Where responses were unclear, the first author and/or one of the senior co-authors of the paper (who were mentors in the course) were contacted via email, telephone and/or skype communication and clarifications were obtained. The verbal responses over Skype/telephone/in-person were transcribed in an email and validated for their accuracy by respondents. This constituted validation of responses by the respondents.

In case of viewpoints led by course faculty, either the first author or one of the senior co-authors was contacted to find out if the work (usually shared between faculty

and participants) contributed to policy change. For every viewpoint, we (AK, RZ and ADH) debated if it had impacted policy and arrived at a consensus.

Claims of policy change were verified by referring to the policy documents or minutes of meetings available in the public domain or by contacting the first authors of the paper participants, wherever feasible.

DATA ENTRY AND ANALYSIS

Data were entered into an MS Excel file (Microsoft, Redmond, WA, USA) and a descriptive content analysis of responses was performed. The e-mail responses satisfied the criterion of 'low inference descriptors' as participants did their own transcribing and the responses were used directly for content analysis.[5] Content analysis was performed manually, given the small dataset, by three authors trained in qualitative research methods. The responses were classified into the following broad themes: change in government policy and/or practice (which is subdivided into national, sub-national and hospital level depending on the level of impact) and change in non-government organizational policy and/or practice (when decisions were made by non-governmental organizations like MSF or The Union).[4] The categorization of responses into themes was done by three authors (AK, HS, JP) together for enhancing interpretive credibility. Any disagreement between the three authors was resolved by consensus after consultation with two senior authors (ADH and RZ). A conservative stance was adopted in assessments – whenever there was doubt, the study was deemed not to have impacted policy/practice. The Ethics Advisory Group of The International Union Against Tuberculosis and Lung Disease, Paris, France, determined that neither ethics clearance nor participant informed consent were required for this type of study.

RESULTS AND DISCUSSION

There were 72 (31 female) participants enrolled in the six courses, of whom 63 (88%) successfully completed the course and submitted one or more papers to a scientific journal. Selected participants came from 36 countries (34 in Asia with 20 from India, 24 in Africa, 12 in the South Pacific and one each from Latin America and Europe). The majority of the participants were medical doctors (48) followed by research officers (6), nurses (3) and other paramedical staff including M&E officers (6). Most were working for government (28) followed by non-governmental organizations (24), academia (10) and donors (1).

OUTPUTS: PUBLICATIONS AND IMPACT ON POLICY/PRACTICE

A total of 81 papers (including nine viewpoints) were submitted for publication, of which 76 (94%) were published by June 30, 2015. The topics covered included tuberculosis (47%), HIV (15%), non-communicable diseases (10%), operational research (10%), maternal and child health (7%) and others (tobacco control, neglected tropical diseases, health system issues). All the 72 research papers were led by the course participants of which 67(93%) were published. This is in line with the previously published reports of high publication outputs

and might be related to strict selection criteria, adherence to timelines and milestones coupled with strong hands-on mentorship offered by the programme faculty.[3,4,6] Of the nine viewpoints, two were led by course participants, one by a former SORT IT participant and current faculty, one by the course administrator and the rest were led by the course faculty and all were published. Very few capacity-building programmes track for outputs, although this is fast changing[7], and SORT IT creates a benchmark in this area.[8]

All study participants responded and of the 81 papers which were assessed, 45(55%) reported to have contributed to a change in policy and/or practice (**Figure**). This is encouraging and can be attributed to several factors including policy-relevance of the research question which was often based on constraints faced by the programmes, engagement of policy makers as co-investigators, ownership of results especially when programme managers were principal investigators of the research project and other windows of opportunity available to individual researchers by virtue of them being in national/state level committees.

However, the outputs are relatively fewer than reported in the previous study which reported nearly three-fourths of the studies having impacted policy.4 We speculate three reasons: 1) increased rigour and conservative stance in our assessments; 2) change in denominator – we used 'all submitted papers' as the denominator in this study as compared to only 'published studies' in the previous assessment. This amendment was made in order to mirror the SORT IT course targets and our belief that policy change can happen even without/before publication; and 3) Varied profile of course participants – a lower proportion of course participants tended to be senior people (including decision makers and national programme managers) in the current cohort as compared to previous cohorts, hence less likely to act on the research findings.

Of the 45 papers having an impact, 29 contributed to a change in government policy or practice (20 at national level, four at sub-national level and five at hospital level),[11] contributed to a change in non-governmental organizational policy or practice and five added additional evidence to existing policies and helped to make national scale-up decisions. The changes ranged from taking new policy decisions to redrafting of national technical and operational guidelines to scaling-up existing policies to changes in recording and reporting leading to improved programme monitoring. Some projects had a policy impact even before publication, possibly indicating the ownership of results by the policy makers engaged as part of the study.

CHANGES IN GOVERNMENT POLICY/PRACTICE

CHANGES IN NATIONAL POLICY/PRACTICE

Three papers from the India SORT IT course generated evidence to support shifting from two sputum samples to one sputum sample during follow-up sputum microscopy among drug-sensitive TB patients.[9-11] To quote the participant from India,

> *"Yes, there has been a national policy change to switch to one specimen from two specimens during follow-up sputum microscopy"*

This was verified by referring to the policy documents and government orders issued by the National TB Programme in India.

Two participants from India[12,13] mentioned change in national guidelines for screening malnourished children for TB,

> *"Yes. The new Strategy document being published for elimination of TB 2020, has taken in to account the screening of all undernourished children in NRCs [Nutritional Rehabilitation Centres]"*

A participant from Mongolia reported that her research led to redrafting of national guidelines for MDR-TB.[14]

CHANGES IN SUBNATIONAL POLICY/PRACTICE CHANGE

Some studies contributed to improvements in record keeping, leading to improved programme implementation at the district level. A participant from Gazeera State in Sudan reported that her study led to modification of monitoring and evaluation tools, including introduction of some new variables in the Asthma card and register, and regular monitoring for completeness of record keeping.[15] A study from Sri Lanka led to the creation of a mid-level programme officer post at sub-district level.[16]

CHANGE IN HOSPITAL LEVEL POLICY/PRACTICE

There were several instances of change in policy at the level of the hospital or institution. A study from China led to prolongation of the treatment of TB patients with co-existing diabetes mellitus in their hospital.[17] In a tertiary hospital in Kenya, management decided to improve care of tuberculosis among health workers by providing dedicated space for treatment, access to new diagnostics and more budgetary allocation for care.[18]

In another experience from Rwanda,[19] the participant mentioned,

> *"A few things that we learned from this evaluation have impacted our newest offering [of research workshops]: 1) Clinical staff were less likely to complete, we believe due to difficulties leaving clinical duties if in the middle of consultations/procedures. Solution - we developed online modules to complement the course. Individuals who missed could make up sessions (up to two out of the 10) using these online modules. 2) Few women enrolled, and were less likely to complete. Solution - we allocated 50% of training slots for women, and online modules added flexibility for their competing demands. 3) Assessment targets were not set. The course was changed to require that participants had an average of 80%+ on all assessments to graduate."*

CHANGE IN NON–GOVERNMENT ORGANIZATIONAL POLICY/PRACTICE

A study from Somalia by MSF on telemedicine led to changes in organizational policy for its wider application in MSF-assisted health care facilities in rural Kenya and Syria.[20] A participant from Ukraine referring to her study[21] reported,

> *"..This research has shown relatively low levels of HIV testing and re-testing among most at-risk populations. A new testing mechanism called "Self-assisted testing" was developed and introduced in 2015 by HIV/AIDS Alliance Ukraine."*

Viewpoints were also reported to have led to policy change – particularly at organizational level. A paper on open access publications led MSF to take an institutional stance.[22] As quoted by the lead author of the author in an email,

> *"MSF has taken an institutional position to support Open Access. Funds have been made available as part of routine country level budgets to cover open access costs. This applies for all SORT IT course publications and also those from routine operational projects."*

Another viewpoint helped in formalizing changes to the structure and content of SORT IT courses run by The Union and MSF.[23]

LACK OF POLICY CHANGE AND REASONS

Most participants (n=22) who reported 'no policy change' did not elaborate on the reasons. Those mentioned by a few participants (n=14) could be classified into the following themes: lack of priority by the national programmes and institutions, need for more time and more evidence for policy change, turnover of decision makers in the ministry and ineffective dissemination. One participant from the South Pacific region mentioned that his research was not policy-relevant and he did not expect any policy change to happen as a result. This underlines the importance of choosing the right research question from a policy perspective. A participant from China[24] mentioned,

> *"No, one reason is that maybe the voice did not reach out to those policy makers enough, another reason is that our policy makers have been focusing on setting up a new standard treatment procedure in the health insurance system which will regulate clinical practice and thus solve the problem brought out by my paper."*

Some course participants were conservative in their assessment as mentioned previously and mentioned a 'no' despite some evidence of impact. A participant from China quoted,[25]

> *"No, not sure about the direct effect on policy and/or practice… But being one of the first large cohort studies among the injection drug users who attended methadone maintenance programme (MMP) in China, our research added the strong and important evidence to the effectiveness of health education in the MMP."*

One participant from India attributed the lack of policy change to his inability to actively follow-up with the national programme,[26]

> *"No. Possible reasons: the findings of my research work were not perceived as a priority issue under the national programme. Other reason, I didn't pursue it further as I am not working directly with the programme."*

One of the viewpoints called for uniformity in referencing styles and in particular criticised PLoS journals and Tropical Medicine and International Health journal for their challenging reference styles in the paper.[27] Though the two journals have changed their referencing styles and aligned themselves with generic Vancouver style, the authors of the viewpoint were not sure if it was due to their paper. Hence they took a conservative stance and decided that their view point did not contribute to policy change.

STRENGTHS AND LIMITATIONS

This study is one of the few attempts to systematically track the effects of operational research on policy and practice.[4] We believe this type of follow up should be the way forward to minimize creation of 'research waste' (research that stops at publication and does not benefit the populations).[28,29] We also call upon journals and researchers to operationalize this process and track their publications for policy impact.[30] We had a 100% response rate and clarifications were sought whenever responses were ambiguous – thus achieving participant validation. Three authors did the content analysis and disagreements were resolved in consultation with two senior authors – this helped to minimize the subjectivity in assessments and to enhance interpretive credibility. An important limitation relates to self-reporting of impact by the authors of the papers. This is especially important in case of viewpoints led by course faculty who are also involved in assessing for policy impact in this paper. While we have tried to mitigate this by verifying official policy documents wherever possible and by adopting a conservative stance in our assessments, responder bias cannot be completely ruled out. It is also important to note that these assessments were for changes in policy and practice, and the further step of determining whether the changes improved the health of the population was not part of this study. Finally, we highlight two important challenges below which may be of use in future assessments.

CHALLENGES IN EVIDENCE–POLICY LINKAGE

While many of the SORT IT studies and viewpoints appear to have contributed to policy change, it was challenging to find documentary evidence linking the evidence to the policy decision. It is one of the limitations of self-reported data. A participant from Swaziland mentioned that the policy decision would have happened based on analysis of routine data irrespective of its publication in a journal, though the publication increased credibility of findings.[31] To quote the participant,

> *"This is a really an issue of how literally you expect respondents to take the question. If I answer the question as it was phrased, then the answer is no*

> *- it was not the study per se that led to policy change, but rather the use of routine data to feed the advocacy efforts of MSF and CHAI - this would have happened regardless of the study. However, it could be argued that the fact that we intended to write up the routine data analysis for publication, meant that we paid increased attention to data quality which made our analysis more reliable, thus improving our advocacy work. In that way, the study could be argued to have had policy impact. So, I guess you know what the question was trying to get at - if you feel that my answer constitutes a 'yes', then that is fine by me."*

In line with our conservative approach to assessment, we took this as 'no'. The response from a participant from Nepal, also highlighted the difficulty in attributing a link between evidence and challenge of evidence-policy change,[32]

> *"Yes - practice changed to screen all retreatment cases and expand Xpert… I am not sure it is because of the study and paper published but there is improvement in situation as it was recommended in the paper. The policy has been changed to screen all retreatment TB patients for MDR TB as much as possible and the Gene Xpert service has been expanded to more places."*

CHALLENGES RELATED TO VARIED INTERPRETATIONS

Different participants interpreted the question of impact differently leading to varied interpretations of the effects of their research on policy. Five participants responded that their studies provided additional evidence for existing policies which led to national scale-up decisions. One example was from India where the study provided additional evidence to scale-up existing policy - use of LED-FM [light emitting diode fluorescent microscopy] in high workload settings of India.[33] Another participant from Bangladesh mentioned,[34]

> *"Yes. It had a great effect on policy and practice. Bangladesh NTP [National Tuberculosis Programme] gave permission to extend the programme in a larger scale."*

In contrast, some participants interpreted that their study did not impact change in policy/practice even though it supported an existing change. For example, a participant from Zimbabwe interpreted the same situation as not having impacted policy change,[35]

> *"No, it provided local evidence to scale up integration of ART in antenatal clinics which was already taking place in Zimbabwe".*

In another instance, a participant from India mentioned his study having impacted policy change even though the study simply reinforced existing policy and did not change practice.[36, 37] On further clarification and discussion over email and phone, he mentioned,

> *"Our study findings called for a need to revisit the WHO recommendation of switching to same-day diagnosis [in tuberculosis]. With the dissemination of this study result, the National TB Control Programme in India took a policy decision not to change its current policy as per WHO recommendation."*

We agreed with this reasoning and considered the study to have had an impact on policy.

In conclusion, over half of course outputs resulting from recent SORT IT OR courses had contributed to a change in policy and/or practice. Given the complexities in interpreting policy impact assessment, future assessments should focus beyond self-reporting of data and use more robust and independent verification of the reported change(s) with all concerned stakeholders to enhance the richness and rigour of the assessments.

Conflicts of Interest: The authors of this paper were also involved as co-investigators in many of the research projects being assessed for impact. We have duly acknowledged this as one of the limitations in the paper.

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REFERENCES

1. Zachariah R, Ford N, Maher D et al. Is operational research delivering the goods? The journey to success in low-income countries. Lancet Infect Dis 2012; 12: 415-421.
2. Ramsay A, Harries AD, Zachariah R et al. The Structured Operational Research and Training Initiative for public health programmes. Public Health Action 2014; 4: 79-84.
3. Guillerm N, Tayler-Smith K, Berger SD et al. What happens after participants complete a Union-MSF structured operational research training course? Public Health Action 2014; 4: 89-95.
4. Zachariah R, Guillerm N, Berger S et al. Research to policy and practice change: is capacity building in operational research delivering the goods? Trop Med Int Health 2014; 19: 1068-1075.
5. Silverman D. Interpreting qualitative data. London: SAGE Publications Ltd; 2006.
6. Bissell K, Harries AD, Reid AJ et al. Operational research training: the course and beyond. Public Health Action 2012; 2: 92-97.
7. Rusen ID, Harries AD, Zachariah R, Ramsay A. Capacity Building in Operational Research: More than One Way to Slice the Cake. Front Public Health 2015; 3: 176.
8. Technopolis Group. Evaluation of the Developing Operational Research Capacity in the Health Sector Project. A Technopolis Group evaluation carried out for the UK Department for International Development (DFID). Final Report, 12 January 2015.
9. Patel J, Dave P, Satyanarayana S et al. Pretreatment sputum smear grade and smear positivity during follow-up of TB patients in Ahmedabad, India. Public Health Action 2013; 3: 308-310.
10. Kumar RS, Kumar AM, Claassens M et al. Number of sputum specimens during treatment follow-up of tuberculosis patients: two or one? Public Health Action 2013; 3: 304-307.
11. Kumar RS, Kumar AMV, Claassens M et al. Are we justified in treating for multidrug-resistant tuberculosis based on positive follow-up smear results? Int J Tuberc Lung Dis 2014; 18: 449-453.
12. Bhat PG, Kumar AMV, Naik B et al. Intensified tuberculosis case finding among malnourished children in nutritional rehabilitation centres of Karnataka, India: missed opportunities. PLoS ONE 2013; 8(12): e84255: doi:10.1371/journal.pone.0084255.
13. Kumar B, Shirivastava J, Satyanarayana S et al. How effective is the integration of facility and community-based management of severe acute malnutrition in India? Public Health Action 2013; 3: 265-270.
14. Ganzaya S, Naranbat N, Bissell K, Zachariah R. Countrywide audit of multidrug-resistant tuberculosis and treatment outcomes in Mongolia. Public Health Action 2013; 3: 333-336.
15. Kodouda SF, Zachariah R, Khogali M et al. How well are asthma treatment cards filled out in public health centres in Gazeera State, Sudan? Public Health Action 2014; 4: 116-121.
16. Abeygunawardena SC, Sharath BN, Van den Bergh R, Naik B, Pallewatte N, Masaima MNN. Management of previously treated tuberculosis patients in Kalutera district, Sri Lanka: how are we faring? Public Health Action 2014; 4: 105-109.
17. Mi F, Tan S, Liang L et al. Diabetes mellitus and tuberculosis: pattern of tuberculosis, two-month smear conversion and treatment outcomes in Guangzhou, China. Trop Med Int Health 2013; 18: 1379-1385.

18. Wahome E, Makori L, Gikera M et al. Tuberculosis treatment outcomes among hospital workers at a public teaching and national referral hospital in Kenya. Public Health Action 2013; 3: 323-327.
19. Iribagiza MK, Manikuzwe A, Aquino T et al. Fostering interest in research: evaluation of an introductory research seminar at hospitals in rural Rwanda. Public Health Action 2014; 4: 271-275.
20. Maalim AM, Zachariah R, Khogali M et al. Supporting 'medicine at a distance' for delivery of hospital services in war-torn Somalia: how well are we doing? Int Health 2014; 6: 70-73.
21. Denisiuk O, Smyrnov P, Kumar AM et al. Sex, drugs and prisons: HIV prevention strategies for over 190 000 clients in Ukraine. Public Health Action 2014; 4: 96-101.
22. Zachariah R, Kumar AM, Reid AJ et al. Open access for operational research publications from low- and middle-income countries: who pays? Public Health Action 2014; 4: 142-144.
23. Kumar AM, Zachariah R, Satyanarayana S et al. Operational research capacity building using 'The Union/MSF' model: adapting as we go along. BMC Res Notes 2014; 7: 819.
24. Xia Y, Goel S, Harries AD et al. Prevalence of extended treatment in pulmonary tuberculosis patients receiving first-line therapy and its association with recurrent tuberculosis in Beijing, China. Trans R Soc Trop Med Hyg 2014; 108: 402-407.
25. Chang YP, Duo L, Kumar AMV et al. Retention and HIV seroconversion among drug users on methadone maintenance treatment in Yunnan,China. Public Health Action 2014; 4: 28-34.
26. Palanivel C, Kumar AMV, Mahalakshmi T et al. Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India. Public Health Action 2013; 3: 220-223.
27. Harries AD, Kumar AMV, Satyanarayana S et al. References for scientific papers: why not standardise to one global style? Public Health Action 2013; 3: 255-257.
28. Galsworthy MJ, Hristovski D, Lusa L et al. Academic output of 9 years of EU investment into health research. Lancet 2012; 380: 971-972.
29. Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009; 374: 86-89.
30. Harries AD, Zachariah R, Ramsay A et al. Does research make a difference to public health? Time for scientific journals to cross the Rubicon. Public Health Action 2014; 4: 2-3.
31. Jobanputra K, Parker LA, Azih C et al. Factors associated with virological failure and suppression after enhanced adherence counselling, in children, adolescents and adults on antiretroviral therapy for HIV in Swaziland. PLoS One 2015; 10: e0116144.
32. Tharu MB, Harries AD, Goel S et al. Screening retreatment tuberculosis patients for drug resistance in mid-west Nepal: how well are we doing? Public Health Action 2014; 4: 60-65.
33. Reza LW, Satyanarayna S, Enarson DA et al. LED-fluorescence microscopy for diagnosis of pulmonary tuberculosis under programmatic conditions in India. PLoS ONE 2013; 8(10): e75566.
34. Siddiquea BN, Islam MA, Bam TS et al. High quit rate among smokers with tuberculosis in a modified smoking cessation programme in Dhaka, Bangladesh. Public Health Action 2013; 3: 243-246.
35. Gunguwo H, Zachariah R, Bissell K, Ndebele W, Moyo J, Mutasa-Apollo T. A 'one-stop shop' approach in antenatal care: does this improve antiretroviral treatment uptake in Zimbabwe? Public Health Action 2013; 3: 282-285.

36. Nayak P, Kumar AMV, Agrawal TK, Chandrakar S, Nair SA. Same-day light-emitting diode fluorescence microscopy for the diagnosis of tuberculosis in Chhattisgarh, India. Int J Tuberc Lung Dis 2014; 18: 666-670.
37. Nayak P, Kumar AMV, Claassens M et al. Comparing same day sputum microscopy with conventional sputum microscopy for the diagnosis of tuberculosis - Chhattisgarh, India. PLoS ONE 2013; 8(9): e74964: doi:10.1371/journal.pone.0074964.

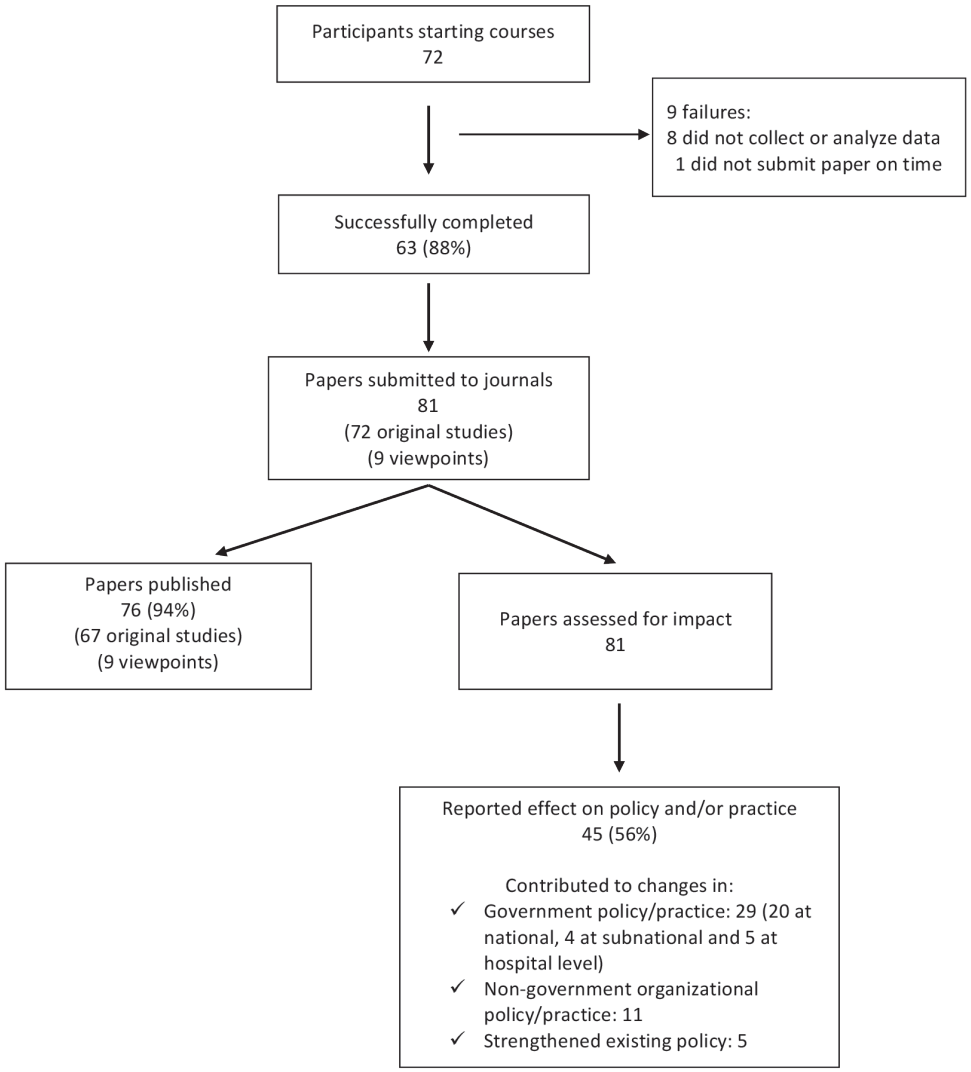

Figure 1. Outputs from six completed SORT IT operational research courses run in Europe, Africa, Asia and the South Pacific during 2012-13[a].

[a] The six courses were run in Chennai-India (1), Paris-France (1), Luxembourg-Luxembourg (1), Addis Ababa-Ethiopia (1), Nadi-Fiji (1) and Kathmandu-Nepal (1); Outputs were assessed as of June 30, 2015

10.

Promoting operational research through fellowships: A case study from South–East Asia Union Office

Kumar AMV, Kumar AM, Satyanarayana S, Berger SD, Chadha SS, Singh RJ, Lal P, Tonsing J, Harries AD.
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SUMMARY

In 2009, The International Union Against Tuberculosis and Lung Disease (The Union) and Médecins Sans Frontières (MSF) jointly developed a new paradigm for operational research capacity building and started a new process of appointing and supporting operational research fellows in the field. This case study describes i) the appointment of two operational research fellows in The Union South-East Asia Office (USEA), New Delhi, India, ii) how this led to the development of an operational research unit in that organization, iii) the achievements over a five year period from June 2009 to June 2014 and iv) challenges and lessons learned. In June 2009, the first operational research (OR) Fellow in India was appointed on a full-time basis and the second was appointed in February 2012 - both had limited previous experience in OR. From 2009 to 2014, annual research output and capacity building initiatives rose exponentially and included: i) facilitation at 61 operational research training courses / modules; ii) publication of 96 papers, several of which had a lasting impact on national policy and practice; iii) providing technical assistance in promoting operational research; iv) building capacity of medical college professionals to manage data; v) support to programme staff for disseminating their research findings; vi) reviewing 28 scientific papers for national or international peer-reviewed journals; and vii) developing 45 scientific abstracts for presentation at national and international conferences. The reasons for this success are highlighted along with on-going challenges. This experience from India provides good evidence for promoting similar models elsewhere.

OPERATIONAL RESEARCH AND IT'S ROLE IN PUBLIC HEALTH

From a public health perspective, operational research can be defined as research into strategies, interventions, tools or knowledge that can enhance the quality, coverage, effectiveness or performance of the health system or disease programme in which the research is being conducted.[1] It can be viewed as a spectrum of activities that encompasses reviews of data already collected in patient registers, treatment cards, patient files or electronic data sets, evaluations of operational practices or assessments of the implementation of new strategies and technologies.

Operational research is often observational in nature, and can involve descriptive or cross-sectional studies, retrospective or prospective cohort studies and sometimes case-control studies. Recent guidelines for the reporting of observational studies (the STROBE statement) provide a logical structured roadmap for this type of research, thereby improving its scientific credibility.[2] In addition, pragmatic, cluster-randomized trial designs and qualitative research methods are also being increasingly viewed as within the ambit of operational research. Operational research also needs to be conducted within a sound ethics framework that includes the principles of informed consent and data confidentiality, and in all cases study results should be fed back to the local communities in an accessible and understandable manner.[3]

The key role of operational research in improving health programme performance is well-recognized, and consequently the subject is strongly promoted by donors and technical agencies. For example, The Global Fund Against AIDS, Tuberculosis and Malaria (GFATM) recommends an allocation of up to 10% of country grants towards monitoring and evaluation including operational research. Given that this is provision is not explicit and hidden under 'monitoring and evaluation', potential users are often unaware and do not make use of this excellent opportunity for programme strengthening. Further, the implementation of operational research is weak in many low- and middle-income countries in most need of it, and lack of operational research capacity is one of the main reasons behind this.

THE UNION'S CENTRE FOR OPERATIONAL RESEARCH

Operational research has always been a priority for the International Union Against Tuberculosis and Lung Disease, Paris, France (The Union) owing to visionary leadership of great public health leaders like Annik Rouillon, Karel Styblo and Don Enarson who served The Union. The initial efforts of OR capacity building included development of a guide,[4] and a training programme that started in 1997 with support of the United States Center for Disease Control's Division of TB Elimination.[5] The vision at the time was to identify and train participants from different countries in quality-assured data capture and analysis and research protocol development and encourage them to conduct multi-centric collaborative operational research projects. There were several challenges including high attrition among the participants and few outputs in terms of publications,[6,7] and the initiative could not be

sustained mainly due to lack of continued funding. Despite these limitations, this initiative sowed the first seeds of OR in the minds of several people who went on to become leaders of organizations and marks the first efforts of The Union in OR capacity building.

On January 1st, 2009, The Union received financial support from Bloomberg Philanthropies to establish the Centre for Operational Research and Strategic Information. One of the objectives was on promoting operational research and was supported by two principal activities: i) to establish a new paradigm for operational research capacity building and ii) to appoint and support operational research fellows in the field.

OPERATIONAL RESEARCH CAPACITY BUILDING:

In March 2009, The Union and Medecins Sans Frontieres Luxembourg (MSF) met in Paris to develop a new course for integrated operational research and training that not only teaches the principles of the "what, why and how of operational research", but also incorporates the development, implementation and writing up of a research project as an integral part of the course.[8] Training is combined with "doing", akin to an apprenticeship. The success of a participant is judged on whether or not a research project has been designed and completed, with a paper submitted to a peer-reviewed journal within the stated time frame of the course. The two organizations also track whether these papers have been published, whether the research has had any impact on policy and practice,[9-11] and whether the skills imparted to the participants and their organizations are used after the course to further develop, implement, write up and publish other relevant studies.[12]

After running courses together for three years, The Union and MSF joined forces with the Special Programme for Research and Training in Tropical Diseases (TDR), which is based at the World Health Organization (WHO), Geneva, Switzerland. In July 2012 the three organizations developed a formal blueprint for training public health programme staff under the Structured Operational Research Training Initiative (SORT IT) and has been described elsewhere.[13]

OPERATIONAL RESEARCH (OR) FELLOWS:

The Union instituted this new cadre of staff called the "operational research fellow", whose task is to strengthen operational research capacity and implementation in the field (**Box 1**). Fellows are appointed using strict selection criteria and they work within disease control programmes or supportive non-governmental organizations in their countries. They work full-time or part-time for The Union and are given support and time to carry out relevant operational research. Fellows must successfully complete one of the operational research courses within their first year of appointment and they are expected to initiate, complete and publish their own operational research as well as drive country-based operational research. They are on one- or two-year performance based contracts, with one of the key milestones being the submission of two papers to peer-reviewed journals by the end of a 12-month period, failure to achieve this resulting in termination of the contract. Fellows start

in junior fellowships, and after two years progress to senior fellowships. After four years, with at least eight papers submitted, fellows may be considered for PhD programmes that allow submission of published papers to count towards the final degree. Following this successful model, MSF also appointed operational research fellows under the same conditions that pertain in The Union.

PURPOSE OF THE CASE STUDY

The main purpose of this manuscript is to describe i) how the appointment of two operational research fellows in the South-East Asia Union Office, Delhi, India, led to the development of an operational research unit in that organization, ii) the achievements and their reasons over a five year period from June 2009 to June 2014 and iii) challenges and lessons learned.

DEVELOPING THE OPERATIONAL RESEARCH UNIT IN INDIA:

OR as a strategic direction was always part of the vision of the leadership of the Union South-East Asia (USEA) Regional office, New Delhi, India and the office of the Executive Director of The Union, Paris and several efforts were being made since 2008 to procure funding for OR capacity building. In June 2009, the first OR Fellow (SS) in India was appointed on a full-time basis. A decision had been made several months earlier between the regional director of The Union South-East Asia (USEA) office, Delhi, India, and the director of operational research in Paris (ADH) to appoint an OR fellow in India. SS was working as a WHO-RNTCP Medical Consultant in the Indian Revised National Tuberculosis Control Programme (RNTCP), was keen to learn about operational research. The national programme manager of Indian RNTCP and the WHO Medical Officer for Tuberculosis displayed exemplary leadership by supporting this appointment, despite human resource constraints at the Central TB Division of Ministry of Health and Family Welfare of Government of India. SS submitted his curriculum vitae along with references, was interviewed and appointed, with the generic terms of reference underpinning the job (**Box 1**). His previous experience with operational research was limited. He had published two papers in peer-reviewed journals, one in 2005 on dengue fever as third author and one in 2008 on initial default in tuberculosis patients in India in which he was eleventh author.[14, 15] He had also had one successful abstract submission for the Annual Conference of the Indian Academy of Preventive and Social Medicine in 2005. He had never acted as a peer reviewer for a scientific paper and had never been a facilitator on an operational research training course. The financial support for his position was through the Bloomberg Philanthropies. This appointment marked the formal beginning of operational research initiatives in the USEA office.

In September 2011, the Department for International Development (DFID), UK, also started to provide support to enhance operational research capacity building at the Union. One of their areas of support was for a regional operational research course for South-East Asia along with an additional OR fellow to support SS in India. At the time, there was a WHO-RNTCP Medical Consultant (AMVK) attending the operational research capacity building

course in Paris. He had proven his competence and enthusiasm for operational research during the course, and following the same procedures as with SS, he was formally appointed in February 2012, with the same generic terms of reference underpinning his tasks. He also had no previous experience with operational research. He had published one paper as sole author on confidence intervals,[16] and had presented a paper at the 22nd Annual conference of the Indian Society for Medical Statistics on prevention of parent to child transmission of HIV/AIDS. He also had never acted as a peer reviewer for a scientific paper and had never been a facilitator on an operational research training course.

At the same time that AMVK was undertaking his operational research training, two senior staff officers of the USEA Office underwent the same operational research training in Paris and this helped in the creation of an enabling environment for operational research in the office. A research associate position was also established and filled to support a tuberculosis knowledge, attitude and practice survey funded by the Global Fund Against AIDS, Tuberculosis and Malaria in 2012. Thus, a small team began to be established in the office. These factors ensured that operational research featured as one of the six strategic goals of the "Vision 2020" document which details the plan, goals and strategic directions for the USEA office for the period 2012-20.

ACHIEVEMENTS AND REASONS FOR SUCCESS:

The achievements are summarised below:

SUCCESSFUL COMPLETION OF THEIR OPERATIONAL RESEARCH COURSES:

SS completed the first ever operational research capacity building course held at The Union Headquarters in Paris with two operational research projects on paediatric tuberculosis and recurrent tuberculosis in India, both of which were published.[17, 18] AMVK similarly completed the second operational research capacity building course in Paris with one project on antiretroviral therapy in HIV-infected TB patients in India.[19]

FACILITATION AND MENTORSHIP ON FURTHER OPERATIONAL RESEARCH COURSES:

Both OR Fellows went on to facilitate at modules of other operational research courses, with SS starting his facilitation career in June 2010 and AMVK in February 2012. The details of the modules at which each fellow facilitated each year are shown in **Table 1**. Up to June 2014, SS facilitated at 21 modules and AMVK facilitated at 40.

In addition to the operational research modules and courses, the OR fellows were invited as resource persons to teach at other capacity building workshops conducted by the World Health Organization, the RNTCP, the National AIDS Control Programme (NACP) and the medical colleges. In May 2012, AMVK and SS were invited by WHO and RNTCP to build data management capacity for about 65 WHO-RNTCP consultants working in India. Following this training, a data management module using the open access software "EpiData" (EpiData Association, Odense, Denmark) was developed by AMVK for the RNTCP to enable the

structured capture of the data collected during the 'programme evaluations' conducted across the country. To institutionalize this mechanism, the Central TB Division of the Ministry of Health of the Government of India issued official directives to train all the data entry operators (more than 650) in using EpiData and how to use the specific data management module to capture the data of Internal Evaluations of RNTCP. The information thus captured is now compiled nationally and used for programme reviews, decision making and research. Several of these WHO-RNTCP consultants, who were instrumental in DOTS expansion in India, became participants in the OR courses and developed as trainers and leaders in OR.[20]

PUBLISHED PAPERS:

The number and details of published papers each year for the two OR fellows are shown in the Supplementary **Annex 1** and **Figure 1**. It should be noted that several of these research projects were mentored by the two OR fellows together. The number of publications increased exponentially between 2009 and 2013, indicating the value of a critical mass of people involved full time in operational research. Altogether over the five years, the OR fellows were co-authors on 75 published research papers and 21 opinion and review papers with a total number of 96 published papers. Of these, 71 (74%) were published in journals offering immediate and free open-access to their readership, with most of the remainder being published in journals offering free open-access after a period of time. In the six years before the OR fellows joined the USEA Office, there was one published paper.

IMPACT OF OPERATIONAL RESEARCH ON POLICY AND PRACTICE:

Several of the operational research studies conducted or mentored by the OR fellows contributed to changes in national policy and practice. Some examples of this impact are highlighted in **Table 2**.

TECHNICAL ASSISTANCE IN PROMOTING OPERATIONAL RESEARCH:

The two OR fellows became known as leaders in operational research by partners and other stakeholders and were invited to be a part of national level technical committees which assist and recommend the national programme. SS participated as a member of the National Standing Committee on Operational Research for the RNTCP, while AMVK participated as a member of National Technical Working Group on TB/HIV for the NACP and as a member of the State level Operational Research Committee of Karnataka State, India. In addition, they provided technical assistance to states in the country for conducting operational research, analysing data and publishing papers. In addition, several research projects (including nationally representative Knowledge, Attitude and Practice surveys on Tuberculosis and projects related to tobacco control) initiated by other departments within USEA office were supported technically by the two OR fellows from design to analysis to publication.

BUILDING CAPACITY OF MEDICAL COLLEGE PROFESSIONALS IN DATA MANAGEMENT:

A collaborative framework was formed between the Karnataka State RNTCP, the Medical Colleges and The Union in 2013 to build the capacity of public health professionals in medical colleges to conduct operational research. One of the first initiatives of this collaboration was to engage with public health professionals in medical colleges and academic institutions in India and conduct a two-day course on EpiData for the residents and faculty of public health departments of medical colleges in and around Bangalore. This workshop, funded by Eli Lilly, was organised by the USEA Office (led by AMVK) in collaboration with the Department of Community Medicine in the Bangalore Medical College and Research Institute (BMCRI), and the Karnataka State Tuberculosis Cell of the RNTCP of the Government of India. A second initiative was replicated in Puducherry in collaboration with Jawaharlal Nehru Institute of Postgraduate Medical Education and Research (JIPMER), one of the premier medical institutions in India, catering to the medical college faculty and scientists of Indian Council of Medical Research from Puducherry. The feedback from the participants suggests that they have begun to use EpiData in their research work and have included it in their teaching curriculum for post-graduate and under-graduate medical students. The sessions in these courses were video-captured, edited and have been posted on YouTube (http://www.youtube.com/watch?v=1SoxNpj-Ncw) to be used as self-learning resource materials by interested public health professionals worldwide. These online learning materials were also shared with the participants of the online virtual operational research training initiated by The Union in North America.

SUPPORT TO PROGRAMME STAFF FOR DISSEMINATING THEIR RESEARCH FINDINGS:

The operational research unit in the USEA office has supported several programme staff officers who are working with the RNTCP and national HIV programme to draft and submit scientific abstracts to national and international conferences. Several abstracts have been accepted for oral or poster presentations. To facilitate dissemination of research findings, a national dissemination workshop was conducted in 2013 by the USEA Office in collaboration with the RNTCP, and this was attended by representatives of all stakeholders working for TB control in India. Such workshops provide a great opportunity for the researchers to share their findings directly with the national programme managers and advocate for policy change.

SCIENTIFIC PAPERS REVIEWED FOR NATIONAL OR INTERNATIONAL PEER–REVIEWED JOURNALS:

The number of papers that each OR fellow reviewed each year is shown in **Figure 2**. Although the OR fellows were invited to review many papers, they could not accept all the offers given their busy schedules. Altogether, 28 papers were reviewed.

SCIENTIFIC ABSTRACTS PRESENTED AT NATIONAL AND INTERNATIONAL CONFERENCES:

The number of abstracts accepted for presentation with OR fellows as co-authors at conferences each year is shown in **Figure 3**. Altogether, 45 conference abstracts were written.

CREATION OF A NATIONAL POOL OF RESOURCE PERSONS:

In the initial courses co-ordinated by the OR fellows, support was provided by external facilitators. Once the fellows became independent facilitators, they started identifying outstanding participants in their operational research courses and provided them with an opportunity to co-facilitate in future courses. This helped in grooming young committed participants as future facilitators. As a result of this facilitator-grooming initiative, there is now a pool of independent, national facilitators in India who can be drawn into facilitating national and regional courses without the need for external (out-of-country) expertise. Several of these facilitators are now able to adapt and replicate the SORT IT model in their own networks. Notable efforts include those made by the Postgraduate Institute of Medical Education and Research, Chandigarh, India, to advance locally relevant research in tobacco control and that of National Institute for Research in Tuberculosis in Madurai, India, to build capacity of medical college professionals in TB research. It augurs well for future sustainability of this model of capacity building.

LESSONS AND CHALLENGES:

There are several important lessons and take home messages from this initiative. First, the fellows had both worked in national disease control programmes before taking up their OR fellowship positions and understood the importance of identifying programmatically relevant operation research questions and ensuring completion of the studies that were initiated.

Second, this experience, combined with their operational research training which focused on study completion and movement of research findings to policy and practice, has ensured that programme managers are engaged at all stages of the operational research (protocol development, data collection, data analysis, data interpretation, paper writing and dissemination). Engagement with programme managers has had a cascading effect in promoting and developing a culture of OR within the national programmes.

Third, an enabling environment for operational research has developed at the USEA office with the regional director strongly supportive of this form of research. In addition to the OR fellows, three senior staff members of the office and one consultant from the Central TB Division of the Ministry of Health and Family Welfare, Government of India, were trained in operational research at Paris, one of whom went on to become the national professional officer for TB control at the WHO-India office. This has enabled strong links to be developed with the key partners, the WHO-country office and the Indian RNTCP.

Fourth, these initiatives have led to the creation of a national pool of resource persons capable of independently facilitating operational research courses without the need

for external international facilitators. The role of the WHO-RNTCP consultant network and the support of WHO-country office lead for tuberculosis in contributing to this resource pool needs special mention.

Finally, there has been strong, on-going and regular mentorship support from the Director of the Centre for Operational Research, Paris, which has included frequent visits to the USEA office. This has provided additional motivation and enthusiasm for the fellows to perform to their full potential.

Despite these lessons, there are on-going challenges. First, even in a country like India, with ample resources of its own, external financial support is needed in the short and medium term to start and sustain this initiative. Donor money is needed both to support OR fellows and the capacity building courses until such time as the national government appreciates the benefits and value of such domestic support. There has, and continues to be, great support from several donor institutions such as Bloomberg Philanthropies, the Global Fund for AIDS, Tuberculosis and Malaria, United States Aid for International Development and the Department for International Development of the United Kingdom for OR capacity building, without which these initiatives could not have been sustained.

The OR fellows have not been successful in tapping into the operations research funds earmarked within the national TB control programme because the latter are cumbersome and time consuming to access. This needs re-thinking as utilising national funds earmarked for operations research may help in undertaking programmatically relevant and challenging operational research studies that require prospective study designs.

Second, building operational research capacity and conducting operational research is a continuous process, with its success and sustainability depending on repeating the process over and over again and again, often due to staff turnover. It is vital for OR fellows to also identify promising individuals at operational research courses and engage them rapidly as facilitators for future courses so that momentum can be maintained.

Third, it is vital that enthusiastic and driven OR fellows are supported in their career paths so that they can attend skills building courses, develop their own capacity and submit their work for masters and PhD degrees. In this regard, adequate and appropriate remuneration is needed to retain such people within their institutions. Fortunately, the 2013 World Health Report explicitly acknowledges the need to strengthen research endeavour not only in academic centres but also in public health programmes, close to the supply of and demand for health services.[21] Important donors, such as the Department for International Development (DFID), UK, recognise this need and are prepared to give the necessary support, provided that value for money is achieved.

CONCLUSION:

This case study testifies to the huge research output that resulted from placing one and then two OR fellows in the USEA Office, Delhi, India. Of particular note, in the six years before the fellows joined there was one published paper from the office while in the first five years since

the fellows joined the cumulative number of published papers reached nearly one hundred. Research publications are an objective way to measure research output, an indicator that the research has been properly designed, implemented, analysed and written up to a high enough standard to get through peer-review and be published in a respectable international journal.[22] Published papers are also a crucial way to disseminate research findings to a wide audience, especially if open-access journals are used as the media for publication.

Before joining as OR fellows, the two individuals had little engagement in operational research. They learnt and subsequently taught their craft as they developed, with a number of factors facilitating this process such as their own enthusiasm and passion for the subject, a supportive and enabling environment and strong mentorship from the leadership. Selecting the right individuals for the job is an essential determinant of success, but the performance-related contracts that The Union offers to all OR fellows allow a way out if a mistake is made in selection and individuals fail to deliver.

Currently, the situation is that one OR fellow is pursuing a PhD training programme in McGill University, Montreal, Canada, and during this time can only spend four months of the year in India. The USEA Office therefore has one full-time resident OR fellow, and although this is not reflected in a decrease in the volume of publications in the first six months of 2014 (24 published papers by 30th June 2014), it nevertheless puts undue strain on the one individual. In an enabling environment in a busy country office, we believe that there should be a minimum of two full-time OR fellows at any one time, and if resources permit this number should be increased to three. We are convinced that in this situation that the whole is greater than the sum of its parts, and total research output will be maximised as good OR fellows will feed off and stimulate each other.

We believe that our experience in India provides good evidence for promoting similar models elsewhere. We need to select highly motivated individuals and, provided they are well supported, mentored and given performance-related contracts, they can facilitate high quality research that impacts not only locally but also at national and international level. Furthermore, it is essential to have a critical mass of OR fellows, with two at any one time being a minimum. We hope that public health institutions and donors will read and learn from this story.

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CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Zachariah R, Harries AD, Ishikawa N et al. Operational research in low-income countries: what, why, and how? Lancet Infect Dis 2009; 9: 711-717.
2. von Elm E, Altman DG, Egger M, Pocock SJ, Cøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007; 370: 1453-1457.
3. Edginton M, Enarson D, Zachariah R, Reid T, Satyanarayana S, Bissell K. Why ethics is indespensible for good-quality operational research. Public Health Action 2012; 2: 21-22.
4. Enarson DA, Kennedy SM, Miller DL, Bakke P. Research methods for promotion of lung health. A guide to protocol development for low-income countries. In: Disease IUATaL, ed. 1 ed. Paris: Les Editions de l'Aulnes; 2001: 1-137.
5. Rieder HL, Lauritsen J. Background, objective, and course history. In (EpiData Software for Operations Research in Tuberculosis Control). 2014. http://www.tbrieder.org/epidata/course_0-2_background.pdf. (Accessed 12 December, 2014.)
6. Rieder HL, Arnadottir T, Tardencilla Gutierrez AA et al. Evaluation of a standardized recording tool for sputum smear microscopy for acid-fast bacilli under routine conditions in low income countries. Int J Tuberc Lung Dis 1997; 1: 339-345.
7. Diop AH, Gakiria G, Pande SB, Malla P, Rieder HL. Dosages of anti-tuberculosis medications in the national tuberculosis programs of Kenya, Nepal, and Senegal. Int J Tuberc Lung Dis 2002; 6: 215-221.
8. Harries AD, Rusen ID, Reid T et al. The Union and Médecins Sans Frontières approach to operational research. [State of the Art Series. Operational Research. Number 2 in the series]. Int J Tuberc Lung Dis 2011; 15: 144-154.
9. Zachariah R, Ford N, Maher D et al. Is operational research delivering the goods? The journey to success in low-income countries. Lancet Infect Dis 2012; 12: 415-421.
10. Zachariah R, Guillerm N, Berger S et al. Research to policy and practice change: is capacity building in operational research delivering the goods? Trop Med Int Health 2014; 19: 1068-1075.
11. Bissell K, Harries AD, Reid AJ et al. Operational research training: the course and beyond. Public Health Action 2012; 2: 92-97.
12. Guillerm N, Tayler-Smith K, Berger D et al. What happens after participants complete a Union-MSF structured operational research training course? Public Health Action 2014; 4: 89-95.
13. Ramsay A, Harries AD, Zachariah R et al. The Structured Operational Research and Training Initiative for public health programmes. Public Health Action 2014; 4: 79-84.
14. Acharya A, Goswami K, Srinath S, Goswami A. Awareness about dengue syndrome and related preventive practices amongst residents of an urban resettlement colony of south Delhi. J Vector Borne Dis 2005; 42: 122-127.
15. Sai Babu B, Satyanarayana AVV, Venkateshwaralu G et al. Initial default among diagnosed sputum smear-positive pulmonary tuberculosis patients in Andhra Pradesh, India. Int J Tuberc Lung Dis 2008; 12: 1055-1058.

16. Kumar AMV. Confidence intervals and test of significance. Indian Journal of Community Medicine 2006; 31: 46.
17. Satyanarayana S, Shivashankar R, Pal Vashist R et al. Characteristics and programme-defined treatment outcomes among childhood tuberculosis (TB) patients under the National TB Programme in Delhi. PLoS ONE 2010; 5(10): e13338: doi:10.1371/journal.pone.0013338.
18. Srinath S, Sharath B, Santosha K et al. Tuberculosis 'retreatment others': profile and treatment outcomes in the state of Andhra Pradesh, India. Int J Tuberc Lung Dis 2011; 15: 105-109.
19. Kumar AMV, Gupta D, Rewari BB et al. Will adoption of the 2010 WHO ART guidelines for HIV-infected TB patients increase the demand for ART services in India? PLoS ONE 2011; 6(9): e24297: doi:10.1371/journal.pone.0024297.
20. Frieden TR, Khatri GR. Impact of national consultants on successful expansion of effective tuberculosis control in India. Int J Tuberc Lung Dis 2003; 7: 837-841.
21. World Health Organization. The World Health Report 2013. Research for Universal Coverage. World Health Organization, Geneva, Switzerland 2013. http://www.who.int/whr/2013/report/en/. (Accessed 14 December, 2014.)
22. Zachariah R, Tayler-Smith K, Ngamvithayapong-Yanai J et al. The published research paper: is it an important indicator of successful operational research at programme level? Trop Med Intern Health 2010; 15: 1274-1277.

BOX 1: TERMS OF REFERENCE FOR OPERATIONAL RESEARCH FELLOWS:

BACKGROUND:

Low and middle income countries of the world, particularly in sub-Saharan Africa, are overburdened with three serious communicable disease epidemics (HIV/AIDS, tuberculosis and malaria) as well as silent, growing epidemics of non-communicable diseases. Many of these countries have very weak health management information systems and are unable to track cases, quality of care, outcomes or results of treatment, or the impact of prevention and treatment. In addition, the use of data that are available to lead directly to actions and policies to promote health (termed operational research) is lacking because few professionals in developing countries have access to appropriate training and mentorship in operational research and resources for this type of research have been largely unavailable. Hence, there is a need for both better collection and tracking of health information and better use of data to improve the health of people in low and middle income countries.

To address these two critical gaps, a new Centre for Strategic Health Information and Operational Research (SCHIOR) has been established within the Union. The work of the Centre will be organised around:-

- developing improved data collection and tracking systems for key infectious and non-communicable disease based on the highly successful model used in international tuberculosis control
- using electronic data systems to accurately supplement, and, where indicated, to replace paper records, based on a successful model that has been used in Malawi for the past 7 years.
- increasing capacity for operational research through in-country training programs and operational research fellowships
- enhancing and expanding vital registration systems (i.e., birth and death registries) which will enable the population impact of health interventions to be assessed
- developing an evaluation component to track the influence of operational research and strategic information in changing policy and practice
- engaging with the World Health Organization to maximise the benefits of this approach to improving health in the developing world

OVERALL ROLE OF AN OPERATIONAL RESEARCH FELLOW:

Operational Research Fellows will conduct and publish research into strategies, interventions, tools and new knowledge that will help to improve health care delivery either in programme settings or important health-related problems.

SPECIFIC RESPONSIBILITIES

Research fellows will specifically:-

- undertake mandatory attendance of the training for all 3 modules conducted by the OR Centre
- develop protocols for research projects under the mentorship of staff at the Centre or within The Union and in collaboration with country colleagues who shall act as local mentors
- submit such proposals to ethical review to ensure that the highest standards are being met
- ensure that protocols, once approved, are implemented in the field within a reasonable time frame

- be responsible for the collection, filing, management and storage of all data, with appropriate back-up strategies, and quality-assured data entry and validation with technically suitable and appropriate electronic application software
- conduct data analysis under the mentorship of staff at the Centre or within The Union and with local mentors
- ensure that within 3 months of completion of any research project that a paper is prepared and ready for submission to an international peer-reviewed journal
- be responsible for the submission, management and follow-up of all papers submitted electronically to journals
- present the results of published work at relevant national and International conferences
- submit each year at least two papers to peer-reviewed journals (see below regarding annual performance assessments)
- attend targeted training on protocol development, data entry, data analysis and paper writing skills and participate / facilitate in Union-sponsored training courses

SKILLS, COMPETENCIES, REQUIREMENTS AND SUPPORT:
Research fellows will be local health care personnel (doctors, paramedical staff or nurses) or health care analysts working in TB or HIV programmes, Ministries of health or larger health care institutions that assist in the national effort to improve the health of ordinary people. They will be enthusiastic and committed to the concept of operational research. They will be fluent in spoken and written English, as this is the most common language of paper writing.

Research fellows will be appointed as Union Fellows a result of recommendations from senior colleagues, an excellent curriculum vitae, an interview process and two satisfactory referee reports. They will have an annual contract for up to 2 years around a programme of work, with an annual assessment of performance. **In particular, failure to submit at least 2 papers to peer-reviewed international journals within each 12-month period will result in failure to renew the annual contract**.

Research fellows will receive financial and other support (for example, lap-top computers) to enable them to undertake research projects in the field.

Research fellows will periodically undertake targeted training on research protocol development, data analysis and paper writing skills, and every attempt will made to include them in Union-conducted training courses or symposia.

Table 1: Operational Research Courses and other training workshops at which the OR fellows facilitated, 2009-14.

Year	OR Fellow (SS)	OR Fellow (AMVK)
2009	None	None
2010	Module 1 PHFI OR Course Module 1 Paris OR 2 Course Module 1 of the India (Bangalore 1) OR course Operational Research Skills in one day (World Lung Conference 2010)	None
2011	Module 1 Paris OR course Module 1 Luxembourg OR course Module 3 India (Bangalore 1) OR course Operational Research Skills in one day (World Lung Conference 2011)	None
2012	Module 3 Paris OR course Module 3 Luxembourg OR course Module 1 of India (Bangalore 2) OR course Modules 1, 2 and 3 of South-Asian OR course 2012 Operational Research Skills in one day (World Lung Conference 2012)	Modules 1, 2 and 3 of South-Asian OR course 2012 Module 2 of African OR course Advanced EpiData course in Paris Module 1 of India (Bangalore 2) OR course Module 2 of the Pacific OR course Modules 1 and 2 of Paris OR course Modules 1 and 2 of India (Chennai 1) OR course EpiData course for WHO-RNTCP consultants in India Operational Research Skills in one day (World Lung Conference 2012) Workshop on "Operational Research" conducted by National AIDS Control Programme in India

2013	Module 1 Luxembourg OR course Module 3 of 2nd Indian OR course Module 1 Luxembourg OR course Paper writing workshop for the staffs of USEA office Paper writing workshop for the staffs of TB-DM pilot project sites (WDF supported) Operational Research Skills in one day (World Lung Conference 2013)	Short course on "Efficient, Quality-assured Data Capture using EpiData" (Bangalore and Puducherry) Workshop on "Operational Research" for medical college professionals working in close collaboration with National TB Programme in Gujarat, India Paper writing workshop for the staffs of USEA office Modules 1, 2 and 3 of South-Asian OR course 2013 Modules 2 and 3 of India (Bangalore 2) OR course Short course on "Efficient, Quality-assured Data Analysis using EpiData" (Bangalore) Advanced EpiData course in New Delhi Paper writing workshop for the staffs of TB-DM pilot project sites (WDF supported) Advanced EpiData course in Paris Module 3 of India (Chennai 1) OR course Module 3 of Paris OR course Module 1 of Estonia OR course Module 1 of Luxembourg OR course EpiData Module for the online virtual OR training (Treat TB) Module 3 of African OR course Modules 1 and 2 of India (Chennai 2) OR course Operational Research Skills in one day (World Lung Conference 2013)
2014 (till June)	None (Joined PhD programme at McGill University, Montreal, Canada)	Modules 1 and 2 of South Asia OR course 2014 Module 3 of Estonia OR Course Module 3 of Luxembourg OR course OR course on tobacco control in collaboration with PGIMER Chandigarh, India

Table 2: Examples of operational research projects co-ordinated and mentored by OR fellows which contributed to changes in policy and practice: 2009-13.

Title and details of the Paper	Policy change sought	Impact
Sachdeva KS, Srinath S, Dewan PK, Nair SA, Reddy R, Kundu D, Chadha SS, Venkatachalaiah AKM, Parmar M, Chauhan LS. Source of previous treatment for re-treatment TB cases registered under the National TB Control Programme, India, 2010. **PLoS ONE 2011; 6: e22061.**	Enhanced efforts towards extending treatment support and supervision to patients treated by private sector treatment providers are urgently required to improve the quality of treatment and reduce the numbers of patients with recurrent tuberculosis.	These two studies highlighted the large numbers of TB patients treated in the huge private sector in India. These studies have contributed to the estimation of the TB burden in the country (as suggested by the WHO's onion peel model). They have also triggered a large number of studies/ models that will help to enhance the notification of TB cases in the country. The Government of India eventually declared TB to be a nationally notifiable disease, mandating all health care providers in the country to inform the RNTCP about the TB cases that they are managing.
Srinath S, Nair SA, Chadha SS, Shivashankar R, Sharma G, Yadav S, Mohanty S, Kamineni V, Wilson NC, Harries AD, Dewan PK. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts. **PLoS ONE 2011; 6: e24160.**	1) Reviewing and revising the scope of the India tuberculosis notification system; 2) Strengthening and monitoring health care delivery systems with periodic assessment of the reach and utilisation of the India RNTCP services especially among rural communities	
Kumar AMV, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, Lal K, Reddy HRR, Naik B, Prasad R, Yaqoob M, Deepak KG, Shastri S, Srinath S, Harries AD, Chauhan LS, Dewan P. Will adoption of the 2010 WHO ART Guidelines for HIV-infected TB patients increase the demand for ART services in India? **PLoS ONE 2011; 6: e24297.**	Antiretroviral therapy (ART) could be extended to all HIV infected TB patients irrespective of the CD4 count with relatively little additional burden to the national ART programme.	National Policy was changed based on this study to initiate ART for all HIV-positive TB patients irrespective of the CD4 count. The number and proportion of HIV-infected TB patients receiving ART has increased over the years.
Chadha SS, Sharath BN, Reddy K, Jaju J, Vishnu PH, Rao S,Parmar M, Srinath S, Sachdeva KS, Wilson N, Harries AD. Operational challenges in diagnosing multi-drug resistant TB and initiating treatment in Andhra Pradesh, India. **PLoS One 2011; 6: e26659**	Amongst patients who are eligible for multidrug-resistant TB (MDR-TB) services, a significant proportion is lost during the diagnostic and treatment initiation pathway due to a variety of operational challenges. The programme needs to urgently address these challenges for effective delivery and utilisation of the MDR-TB services.	The study highlighted the need for a) line listing all patients who are suspected to have MDR-TB and b) for tracking sputum collection, transportation and ensuring that the patients do not get missed out in the journey from identification to diagnosis. The process outlined in the paper has now become a routine practice under the RNTCP.

Naik B, Kumar A, Kumaraswamy L, Doddamani S, Krishnappa M, Indander V, Satyanarayana S, Gupta D, Dewan PK. HIV prevalence among persons suspected of tuberculosis: policy implications for India. J Acquir Immune Defic Syndr **2012; 59: e72-76.**	HIV testing should be routinely offered to all TB suspects in high HIV settings	
Achanta S, Kumar AM, Nagaraja SB, Jaju J, Shamrao SR, Uppaluri R, Tekumalla RR, Gupta D, Kumar A, Satyanarayana S, Dewan PK. Feasibility and Effectiveness of Provider Initiated HIV Testing and Counseling of TB Suspects in Vizianagaram District, South India. **PLoS One 2012; 7: e41378.**	HIV testing should be routinely offered to all TB suspects in high HIV settings	A policy decision has been taken that HIV testing should be offered routinely to all patients who are suspected as having tuberculosis in high HIV settings of India
Kumar AMV, Gupta D, Gupta RS, Satyanarayana S, Wilson N, Zachariah R, Lawn SD, Harries AD. HIV testing in people with presumptive tuberculosis: time for implementation. **Lancet Respiratory Diseases 2012, October 24: doi: 10.1061/S2213-2600(12)70050-4.**	HIV testing should be routinely offered to all TB suspects in high HIV settings	
India Tuberculosis – Diabetes Study Group. Screening of patients with tuberculosis for diabetes mellitus in India **Tropical Medicine and International Health 2013; 18: 636 – 645**	TB patients should be routinely screened for Diabetes Mellitus	These studies contributed towards a national policy decision that all TB patients in India should be screened routinely for Diabetes Mellitus. Treatment cards and registers for the country were amended to accommodate the recording and reporting necessary for policy implementation.
Balakrishnan S, Vijayan S, Nair S, Subramoniapillai J, Mrithyunjayan S, Wilson N, Satyanarayana S, Dewan PK, Kumar AMV, Karthickeyan D, Willis M, Harries AD, Nair SA. High diabetes prevalence among tuberculosis cases in Kerala, India. **PLoS One 2012; 7: e46502.**	TB patients should be routinely screened for Diabetes Mellitus	

Reza LW, Satyanarayana S, Pandey A, Kumar S, Devendrappa NM, Anand L, Singh G, Kumar AMV, Chadha SS, Wilson N, Sachdeva KS, Nair SA. LED fluorescence microscopy increase the detection of smear-positive pulmonary tuberculosis in medical colleges of India. **Public Health Action 2013; 3: 240-242.**	A decision to scale-up the use of light-emitting diode-fluorescent microscopy (LED-FM) in all high-workload settings of India	The decision to use LED-FM microscopy has already been reflected in the national strategic plan of RNTCP 2012-17.
Reza LW, Satyanarayana S, Enarson DA, Kumar AMV, Sagili K, Kumar S, Prabahakar LA, Devendreppa NM, Pandey A, Wilson N, Chadha S, Thapa B, Sachdeva KS, Kohli MP. LED-Fluorescence microscopy for diagnosis of pulmonary tuberculosis under programmatic conditions in India **PLoS ONE 2013; 8: e75566.**	A decision to scale-up the use of light-emitting diode-fluorescent microscopy (LED-FM) in all high-workload settings of India	
Nayak P, Kumar AMV, Claassens M, Enarson DA, Satyanarayana S, Kundu D, Khaperde K, Agrawal TK, Dapkekar S, Chandraker S, Nair SA. Comparing same day sputum microscopy with conventional sputum microscopy for the diagnosis of tuberculosis – Chhattisgarh, India. **PLoS ONE 2013; 8: e74964.**	To continue with the current strategy of the spot-early morning system of sputum specimen collection, contrary to WHO recommendations of same-day sputum collection	Given similar evidence from multiple sources, RNTCP has decided to continue with the current strategy and not change to same-day strategy

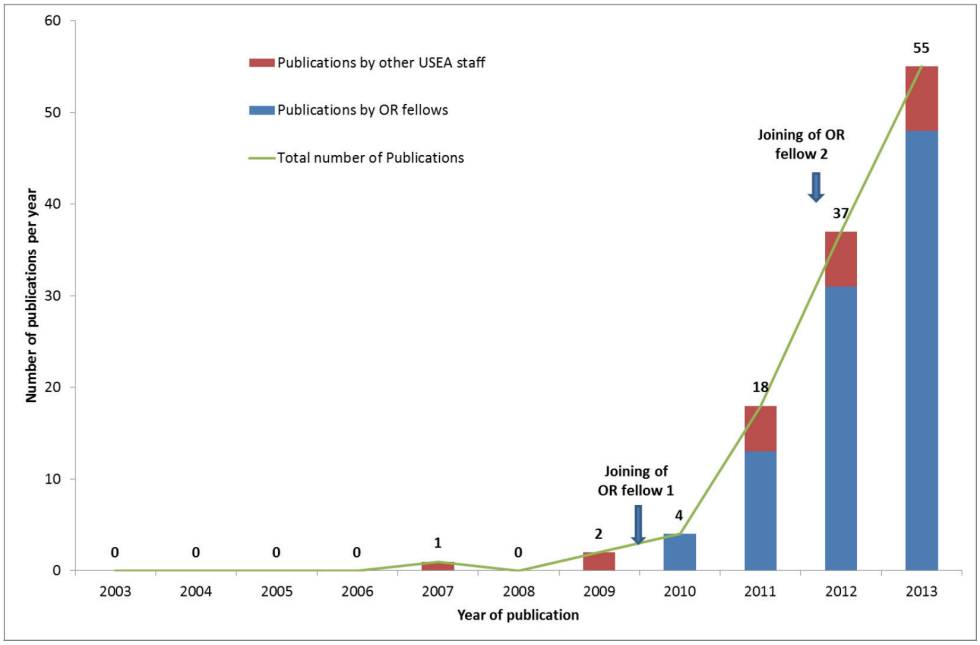

Figure 1. Annual number of publications co-authored by the staffs of The Union South-East Asia (USEA) office and contribution of operational research (OR) fellows, 2003-13

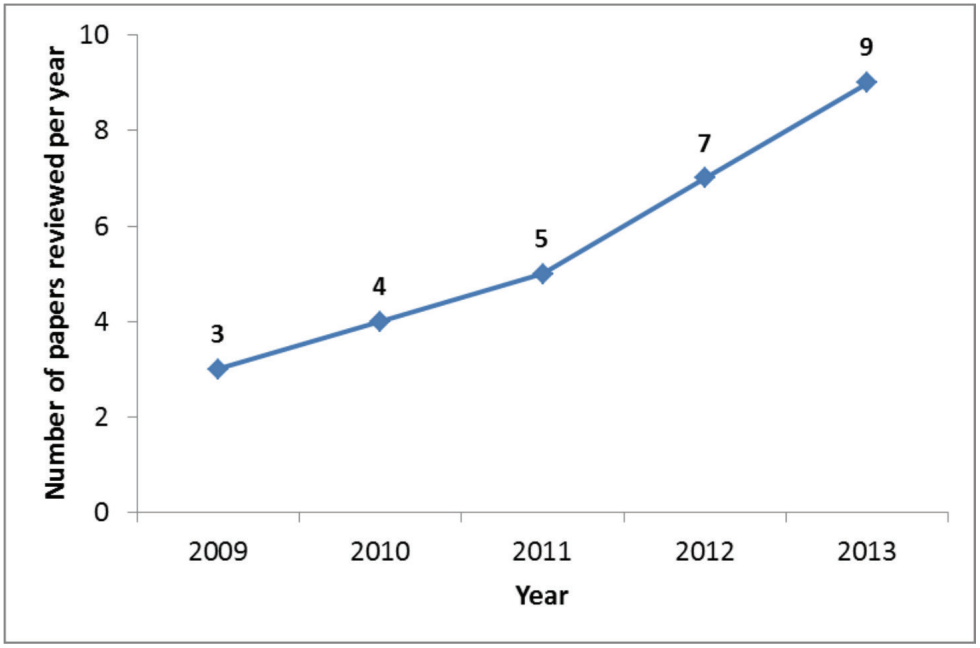

Figure 2. Annual number of papers reviewed by the operational research (OR) fellows of The Union South-East Asia (USEA) office, 2009-13

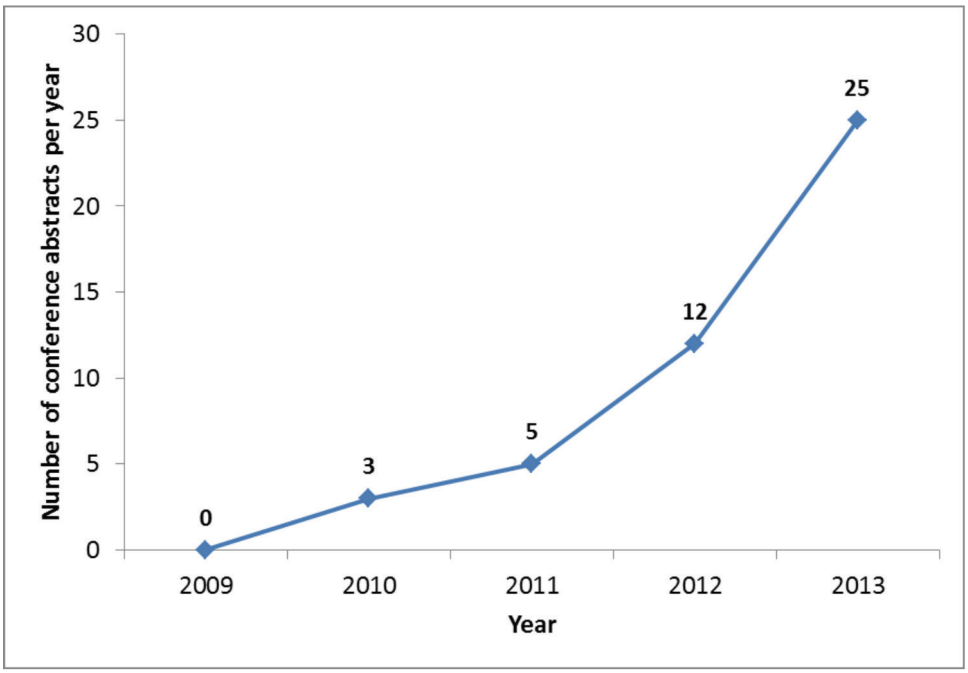

Figure 3. Annual number of conference abstracts co-authored by the operational research (OR) fellows of The Union South-East Asia (USEA) office, 2009-13

SUPPLEMENTARY ANNEX 1: LIST OF PUBLICATIONS EACH YEAR BY OPERATIONAL RESEARCH FELLOWS OF THE UNION SOUTH–EAST ASIA REGIONAL OFFICE, 2009–13

RESEARCH PAPERS:

2009: [0]

None

2010: [2]

1. Jha UM, S Srinath, Dewan PK, Chadha S, Wares F, Sahu S, Gupta D, Chauhan LS. Risk factors for treatment default among re-treatment tuberculosis patients in India, 2006.
   PLoS One 2010; 5: e8873
2. Satyanarayana S, Shivashankar R, Vashist RP, Chauhan LS, Chadha SS, Dewan PK, Wares F, Sahu S, Singh V, Wilson NC, Harries AD. Characteristics and programme-defined treatment outcomes among childhood tuberculosis (TB) patients under the national TB Programme in Delhi.
   PLoS One 2010; 5: e13338.

2011: [11]

1. Srinath S, Sharath B, Santosha K, Chadha SS, Roopa S, Chander K, Wares F, Chauhan LS, Wilson NC, Harries AD. Tuberculosis "retreatment others": profile and treatment outcomes in the state of Andrha Pradesh, India.
   Int J Tuberc Lung Dis 2011; 15: 105-109.
2. Kamineni VV, Turk T, Wilson N, Satyanarayana S, Chauhan LS. A rapid assessment and response approach to review and enhance Advocacy, Communication and Social Mobilisation for Tuberculosis control in Odisha state, India.
   BMC Public Health 2011; 11: 463
3. Sachdeva KS, Srinath S, Dewan PK, Nair SA, Reddy R, Kundu D, Chadha SS, Venkatachalaiah AKM, Parmar M, Chauhan LS. Source of previous treatment for re-treatment TB cases registered under the National TB Control Programme, India, 2010.
   PLoS ONE 2011; 6: e22061.
4. Pothukuchi M, Nagaraja SB, Kelamane S, Srinath S, Babu S, Dewan P, Wares F. Tuberculosis contact screening and isoniazid preventive therapy in a South Indian District: operational issues for programme consideration.
   PLoS ONE 2011; 6: e22500.
5. Srinath S, Nair SA, Chadha SS, Shivashankar R, Sharma G, Yadav S, Mohanty S, Kamineni V, Wilson NC, Harries AD, Dewan PK. From where are tuberculosis patients accessing treatment in India? Results from a cross-sectional community based survey of 30 districts.
   PLoS ONE 2011; 6: e24160.
6. Kumar AMV, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, Lal K, Reddy HRR, Naik B, Prasad R, Yaqoob M, Deepak KG, Shastri S, Srinath S, Harries AD, Chauhan LS, Dewan P. Will

adoption of the 2010 WHO ART Guidelines for HIV-infected TB patients increase the demand for ART services in India?

PLoS ONE 2011; 6: e24297.

7. SB Nagaraja, S Srinath, SS Chadha, S Kalemane, J Jayu, S Achanta, K Reddy, V Potharaju, SRM Shamrao, P Dewan, R Zachariah, S Tetali, R Anchala, NK Kannuri, AD Harries, SK Singh. How do patients who fail first line TB treatment but who are not placed on an MDR-TB Regimen fare in south India?

   PLoS One 2011; 6: e25698

8. Chadha SS, Sharath BN, Reddy K, Jaju J, Vishnu PH, Rao S,Parmar M, Srinath S, Sachdeva KS, Wilson N, Harries AD. Operational challenges in diagnosing multi-drug resistant TB and initiating treatment in Andhra Pradesh, India.

   PLoS One 2011; 6: e26659

9. Jonnalagada S, Harries AD, Zachariah R, Srinath S, Tetali S, Chander K, Rao S, Rao R, Peri S, Anchala R, Kannuri NK. The timing of death in patients with tuberculosis who die during anti-tuberculosis treatment in Andhra Pradesh, South India

   BMC Public Health 2011; 11: 921 doi: 10.1186/1471-2458-11-921

10. Satyanarayana S, Nagaraja SB, Kelamane S, Jaju J, Chadha SS, Chnader K, Vishnu H, Wilson N, Harries AD. Did successfully treated pulmonary tuberculosis patients undergo all follow-up sputum smear examinations?

    Public Health Action 2011; 1: 27 – 29.

11. Takarinda KC, Harries AD, Srinath S, Mutasa-Apollo T, Sandy C, Mugurungi O. Treatment outcomes of new adult tuberculosis patients in relation to HIV status in Zimbabwe.

    Public Health Action 2011; 1: 34-39.

2012: [20]

1. Kondapaka KK, Prasad SV, Srinath S, Kandi S, Zachariah R, Harries AD, Nagaraja SB, Tetali S, Anchala R, Kannuri NK, Murthy K, Koppu D, Vangari L, Sreenivas R. Are tuberculosis patients in a tertiary care hospital in Hyderabad, India, being managed accoridng to national guidelines?

   PloS ONE 2012; 7: e30281.

2. Takarinda K, Harries AD, Srinath S, Mutasa-Apollo T, Sandy C, Mugurungi O. Treatment outcomes of adult patients with recurrent tuberculosis in relation to HIV status in Zimbabwe: a retrospective record review.

   BMC Public Health 2012; 12: 124.

3. Naik B, Kumar A, Kumaraswamy L, Doddamani S, Krishnappa M, Indander V, Satyanarayana S, Gupta D, Dewan PK. HIV prevalence among persons suspected of tuberculosis: policy implications for India.

   J Acquir Immune Defic Syndr 2012; 59: e72-76.

4. Kamineni VV, Wilson N, Das A, Satyanarayana S, Chadha S, Sachdeva KS, Chauhan LS. Addressing poverty through disease control programmes: examples from Tuberculosis control in India

   Int J Equity Health 2012; 11: 27

5. Quazi TA, Sarkar S, Borgohain G, Sreenivas A, Harries AD, Srinath S, Khan K, Bishnu B, Tapader S, Phukan AC, Kabir A, Chaddha V, Paul D, Dewan P. Are all medical patients diagnosed with tuberculosis in Indian medical colleges referred to the RNTCP?
Int J Tuberc Lung Dis 2012: 16: 1083-1085
6. Durba P, Busireddy A, Nagaraja SB, Satyanarayana S, Dewan PK, Nair SA, Sarkar S, Ahmed QT, Sarkar S, Sreenivas SRM, Harries AD, Oeltmann JE. Factors associated with delays in treatment initiation after tuberculosis diagnosis in two districts in India.
PLoS ONE 2012; 7: e39040.
7. Kapoor SK, Raman AV, Sachdeva KS, Satyanarayana S. How did the TB patients reach DOTS services in Delhi? A study of patient treatment seeking behaviour
PLoS ONE 2012; 7: e42458
8. Achanta S, Kumar AM, Nagaraja SB, Jaju J, Shamrao SR, Uppaluri R, Tekumalla RR, Gupta D, Kumar A, Satyanarayana S, Dewan PK. Feasibility and Effectiveness of Provider Initiated HIV Testing and Counseling of TB Suspects in Vizianagaram District, South India.
PLoS One 2012; 7: e41378.
9. Gandhi MP, Kumar AM, Toshniwal MN, Reddy RH, Oeltmann JE, Nair SA, Satyanarayana S, Dewan PK, Mannan S. Sputum smear microscopy at two months into continuation-phase: should it be done in all patients with sputum smear-positive tuberculosis?
PLoS One 2012; 7: e39296.
10. Nagaraja SB, Kumar AMV, Sachdeva KS, Ramachandran R, Satyanarayana S, Bansal A, Parmar M, Chadha S, Nair S, Kumar A, Hinderaker S, Edginton M, Dewan PK. Is one sputum specimen as good as two during follow-up cultures for monitoring multi drug resistant tuberculosis patients in India?
PLoS One 2012; 7: e45554.
11. Balakrishnan S, Vijayan S, Nair S, Subramoniapillai J, Mrithyunjayan S, Wilson N, Satyanarayana S, Dewan PK, Kumar AMV, Karthickeyan D, Willis M, Harries AD, Nair SA. High diabetes prevalence among tuberculosis cases in Kerala, India.
PLoS One 2012; 7: e46502.
12. Malhotra S, Zodpey SP, Chandra S, Vashist RP, Satyanarayana S, Zachariah R, Harries AD. Should sputum smear examination be carried out at the end of the intensive phase and end of treatment in sputum smear negative pulmonary TB patients?
PLoS One 2012; 7: e49238.
13. Ali E, Zachariah R, Hinderaker SG, Satyanarayana S, Kizito W, Alders P, Shams Z, Allaouna M, Draguez B, Delchevalerie P, Enarson DA. Does the 65cm height cut-off as age proxy exclude children eligible for nutritional assessment in Bangladesh?
Public Health Action 2012; 2: 103 – 106.
14. Shams Z, Zachariah R, Enarson DA, Satyanarayana S, van den Bergh R, Ali E, Alders P, Manzi M, Allaouna M, Draguez B, Delchevalerie P, Vernaeve L, Harries AD. Severe malnutrition in children presenting to facilities in an urban slum in Bangladesh.
Public Health Action 2012; 2: 107– 111.

15. Ram S, Kishore K, Batio I, Bissell K, Zachariah R, Satyanarayana S, Harries AD. Pre-treatment loss to follow-up among smear-positive pulmonary tuberculosis cases: a 10-year audit of national data from Fiji.
Public Health Action 2012; 2: 138– 141.
16. Satyanarayana S, Nair SA, Chadha SS, Sharma G, Yadav S, Mohanty S, Kamineni V, Wilson NC, Harries AD. Health-care seeking among people with cough of 2 weeks or more in India: Is passive case finding sufficient?
Public Health Action 2012; 2: 157 – 161.
17. Satyanarayana S, Kumar AMV, Sharath BN, Harries AD. Fast-track writing of a scientific paper with 30 authors: how to do it.
Public Health Action 2012; 2: 186 – 187.
18. Rani MA, Shriraam V, Zachariah R, Harries AD, Satyanarayana S, Tetali S, Anchala R, Muthukumar D, Sathiyasekaran BWC. Does a nutrition education programme change the knowledge and practice of healthy diets among high school adolescents in Chennai, India?
Health Education Journal 2012: 72; 733-741. doi: 10.1177/0017896912461093.
19. Kundu D, Kumar AV, Satyanarayana S, Dewan PK, Nair SA, Khaparde K, Nayak P, van der Bergh R, Manzi M, Enarson DA, Deshpande MR, Chandraker S. Can follow-up examination of tuberculosis patients be simplified? A study in Chhattisgarh, India
PLoS One 2012; 7: e51038.
20. Bissell K, Harries AD, Reid AJ, Edginton M, Hinderaker SG, Satyanarayana S, Enarson DA, Zachariah R. Operational research training: the course and beyond.
Public Health Action 2012: 2(3); 92-97.

2013: [42]

1. Bishnu B, Bhaduri S, Kumar AMV, Click ES, Chadha VK, Srinath S, Nair SA, Gupta D, Ahmed QT, Sarkar S, Paul D, Dewan P. What are the reasons for poor uptake of HIV testing among patients with TB in an Eastern India District?
PLoS ONE 2013; 8: e 55229.
2. India Tuberculosis – Diabetes Study Group. Screening of patients with tuberculosis for diabetes mellitus in India
Trop Med Int Health 2013; 18: 636 - 645
3. India Diabetes Mellitus – Tuberculosis Study Group. Screening of patients with diabetes mellitus for tuberculosis in India
Trop Med Int Health 2013; 18: 646-654
4. Dendup T, Dorji T, Edginton ME, Kumar AMV, Wangchuk D, Dophu U, Jamtsho T, Rinzin C. Childhood tuberculosis in Bhutan : profile and treatment outcomes.
Public Health Action 2013; 3: 11-14.

5. Shah SK, Kumar AMV, Dogar OF, Khna MA, Qadeer E, Tahseen S, Masood F, Chandio AK, Edginton ME. Xpert MTB/RIF under routine conditions in diagnosing pulmonary tuberculosis: a study in two hospitals in Pakistan.
Public Health Action 2013; 3: 20-22.
6. Vishnu PH, Bhat P, Bansal A, Satyanarayana S, Alavadi U, Ohri BS, Shrinivas MSR, Desikan P, Jaju J, Rao VG, Moonan PK. Is bleach-sedimented smear microscopy an alternative to direct microscopy under programme conditions in India?
Public Health Action 2013; 3: 23-25.
7. Kumar AMV, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, Lauritsen JM, Rieder HL. Efficient, quality-assured data capture in operational research through innovative use of open-access technology.
Public Health Action 2013; 3: 60-62.
8. Basnet R, Shrestha BR, Nagaraja SB, Basnet B, Satyanarayana S, Zachariah R. Universal health coverage in a regional Nepali hospital: who is exempted from payment?
Public Health Action 2013; 3: 90-92.
9. Khann S, Tan Mao E, Rajendra YP, Satyanarayana S, Nagaraja BN, Kumar AMV. Linkage of presumptive multidrug resistant tuberculosis (MDR-TB) patients to diagnostic and treatment services in Cambodia
PLoS ONE 2013; 8: e59903.
10. Sharma SK, Mohan A, Chauhan LS, Narain JP, Kumar P, Behera D, Sachdeva KS, Kumar A, Agarwal P, Awadh NT, Bansal A, Baruah S, Baruwa P, Balasangameshwara VH, Balasubramanian R, Bhardwaj AK, Bhargav S, Chadha S, Chaddha VK, Chhatwal M, Da Costa AL, Dash DP, Dep J, Dhingra S, Dhooria Harmeet S, Frieden TR, Garg A, Granich R, Gulati V, Gupta D, Gupta D, Gupta KB, Gupta KN, Jaikishan, Janmeja AK, Jawahar MS, Jethani SL, Jindal SK, John KR, Kalra OP, Kalra VP, Kannan AT, Kayshap S, Keshav Chander G, Khushwa SS, Kushwaha RS, Kumar V, Laskar B, Leela Itty Amma KR, Leuva AT, Maitra Malay K, Mesquita AM, Mathew T, Mundade Y, Munje R, Nagpal S, Nagaraja C, Nair S, Narayanan OR, Paramasivan CN, Parmar M, Prasad R, Phukan AC, Prasanna R, Purty A, Ramachandran R, Ramachandran R, Ravindran C, Reddy Raveendra HR, Sahu S, Santosha, Sarin R, Sarkar S, Sarma KC, Saxena P, Sehgal S, Sharath N, Sharma G, Sharma N, Shridhar PK, Shukla RS, Singh O, Singh NT, Singh V, Singla R, Sinha N, Sinha P, Sinha S, Solanki R, Sreenivas A, Srinath S, Subhakar K, Suri JC, Talukdar P, Tonsing J, Tripathy SP, Vaidyanathan P, Vashist RP, Venu K.Contribution of medical colleges to tuberculosis control in India under the Revised National Tuberculosis Control Programme (RNTCP): Lessons learnt & challenges ahead.
Indian J Med Res. 2013; 137: 283-94
11. Mlilo N, Sandy C, Harries AD, Kumar AMV, Masuka N, Nyathi B, Edginton M, Isaakidis P, Manzi M, Siziba N. Does the type of treatment supporter influence tuberculosis treatment outcomes in Zimbabwe?
Public Health Action 2013; 3: 146-148.

12. Kilale AM, Ngowi BJ, Mfinanga GS, Egwaga S, Doulla B, Kumar AMV, Khogali M, van Griensven J, Harries AD, Zachariah R, Hinderaker SG. Are sputum samples of retreatment tuberculosis reaching the reference laboratories? A 9-year audit in Tanzania.
Public Health Action 2013; 3: 156-159.
13. Kumar AMV, Satyanarayana S, Wilson N, Zachariah R, Harries AD. Operational research capacity building in Asia: innovations, successes and challenges of a training course.
Public Health Action 2013; 3: 186-188.
14. Ananthakrishnan R, Kumar K, Ganesh M, Kumar AMV, Krishnan N, Swaminathan S, Edginton M, Arunagiri K, Gupta D. The profile and treatment outcomes of the older (aged 60 years and bove) tuberculosis patients in Tamilnadu, South India.
PLoS ONE 2013; 8: e67288
15. Shastri S, Boregowda PH, Rewari BB, Tanwar S, Shet A, Kumar AMV. Scaling up antiretroviral treatment services in Karnataka, India: impact on CD4 counts of HIV-infected people.
PLoS ONE 2013; 8: e72188.
16. Achanta S, Jaju J, Kumar AMV, Nagaraja SB, Shamrao SRM, Bandi SK, Kumar A, Satyanarayana S, Harries AD, Nair SA, Dewan PK. Tuberculosis management practices by private practitioners in Andhra Pradesh, India.
PLoS ONE 2013; 8: e71119.
17. Shastri S, Satyanarayna S, Nagaraja SB, Kumar AMV, Rewari B, Harries AD, Zachariah R. The journey to antiretroviral therapy in Karnataka, India: who was lost on the road?
J Int AIDS Soc 2013; 16: 18502.
18. Palanivel C, Kumar AMV, Mahalakshmi T, Govindarajan S, Claassens M, Satyanarayana S, Gurumurthy D, Vasudevan K, Purty A, Paulraj AK, Raman KV. Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India.
Public Health Action 2013; 3: 220 - 223.
19. Tripathy JP, Srinath S, Naidoo P, Ananthakrishnan R, Bhaskar R. Is physical access an impediment to tuberculosis diagnosis and treatment? A study from a rural district in North India.
Public Health Action 2013; 3: 235 – 239. .
20. Reza LW, Satyanarayana S, Pandey A, Kumar S, Devendrappa NM, Anand L, Singh G, Kumar AMV, Chadha SS, Wilson N, Sachdeva KS, Nair SA. LED fluorescence microscopy increase the detection of smear-positive pulmonary tuberculosis in medical colleges of India.
Public Health Action 2013; 3: 240-242.
21. Siddiquea BN, Islam MA, Bam TS, Satayanrayana S, Enarson DA, Reid AJ, Husain MdA, Ahmed SM, Ferdous S, Ishikawa N. High quit rate among smokers with tuberculosis in a modified smoking cessation programme in Dhaka, Bangladesh.
Public Health Action 2013; 3: 243 – 246.
22. Nayak P, Kumar AMV, Claassens M, Enarson DA, Satyanarayana S, Kundu D, Khaperde K, Agrawal TK, Dapkekar S, Chandraker S, Nair SA. Comparing same day sputum microscopy with conventional sputum microscopy for the diagnosis of tuberculosis – Chhattisgarh, India.
PLoS ONE 2013; 8: e74964.

23. Sun AY, Pai M, Salje H, Satyanarayana S, Deo S, Dowdy DW. Modelling the impact of alternative strategies for rapid molecular diagnosis of tuberculosis in South east Asia
Am J Epidemiol 2013; 178: 1740 - 1749.
24. Kumar R, Chauhan G, Satyanarayana S, Lal P, Singh RJ, Wilson NC. Assessing compliance to smoke-free legislation: results of a sub-national survey in Himachal Pradesh, India
WHO South-East Asia Journal of Public Health 2013; 2: 52-56.
25. Reza LW, Satyanarayana S, Enarson DA, Kumar AMV, Sagili K, Kumar S, Prabahakar LA, Devendreppa NM, Pandey A, Wilson N, Chadha S, Thapa B, Sachdeva KS, Kohli MP. LED-Fluorescence microscopy for diagnosis of pulmonary tuberculosis under programmatic conditions in India
PLoS ONE 2013; 8: e75566.
26. Deepa D, Achanta S, Jaju J, Rao K, Samyukta R, Kumar AMV, Vishnu PH. The impact of isoniazid resistance on the treatment outcomes of smear-positive re-treatment tuberculosis patients in the State of Andhra Pradesh, India
PLoS ONE 2013; 8: e76275.
27. Nandakumar KV, Duraisamy K, Balakrishnan S, Sagili KD, Satyanarayana S, Kumar AMV, Enarson DA. Outcome of tuberculosis treatment in patients with diabetes mellitus treated in the revised national tuberculosis control programme in Malappuram District, Kerala, India.
PLoS ONE 2013; 8: e76189.
28. Patra S, Lukhmana S, Tayler-Smith K, Kannan AT, Satyanarayana S, Enarson DA, Nagar RK, Marcel M, Reid T. Profile and treatment outcomes of elderly patients with tuberculosis in Delhi, India: implications for their management.
Trans Roy Soc Trop Med 2013; 107: 763 - 768.
29. Prakash BC, Ravish KS, Prabhakar B, Ranganath TS, Naik B, Satyanarayana S, Isakidis P, Kumar AMV. Tuberculosis-diabetes mellitus bidirectional screening at a tertiary care centre, South India.
Public Health Action 2013; 3 (Suppl 1): S18 – S22.
30. Kumpatla S, Sekar A, Achanta S, Sharath BN, Kumar AMV, Harries AD, Viswanathan V. Characteristics of patients with diabetes screened for tuberculosis in a tertiary care hospital in South India.
Public Health Action 2013; 3 (Suppl 1): S23 - S28.
31. Dave P, Shah M, Chauhan M, Kumar AMV, Harries AD, Malhotra S, Pujara K, Patel P, Mane M, Thakkar A. Bharaswadkar S, Sharath BN, Achanta S. Screening patients with tuberculosis for diabetes mellitus in Gujarat, India
Public Health Action 2013; 3 (Suppl 1): S29 – S33.
32. Naik B, Kumar AMV, Satyanarayana S, Suryakant MD, Swamy NMV, Nair S, Isaakidis P, Harries AD. Is screening for diabetes among tuberculosis patients feasible at the field level?
Public Health Action 2013; 3 (Suppl 1): S34 – S37.
33. Nair S, Kumari AK, Subramonianpillai J, Shabna DS, Kumar SM, Balakishnan S, Naik B, Kumar AMV, Isaakidis P, Satyanarayana S. High prevalence of undiagnosed diabetes among tuberculosis patients in peripheral health facilities in Kerala.
Public Health Action 2013; 3 (Suppl 1): S38 – S42.

34. Achanta S, Tekumalla RR, Jaju J, Purad C, Chepuri R, Samyukta R, Malhotra S, Nagaraja SB, Kumar AMV, Harries AD. Screening tuberculosis patients for diabetes in a tribal area in South India. **Public Health Action 2013; 3 (Suppl 1): S43 – S47.**
35. Jali MV, Mahishale VK, Hiremath MB, Satyanarayana S, Kumar AMV, Nagaraja SB, Isaakidis P. Diabetes and smoking among tuberculosis patients in a tertiary care centre in Karnataka, India. **Public Health Action 2013; 3 (Suppl 1): S51 – S53**
36. Bhat PG, Kumar AMV, Naik B, Satyanarayana S, Deepak KG, Nair SA, Suryakanth MD, Heldal E, Enarson DA, Reid AJ. Intensified tuberculosis case finding among malnourished children in nutritional rehabilitation centres of Karnataka, India: missed opportunities. **PLOS ONE 2013; 8: e84255**
37. Kumar B, Shrivastava J, Satyanarayana S, Reid AJ, Ali E, Zodpey S, Agnani M. How effective is the integration of facility and community-based management of severe acute malnutrition in India? **Public Health Action 2013; 3: 265 – 270.**
38. Njagi SK, Mugo NR, Reid AJ, Satyanarayana S, Tayler-Smith K, Kizito W, Kwatampora J, Waweru W, Kimani J, Smith JS. Prevalence and incidence of cervical intra-epithelial neoplasia among female sex workers in Korogocho, Kenya. **Public Health Action 2013; 3: 271 – 275.**
39. Kumar RS, Kumar AMV, Claassens M, Banurekha VV, Gomathi NS, Venkatesan P, Swaminathan S. Number of sputum specimens during treatment follow-up of tuberculosis patients: two or one? **Public Health Action 2013; 3: 304-307.**
40. Patel J, Dave P, Satyanarayana S, Kumar AMV, Shah A, Ananthakrishnan R, Ratnu A. Pretreatment sputum smear grade and smear positivity during follow-up of TB patients in Ahmedabad, India. **Public Health Action 2013; 3: 308 – 310.**
41. Lim LK-Y, Enarson DA, Reid AJ, Satyanarayana S, Cutter J, Kyi Win KM, Chee CB-E, Wang YT. Notified tuberculosis among Singapore residents by ethnicity, 2002- 2011. **Public Health Action 2013; 3: 311-316.**
42. Wahome E, Makori L, Gikera M, Wafula J, Chakaya J, Edginton ME, Kumar AMV. Tuberculosis treatment outcomes among hospital workers at a public teaching and national referral hospital in Kenya. **Public Health Action 2013; 3: 323-327.**

VIEWPOINT, OPINION AND REVIEW PAPERS:

2009: [0]

None

2010: [2]

1. Edginton ME, Miller DL, Burney P, El Sony AI, Lwilla FI, O'Brien R, Roldan MB, Roldan A, Srinath S. Surveillance for MDR-TB: is there an obligation to ensure treatment for individuals identified with MDR-TB?
   Int J Tuberc Lung Dis 2010; 14: 1094-1096.
2. Edginton ME, O'Brien R, El SA, Roldan A, Srinath S. Informed consent.
   Int J Tuberc Lung Dis 2010; 14: 938.

2011: [2]

1. Zachariah R, Reid T, Srinath S, Chakaya J, Legins K, Karunakara U, Harries AD. Building leadership capacity and future leaders in operational research in low-income countries: why and how?
   Int J Tuberc Lung Dis 2011; 15: 1426 - 1435.
2. Harries AD, Lin Y, S Srinath, Lonnroth K, Liang Li, Wilson N, Chauhan LS, Zachariah R, Baker MA, Jeon CY, Murray MB, Maher D, Bygbjerg IbC, Enarson DA, Billo NE, Kapur A. The looming epidemic of diabetes-associated tuberculosis – learning lessons from HIV-associated tuberculosis
   Int J Tuberc Lung Dis 2011; 15: 1436 – 1444.

2012: [11]

1. Zachariah R, Ali E, Dahmane E, Srinath S, Reid T, Harries AD. The need for building design professionals in operational research in low-income countries [correspondence]
   Int J Tuberc Lung Dis 2012; 16: 565-566.
2. Kumar A, Kumar AMV, Gupta D, Kanchar A, Mohammed S, Srinath S, Tripathy S, Rajacekaran S, Chan PL, Swaminathan S, Dewan PK. Global guidelines for treatment of tuberculosis among persons living with HIV: unresolved issues.
   Int J Tuberc Lung Dis 2012; 16: 573-578.
3. Edginton M, Enarson D, Zachariah R, Reid T, Satyanarayana S, Bissell K, Hinderaker SG, Harries T. Why ethics is indispensible for good quality operational research.
   Public Health Action 2012; 2: 21-22.
4. Zachariah R, Harries AD, S Srinath, Ram S, Viney K, Singogo E, Lal P, Mendoza-Tikona A, Sreenivas A, Aung NW, Sharath BN, Kanyerere H, van Soelen N, Kirui N, Ali E, Hinderaker SG, Bissell K, Enarson DA, Edginton ME. Language in tuberculosis services: can we change to patient-centred terminology and stop the paradigm of blaming patients?
   Int J Tuberc Lung Dis 2012; 16: 714-717.
5. Sachdeva KS, Kumar A, Dewan P, Kumar A, Satyanarayana S. New vision for the Revised National Tuberculosis Control Programme (RNTCP): universal access – "reaching the unreached".
   Indian J Med Res 2012; 135: 690-694.
6. Kumar AMV, Gupta D, Gupta RS, Satyanarayana S, Wilson N, Zachariah R, Lawn SD, Harries AD. HIV testing in people with presumptive tuberculosis: time for implementation.
   Lancet Respir Dis 2012, October 24: doi: 10.1061/S2213-2600(12)70050-4.

7. Zachariah R, Srinath S, Edginton ME (2012) In reply to 'Language in tuberculosis services'.
Int J Tuberc Lung Dis 2012; 16: 1129-1130.
8. Edginton ME, El Sony AI, Kim SJ, Roldan A, Satyanarayana S. Important research, but did the participants consent?
Int J Tuberc Lung Dis 2012; 16(4) :427
9. Hans L Rieder, Ajay MV Kumar. EpiData Software for Operations Research in Tuberculosis Control: A course manual developed by EpiData Promoters in collaboration with the EpiData Association and the International Union Against Tuberculosis and Lung Disease. Accessed on 15.12.2012 from **http://tbrieder.org/epidata/course_abcd.pdf**
10. Kumar AMV. UNIT 13: Three I's – Reducing the burden of TB among HIV-infected patients. Block 3: Tuberculosis. Course manual of Post-Graduate Diploma in HIV Medicine. Indira Gandhi National **Open University (IGNOU), New Delhi, 2012.**
11. Kumar AMV. UNIT 12: National Programme of collaborative TB/HIV activities. Block 3: Tuberculosis. Course manual of Post-Graduate Diploma in HIV Medicine. Indira Gandhi National Open University **(IGNOU), New Delhi, 2012.**

2013: [6]

1. Zachariah R, Reid T, Van den Bergh R, Dahmane A, Kosgei RJ, Hinderaker SG, Tayler-Smith K, Manzi M, Kizito W, Khoghali M, Kumar AM, Baruani B, Bishinga A, Kilale A, Nqobile M, Patten G, Sobry A, Cheti E, Nakanwagi A, Enarson DA, Edginton ME, Upshur R, Harries AD. Applying the ICMJE authorship criteria to operational research in low-income countries: the need to engage programme managers and policy makers.
Trop Med Int Health 2013; 18: 1025 – 1028.
2. Harries AD, Kumar AMV, Satyanarayana S, Bissell K, Hinderaker SG, Edginton M, Reid AJ, Zachariah R. References for scientific papers: why not standardise to one global style?
Public Health Action 2013; 3: 255 – 257.
3. Satyanarayana S, Kumar AMV, Wilson N, Kapur A, Harries AD, Zachariah R. Taking on the diabetes – tuberculosis epidemic in India: paving the way through operational research.
Public Health Action 2013; 3 (Suppl 1): S1 – S2.
4. Harries AD, Satyanarayana S, Kumar AMV, Nagaraja SB, Isaakidis P, Malhotra S, Achanta S, Naik B, Wilson N, Zachariah R, Lönnroth K, Kapur A. Epidemiology and interaction of diabetes mellitus and tuberculosis and the challenges for care: a review.
Public Health Action 2013; 3 (Suppl 1): S3 – S9.
5. Kumar AM, Satyanarayana S, Wilson N, Zachariah R, Harries AD. Operational research capacity building in Asia: innovations, successes and challenges of a training course.
Public Health Action 2013; 3(2): 186-188.
6. Central TB Division, Directorate General Health Services, Ministry of Health and Family Welfare, Government of India. Screening of Tuberculosis Patients for Diabetes Mellitus (A training module for staff of Revised National TB Control Programme. March 2013.)

11.

Operational research capacity building in Asia: Innovations, successes and challenges of a training course

Kumar AMV, Satyanarayana S, Wilson N, Zachariah R, Harries AD.
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SUMMARY

A structured training course on Operational Research (OR), based on the Union/MSF model, was conducted in the South Asian region in 2012. Many innovations were introduced into the administration, structure and content of the course. 11 of 12 participants successfully completed all pre-defined milestones. Several challenges were identified. The main challenges included shortage of time, especially for data analysis and interpretation, and insufficient numbers of experienced facilitators. Appropriate modifications have been made to the structure and processes of the next course being run in 2013. We describe these modifications and the innovations, successes and challenges of this model of training.

INTRODUCTION

Operational Research (OR) is increasingly recognized as a science that is important to reduce the gap between knowledge and implementation, to optimize the performance of health programmes and to achieve improved health outcomes.[1] Despite recognition of the necessity of OR by global health organizations, donor agencies and national health programmes, the amount of research in global health that actually happens and gets published in both resource-limited and industrialised countries still remains limited.[2-4] This may be partly due to the limited capacity of health professionals to conduct and publish OR. Drawing on lessons from several OR capacity building initiatives in the past,[5-7] the Union/MSF model was conceived and has been implemented since 2009 with excellent outputs – trained participants in low- and middle-income countries who have become independent facilitators and mentors in subsequent courses; presentation at international conferences; publications in peer-reviewed journals; more importantly, impacting national/local policy and practice.[8] In 2012, we replicated this training model for health professionals in the South Asian region with several innovative modifications drawn from lessons learnt from previous courses. In the spirit of applying operational research thinking to 'OR capacity building', we describe the innovations, the successes and the challenges of the first South Asian OR course.[9]

METHODS

The Union/MSF training model has been described in detail elsewhere.[2, 8] In brief, this is an output-oriented mentorship programme with three 5-day modules interspersed over a period of 9-12 months – module 1 on 'research protocol development', module 2 on 'data entry and analysis' and module 3 on 'scientific paper writing'. Participants who submitted a scientific manuscript for publication to a peer-reviewed journal within 4 weeks of completion of module 3 were considered to have successfully completed the course.

RESULTS

In this first Asian course held in Nepal in 2012, twelve participants, mostly health professionals (physicians, programme managers, paramedical workers and data analysts) working in health programmes from India, Nepal, Bhutan, Bangladesh, Pakistan, Sri Lanka, Indonesia, Timor Leste and Cambodia, selected through a competitive process, were required to attend the three modules and achieve interim milestones linked to each module to remain in the course. The number of facilitators varied from module to module – six for modules 1 and 3 and two for module 2.

Eleven of twelve participants successfully completed all the milestones and submitted 12 scientific manuscripts (one participant completed two projects) on topics ranging from tuberculosis, HIV and tobacco control to health system financing, for publication in international peer-reviewed journals. Of these, six papers were accepted for publication within three months of submission; how many more will be published and what their impact

on policy and practice will be is being tracked. One participant met milestones for modules 1 and 2 successfully, but was not able to complete the project in time; the long delays in local ethics approval demotivated the participant to continue on the project.

Three junior facilitators from this course will facilitate independently and two participants from this course will participate as junior facilitators in the next course scheduled to start in February 2013.

There were several innovations introduced into the structure and process of the OR course, which are summarized in the **Table**. We also faced several challenges during the course, which are listed in the **Box**.

DISCUSSION

The success of the Union-MSF Courses was replicated in Asia with most participants completing their milestones. There were several innovations with this course. The positioning of modules 1 and 2 back-to-back helped in two ways – one technical and other logistical. First, the 2-3 month gap between module 1 and module 2 in the original Union/MSF model meant that some participants started data collection and capture before module 2 with several errors. This often meant that they had to repeat their data capture efforts once they learnt more appropriate ways of data management in module 2. Having modules 1 and 2 back-to-back meant that the participants were equipped right from the start with not only a clear study protocol but also with the necessary quality-assured tools for data capture and analysis. Second, the positioning of the two modules also meant that only two trips were required to the course location instead of three, thus saving on resources and travel costs with an overall reduction by 25-30%. However, this change posed challenges for female participants, especially those with young children, who had to be away from family for two weeks.

The peer support strategy was widely appreciated and had multiple advantages. It promoted the concept of peer support and learning, and this provided opportunities for fast learners to start getting trained as facilitators. Often, the fast learner was quick to understand the point and thus was able to engage in the support and teaching of his/her peer. This took some of the pressure off facilitators, and was one of the reasons why module 2 could be managed with just two facilitators.

Organizing course content in the form of a website and sharing it via Dropbox, a file-sharing service, promoted easy access for facilitators (often from different countries) prior to the module for their review and inputs. Its offline access feature is advantageous obviating the need for continuous internet connectivity.

There were also challenges. The main challenge was that of shortage of time (especially for the data analysis component) and facilitators experienced in conducting and publishing OR. To address these challenges, the following modifications were made to the course structure in 2013. Module 2 has been extended by a day and module 3 by two days – with the additional time to be used for teaching participants about data analysis and

supporting individual projects with data analysis support. We have also increased the number of facilitators to 8 for each module – divided into 4 groups of two (one junior and one senior facilitator), with each group having to mentor three participants. From the feedback of the participants, we will also provide module 2 course materials as a spiral-bound book instead of a course folder and examine how this works. If participants find it more user-friendly than the folders, we intend to adopt this for the other modules as well. Paying up-front costs for open access publications (500-1500 USD) had also been a problem and the way forward is to plan this within the course budget.

While this description is limited by low numbers, we believe that the experience will be of value to people involved in or interested in conducting similar courses across the globe. Overall, the South Asian OR course successfully achieved its outputs and provided several lessons for optimizing it further. We hope that the participants inspired by this course continue their work and become leaders in OR in their own networks and countries.[10]

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AUTHOR CONTRIBUTIONS:

Ajay Kumar wrote the first draft. All the other co-authors reviewed the draft, provided critical inputs and helped in revision of the manuscript. All authors approved the final version.

CONFLICTS OF INTEREST:

None declared.

REFERENCES

1. Zachariah R, Ford N, Maher D, Bissell K, Van den Bergh R, Van Den Boogaard W, et al. Is operational research delivering the goods? The journey to success in low-income countries. Lancet Infect Dis 2012;DOI:10.1016/S1473-3099(11)70309-7.
2. Harries A D, Rusen I D, Reid T, Detjen A K, Berger S D, Bissell K, et al. The Union and Médecins Sans Frontières approach to operational research. [State of the Art Series. Operational Research. Number 2 in the series]. Int J Tuberc Lung Dis 2011;15:144-54.
3. Galsworthy M J, Hristovski D, Lusa L, Ernst K, Irwin R, Charlesworth K, et al. Academic output of 9 years of EU investment into health research. Lancet 2012;380:971-2.
4. Royston G. Meeting global health challenges through operational research and management science. Bull World Health Organ 2011;89:683-8.
5. Laserson K F, Binkin N J, Thorpe L E, Laing R, Iademarco M F, Bloom A, et al. Capacity building for international tuberculosis control through operations research training. Int J Tuberc Lung Dis 2005;9:145-50.
6. Ohkado A, Pevzner E, Sugiyama T, Murakami K, Yamada N, Cavanaugh S, et al. Evaluation of the international training course to build programmatic capacity for tuberculosis control. Int J Tuberc Lung Dis 2010;14:371-3.
7. Zachariah R, Harries A D, Ishikawa N, Rieder H L, Bissell K, Laserson K, et al. Operational research in low-income countries: what, why, and how? Lancet Infect Dis 2009;9:711-7.
8. Bissell K, Harries A D, Reid A J, Edginton M, Hinderaker S G, Satyanarayana S, et al. Operational research training: the course and beyond. Public Health Action 2012;2:92-7.
9. Rusen I D. Operational research on operational research: much more to be learned. (Editorial). Int J Tuberc Lung Dis 2011;15:1421.
10. Zachariah R, Reid T, Srinath S, Chakaya J, Legins K, Karunakara U, et al. Building leadership capacity and future leaders in operational research in low-income countries: why and how? [State of the Art Series. Operational Research. Number 11 in the series]. Int J Tuberc Lung Dis 2011;15:1426-35.

Table: Innovations introduced into the Union-MSF model of operational research training in South Asia, 2012.

Innovation	Description	Advantage
Adjoining the first two modules	Modules 1 and 2 were conducted back-to-back with a weekend break in between.	This reduced overall costs by 25-30%
Course venue	Nepal was chosen as the course venue which provided for 'VISA on arrival' for all the participants and facilitators.	This simplified travel logistics and saved time and inconvenience for participants and organizers.
Introducing new sessions into the curriculum	While the core modules remained the same, some new sessions were introduced. For example, a session on 'how to take back-up of data' using a combination of open-access tools like Dropbox (http://www.dropbox.com) and FreeCommander (http://www.freecommander.com) was taught in module 2. A session on organizing and managing references was taught in module 3 using another open access tool, Mendeley (http://www.mendeley.com).	This met some of the felt-needs of the participants in the described areas.
Organization of course materials	All participants, in addition to a hard back course folder, were provided a CD-ROM containing all the course materials organized like a website, which was then shared via Dropbox, a file-sharing service	This facilitated user-friendly access for participants and facilitators (often from different countries) of course material prior to and during the module
Introducing a milestone for Module 2	For the first time, participants were required to submit the following as outputs of Module 2 - data collection plan, electronic data capture formats in EpiData (http://www.epidata.dk) and a plan for data analysis including dummy tables and figures.	This helped in emphasizing the value of quality-assurance in data capture and analysis in operational research, one of the key objectives of the course.
Mentoring junior facilitators	The facilitators were paired to provide mentorship to four participants in such a way that one senior facilitator* was paired with a junior facilitator. All the junior facilitators were participants in previous courses.	This helped in grooming the junior facilitator to become an independent trainer in the future.
Using SurveyMonkey	SurveyMonkey (http://www.surveymonkey.com), an online survey entry and analysis software was used for participant evaluation at the end of the course.	This saved time in analysing evaluations and providing feedback

*A senior facilitator is one who is experienced in both conducting and publishing papers and has excellent writing skills.

BOX: CHALLENGES FACED DURING IMPLEMENTATION OF THE UNION–MSF MODEL OF OPERATIONAL RESEARCH TRAINING IN SOUTH ASIA, 2012

- **Burden of work for facilitators:** Having only two facilitators in module 2 created a large burden of work. Similarly, six facilitators in module 1 and 3 were also insufficient, especially in Module 3, as each facilitators' group had four participants. With each group writing four papers, in literally five days, this number was too small.
- **Data analysis and interpretation:** Most participants complained that not enough time was given in class to this important subject.
- **Better organization of course material:** Several participants requested that the course material be organized as a book instead of a course folder in order to increase its shelf life.
- **Delays in local ethics approval:** Some participants had to wait for a long time (ranging from 1-6 months) before obtaining ethics approval from their national/local ethics committees. Given the tight timelines of the course, this left them with very little time for the actual conduct of the project.
- **Scheduling of the sessions on 'literature search and managing references:** Several participants commented on the need for bringing this session upstream to module 1 rather than module 3. This has now been done.
- **Publication in open access journals for enhanced dissemination in resource-limited settings:** This implies additional load on the course budget (ranging from 500-1500 USD per article).
- **Portal of call for applications:** We received only 15 applications to our initial call which was through the national tuberculosis programme managers of countries in the region. We then informed the WHO focal points of countries and the contacts of non-governmental organizations and extended the deadline for application by a week. The number of applications rose to 50 in a week's time. Drawing on these lessons, we advertised on http://www.devnetjobs.org/ in 2013 and got 128 applications.

WHO – World Health Organisation

12.

Operational research capacity building using 'The Union/MSF' model: Adapting as we go along

Kumar AMV, Zachariah R, Satyanarayana S, Reid AJ, Van den Bergh R, Tayler-Smith K, Khogali M, Harries AD. BMC research notes. 2014;7(1):819.

Background

We have conducted 23 operational research (OR) courses since 2009, based on 'The Union/ Médecins sans Frontières (MSF)' model, now popularly known as SORT-IT (Structured Operational Research and Training Initiative) model - wherein participants are mentored through the whole research process from protocol development (module 1) to data analysis (module 2) to publication (module 3) over a period of 9-12 months. We have faced a number of challenges including shortage of time, especially for data analysis and interpretation, and a heavy mentorship burden on limited numbers of experienced facilitators. To address these challenges, we have made several modifications to the structure of the OR course. In this article, we describe the revised structure and our experience (successes and challenges) of implementing it in Asia in 2013.

Findings

The key changes introduced included extending the duration of the course modules (by a day each in module 1 and 2 and by three days in module 3), increasing the numbers of facilitators and standardizing milestones related to data entry and analysis. We successfully implemented this revised structure in the second Asian OR Course held in Nepal in 2013. Eleven of twelve participants successfully completed all the milestones and submitted 13 scientific manuscripts (two participants completed two projects) to international peer-reviewed journals. Though, this posed two challenges – increased costs and increased time away for faculty and participants.

Conclusions

The revised structure of 'The Union/MSF' model of OR capacity building addressed previous issues of insufficient time and overburdened mentors and we intend to continue with this model for future courses.

BACKGROUND

Since 2009, the International Union Against Tuberculosis and Lung Disease (The Union) and Médecins sans Frontières (MSF) have been involved in building capacity of health professionals in low- and middle-income countries to conduct and publish operational research (OR). We use a practical and output-based approach with hands-on mentorship and has been described in detail elsewhere. [1-3] In brief, this model is implemented over a period of 9-12 months and consists of three modules – Module 1 on 'research protocol development', Module 2 on 'data entry and analysis' and Module 3 on 'scientific paper writing'. To be successful, participants have to design and conduct an OR project and at the end of the course submit a scientific manuscript to a peer-reviewed journal. We have achieved excellent results with this model, with more than 85% of participants completing the course and more than 80% of submitted manuscripts being published. The Special Programme for Research and Training in Tropical Diseases (TDR) at the World Health Organization (WHO) has adopted this model as "The Structured Operational Research and Training InitiaTive (SORT IT)" and is committed to its global expansion.[3]

To date, we have conducted 23 courses (17 courses completed and six on-going) based on The Union/MSF model. Over the years, we have faced a number of challenges in implementation of these courses, including shortage of time for data analysis, data interpretation and manuscript drafting, and a high mentorship burden on a limited pool of facilitators.[4] To address these challenges, we have introduced several changes to the structure of the OR course. In this article, we summarize these changes and share our experience of implementing a revised OR course structure in Asia.

CONTENTS OF THE ADAPTED COURSE

The changes made to the course structure are summarized in the **Table 1**. They include an increase in the number of days for each module, an increase in the number of facilitators and strengthened milestones related to Module 2. In Module 1, an additional day was used to introduce new sessions on how to systematically search for published literature and organize references. In Module 2, an added day was dedicated entirely to data analysis. Module 3 was extended by three days in order to a) provide more intensive and tailored support to participants for analysing their data, b) give participants more time to conduct a thorough on-line literature review and c) include a new plenary session on manuscript 'titles and abstracts'. The number of facilitators was increased and standardised for each module, in order to ensure similar standard mentor-participant pairings in Modules 1 and 3, and to allow junior facilitators the opportunity to be trained by senior facilitators within each pairing group. The milestones relating to Module 2 were strengthened and standardized (**Table 1**).

We implemented this revised structure in the second Asian OR Course held in Nepal in 2013. We had twelve participants, mostly health professionals working in programmes from India, China, Nepal, Bhutan, Bangladesh, Pakistan and Sri Lanka. Eleven of twelve participants

successfully completed all the milestones with two of them completing two research projects each. Thus a total of 13 scientific manuscripts were submitted to international peer-review journals. One participant was not able to complete the research project in time due to changing her place and institution of work. The key advantages and challenges of the revised structure, as mentioned in the end-of–module feedback of participants and facilitators are summarized in the **Table 2**.

DISCUSSION

There were two main problems in our courses - shortage of time for data analysis and interpretation and high mentorship load. The problem of time shortage for data analysis was addressed in several ways. First, the additional days in Module 2 and 3 were primarily used to provide tailored data analysis support for research projects. Second, the number of facilitators for Module 2 was increased to six so that each facilitator supported only two participants in data analysis. Third, the strengthened milestone focussing on data analysis just before Module 3 increased the priority level and attention accorded to data analysis by participants and their mentors.

To reduce the high mentorship load, the module duration was extended which took pressure off both facilitators and participants, who on previous courses often worked late into the night and way beyond the course timetable. In the revised structure, participants had sufficient time to develop the first drafts of their protocols, carry out the data analysis and draft their manuscript before facilitators provided their inputs, thus enhancing the iterative learning experience. The revised structure also demonstrated the increased emphasis on reviewing published literature and organizing references, which had a limited focus in previous courses. This led to increased familiarity with previously published literature and improvements to both the introduction and discussion sections of the final papers. With the perspective of decentralizing OR courses to settings with relatively inexperienced and junior facilitators, and with growing diversification of the research portfolio beyond the current focus of HIV and tuberculosis, additional days have proved necessary to ensure the quality of outputs.

The two key challenges in implementing the revised structure were the associated increased costs (primarily for hotel and per-diem on additional days) and faculty having to commit to being away from duty stations for a longer period of time. The increased costs need to be included in future funding proposals to donors. Faculty commitment will be an ongoing challenge but will be partly solved by developing and nurturing a pool of senior and junior facilitators. It will be important to encourage facilitators who attend Module 1 to also attend Module 3 so that there is continuity and familiarity of faculty with the OR protocols.

In conclusion, the revised structure of 'The Union/MSF' model of OR capacity building addressed previous issues of insufficient time and overburdened mentors and we intend to continue with this model for future courses. We will continue to evaluate the revised model of capacity building using the standard SORT-IT indicators.[3]

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AUTHOR CONTRIBUTIONS:

AK conceived and wrote the first draft. RZ, SS, AJR, RV, KT, MK, ADH reviewed the draft, provided critical inputs and helped in revision of the manuscript. All authors approved the final version.

CONFLICTS OF INTEREST:

None declared.

REFERENCES

1. Harries AD, Rusen ID, Reid T, Detjen AK, Berger SD, Bissell K, Hinderaker SG, Edginton M, Fussell M, Fujiwara PI, Zachariah R: The Union and Médecins Sans Frontières approach to operational research. [State of the Art Series. Operational Research. Number 2 in the series]. Int J Tuberc Lung Dis 2011, 15:144-154.
2. Bissell K, Harries AD, Reid AJ, Edginton M, Hinderaker SG, Satyanarayana S, Enarson DA, Zachariah R: Operational research training: the course and beyond. Public Health Action 2012, 2:92-97.
3. Ramsay A, Harries AD, Zachariah R, Bissell K, Hinderaker SG, Edginton M, Enarson DA, Satyanarayana S, Kumar AMV, Hoa NB, et al: The Structured Operational Research and Training Initiative for public health programmes. Public Health Action 2014, 4:79-84.
4. Kumar AMV, Satyanarayana S, Wilson N, Zachariah R, Harries AD: Operational research capacity building in Asia: innovations, successes and challenges of a training course. Public Health Action 2013, 3:186-188.

Table 1: Comparison of the initial and revised structure of the Union-MSF model of operational research course.

Aspect	Initial Model	Revised Model
Duration of the module	Each module was five days in duration. In Module 2, about 3.5 days were used on data entry and the rest on data analysis. While some courses offered tailored support on data entry and data presentation in function of the participant OR projects, no focus could be placed on data analysis in function of the specific projects.	Duration of Module 1 and 2 increased to six days while that of Module 3 increased to eight days. In Module 1, the extra day was used to introduce two new sessions – one on the systematic search of published literature and another on organizing references. In Module 2, we allocated two days for data entry, two days for data analysis, one day to develop data entry tools and the data-analysis plan for the participants' research projects, and one day for plenary for presenting the data entry formats and dummy analytic tables. In Module 3, the first two days (Friday and Saturday) were dedicated to data analysis and interpretation followed by a day's break (Sunday) for self-study and reading published literature. Projects requiring 'multivariate regression analyses' were supported on a case-to-case basis. This was followed by five days (Monday to Friday) for drafting the manuscript. A new plenary was introduced for presenting 'titles and abstracts'.
Number of facilitators	In previous courses, the number of facilitators for Modules 1 and 3 varied from 6 to 9 and the number of mentor groups varied from 3 to 4. The facilitators worked in pairs - one senior (relatively more experienced in conducting and publishing OR) and one junior facilitator (usually one of the successful participants in the previous courses).	Number of facilitators in Modules 1 and 3 was standardized to eight (each pair of facilitators with three mentees)
	For Module 2, facilitators varied in number from two to six and there were a variable number of participants per facilitator.	Number of facilitators in Module 2 was increased and standardized to six – each had two mentees
Strengthened milestones	The milestones attached to Module 2 were weak, subjective and relied upon a self-declaration by the participant prior to Module 3 that the data collection had been completed.	The milestones related to Module 2 were modified and made more objective – one to be met within two weeks of Module 2 (submission of a plan for data collection, electronic data capture formats in EpiData (http://www.epidata.dk) and dummy tables and figures to facilitate analysis and reporting). The second milestone at least six weeks prior to Module 3 included submission of proof of study completion including the dataset and a draft analysis.

Table 2: Advantages and disadvantages of the revised strucutre of the Union-MSF model in Asia, 2013.

Revised structure	Advantages	Disadvantages
Extended duration of module	• Allowed new knowledge on sourcing published literature and organizing references to be imparted to participants • More individualized time devoted to analysing and interpreting data • Improved manuscript titles and abstracts. Less stress and fewer hours worked beyond course schedule for both participants and faculty • Improved opportunities for social networking and alumni links between participants and mentors	• Increased costs due to additional accomodation conferencing and per-diem expenses • Increased time away from duty station for faculty and participants
Increased number of facilitators	• For Modules 1 and 3, facilitator numbers were standardized to two for three participants allowing more individual time per participant	• Increased costs
Strengthened milestones for Module 2	• Increased priority accorded to data entry and analysis • Increased hands-on support to participants in analyzing data	• Increased burden on the participants and the facilitators to meet milestones • Increased burden on the module coordinator and course co-ordinator to monitor the achievement of milestones

13.
Discussion and Conclusion

SUMMARY OF STUDY FINDINGS AND COMPARISONS WITH PREVIOUS LITERATURE

This dissertation documents several operational research studies on HIV-associated TB that were conducted in India between 2010 and 2012. These studies had a major impact in shaping the national policy on TB/HIV collaborative activities in India and thus contributing to overall goals of ending TB and HIV epidemics, in line with the sustainable development goals of the United Nations. In this section, we summarise and discuss the key findings of each study and their policy implications. (See **Table**) Since these studies were conducted under an overarching operational research capacity building initiative, we also discuss the key capacity building initiatives, their evolution and outcomes.

ART FOR ALL HIV–INFECTED TB PATIENTS

In 2010, WHO ART Guidelines recommended that ART be initiated in all HIV-infected TB patients, irrespective of CD4 count.[1] While Indian national TB and HIV programmes wanted to make the change, they had major concerns about whether this change would have major resource implications in terms of the additional number of people who would need to be started on ART, drugs, costs, staff workload and accompanying logistics. In the study that we conducted (chapter 2), we found out that nine out of ten HIV-infected TB patients were already eligible for ART based on the 2006 WHO ART guidelines and adopting the 2010 guidelines would add only one additional person (out of ten) requiring ART.[2] As a public health approach to ART, this strongly justified the adoption of the WHO 2010 ART Guidelines, meaning that ART could be extended to all HIV-TB patients with relatively little additional burden to the national ART programme.

The findings of this study were shared with the key policy makers in a national technical working group of TB/HIV collaborative activities. Following this, a national policy decision was made to provide ART to all HIV-infected TB patients in India.[3] There were several factors which might have contributed to this decision which included: i) strong national evidence from the routine programmatic setting of a large state in India; ii) ownership of study findings by the national TB and HIV programme managers who were engaged right from the conception of the study until the end and were included as co-investigators and co-authors; iii) supporting evidence from other settings in Africa;[4] and iv) the supportive policy recommendation from WHO.[1] Although we did not undertake a costing analysis which would have provided useful information, this did not deter the policy makers from making the decision as the 'numbers of additional people requiring ART' were small and it was believed that the additional costs could easily be absorbed by the programme.

Following the implementation of this policy and several other health system strengthening measures to improve access to ART (which also included providing transport reimbursements for patients travelling to ART centres), there has been a steady increase in the number and proportion of HIV-TB patients who are receiving ART during TB treatment from less than 50% in 2009 to 98% in 2016.[5,6] While the case fatality among HIV-TB patients has declined during the same period, it still remains high at 12%.[5] This might be related

to delays in making the diagnosis of HIV and TB. Several interventions have been initiated to address the delays including the provider-initiated HIV testing among presumptive TB patients and use of Xpert MTB/RIF as the primary tool for diagnosing TB among PLHIV in India.[7] There has been an increase in the number of 'TB patients with a known HIV status' over the years and has reached 72% for 2016.[6] However, the impact of all these interventions on HIV-TB mortality is yet to be assessed.

HIV TESTING AMONG PRESUMPTIVE TB PATIENTS AND LINKAGE TO ART

In 2010, HIV testing was offered routinely to all TB patients in India, but not to all patients with presumptive TB (people with symptoms suggestive of TB and investigated for TB, who previously were referred to as "TB suspects").[8] There were many reasons for this stance by the Indian TB and HIV programmes. First, the WHO recommendation was mainly based on studies from the African region [9–35] which faced a generalized HIV epidemic and other settings in Asia[36] and America,[37,38] which could not be generalised to India. Second, there had not been any previous studies on this issue from India barring an incidental finding in a study from South India (which reported a HIV prevalence of 8.5% among presumptive TB patients).[39] So the Indian policy makers sought national evidence before making a decision.

As a first step towards filling this evidence gap, it was decided to study the HIV prevalence among presumptive TB patients in two districts of South India – one district in Karnataka State and another in Andhra Pradesh State – both known to have high HIV prevalence in the country. The rationale for choosing these districts was that if HIV prevalence among presumptive TB patients was low in these settings, then it could be safely assumed that the HIV prevalence in other parts of the country would be lower and the policy of routine HIV testing in this group of patients would not be worthwhile in the entire country. The findings of these studies have been described in chapters 3 and 4 and are discussed here.[40,41]

HIV TESTING IN PRESUMPTIVE TB PATIENTS IN HIGH HIV SETTINGS

Chapter 3 describes the findings from Mandya district (Karnataka State), where we found that 7% of presumptive TB patients were HIV positive as compared to 15% HIV prevalence among TB patients. Nearly 90% of all presumptive TB patients who were offered HIV testing accepted it, indicating that HIV testing was acceptable. Even though the strategy of 'HIV testing among presumptive TB patients' was not as efficient as 'HIV testing among TB patients' in terms of NNS to detect an additional case of HIV, it remained reasonably efficient given the context of a concentrated epidemic. In certain age groups (25-54 years), the NNS was lower at 20. More importantly, in the context of overall district HIV case-finding efforts, a policy of HIV testing of presumptive TB patients had the potential to substantially increase HIV case detection relative to existing practice. Thus, all the findings favoured a policy decision of routine HIV testing among presumptive TB patients in high HIV-prevalence settings in India. However, the evidence was limited to a single district in India and needed additional evidence from other parts of the country.[40]

Chapter 4 provides the additional evidence from Vizianagaram district of Andhra Pradesh State where the same research was conducted and the findings were replicated.[41] About 85% of presumptive TB patients accepted HIV testing and among them, about 10% were diagnosed HIV positive as compared to 8% among TB patients. Thus, the HIV-prevalence in 'presumptive TB patients' was higher than that found in 'TB patients'. A workload analysis showed that most of the HIV testing centres (27/31) would have a minimal increase in workload with an average of only 1-2 extra clients needing to be counselled and tested in a day. This meant that the strategy could be implemented using the existing human resources with negligible additional burden on the health staff delivering these services. Given these findings, it was concluded that routine HIV testing was feasible and effective, detecting a large number of new HIV cases with minimal additional workload on staff working in HIV testing centres.

Although, not formally studied, there were other positive implications of this strategy. First, the early diagnosis of HIV-infected TB patients and linkage to HIV care and support could potentially be life-saving. Second, this strategy identified HIV-infected individuals in whom TB had been ruled out and who were therefore potentially eligible for Isoniazid preventive therapy (IPT) as per WHO guidelines.[42] Third, these individuals might also have been eligible for ART, as has been shown in sub-Saharan Africa,[43] and getting them initiated on this treatment early on might have prevented TB as well as saved their lives.[44]

The results of both these studies were presented to the policy makers. Acknowledging the strong evidence from the operational research studies, the National Technical Working Group (NTWG) of TB/HIV collaborative activities took a policy decision to implement provider-initiated HIV testing and counselling (PITC) among patients with "presumptive TB" in high HIV settings (states of Karnataka, Andhra Pradesh, Tamil Nadu, Maharashtra, Manipur and Nagaland) in India.[45] It was clear from the two studies that a pre-requisite for effective implementation of this strategy was availability of HIV testing services at every health facility where presumptive TB patients were being evaluated. Thus, the study findings made a strong case and supported the national strategy for scaling up HIV testing services across the country. Another study from Delhi published around the same time in 2012 showed that the prevalence of HIV among presumptive TB patients was 31% (42% in culture positive TB patients and 26% among those culture negative) providing additional evidence in favour of the policy decision.[46]

PITC AMONG PRESUMPTIVE TB PATIENTS: THE IMPLEMENTATION MODEL

While PITC was of value in high HIV settings, how this was best implemented and monitored in routine health care settings, especially when taken to large scale, was not known, and this implementation-knowledge gap needed to be addressed. Accordingly, a pilot study was implemented in the entire state of Karnataka (South India, population 64 million, high HIV prevalence).

Chapter 5 describes the results of this research and we discuss the key findings here.[47] As part of this pilot, the strategy was implemented in all 645 microscopy centres of 31 districts and a total of ~115,000 patients with presumptive TB were offered HIV testing, of whom HIV status was ascertained for 62,847 (55%) and 7,559 (12%) were found to be HIV positive. Of the latter, about 40% were newly diagnosed and about 90% of them were found to be eligible for ART as per the existing guidelines at the time.

Despite the apparent low levels of HIV testing, the intervention was considered feasible and effective. It was considered feasible because: 1) all the interventions including the recording and reporting were implemented in a large state by the existing staff and resources (including budgets); 2) there was minimal additional workload on the staff except in tertiary centres; and 3) only 4% of the patients refused HIV testing. The intervention was considered effective as it identified thousands of new HIV-positive, ART-eligible patients who would not have otherwise been detected. These findings were presented back to NTWG and a decision to nationally scale up this intervention across all high HIV settings was made.[3] Changes in recording and reporting have also been adopted by the national TB and HIV programmes in India following the study.[7] While it cannot be attributed directly, we note that some of these changes are now reflected in global guidance as well, which includes documenting HIV status in the laboratory form requesting for examination of biological specimen for TB and the laboratory register (for smear microscopy and Xpert MTB/RIF).[48]

This study provided insights into the reasons for non-testing among presumptive TB patients. Not surprisingly, HIV testing was more likely in sputum microscopy centres with co-located HIV testing facilities. This justified the ongoing efforts of the national programmes to prioritise the setting up of new HIV testing facilities at hospitals having sputum microscopy facilities. This, however, did not address the major reason for non-testing in a substantial proportion of presumptive TB patients for whom sputum samples were collected and transported from peripheral health institutions to microscopy centres – such patients missed the opportunity of getting HIV tested at microscopy centres. This called for further decentralization of the HIV testing services to all peripheral health institutions and sputum collection centres. The other programmatic challenge was to improve the procurement and supply chain management of HIV test kits to enhance HIV testing uptake. Unavailability of the laboratory technician or counsellors at the microscopy centre or HIV testing centre was another reason for lack of HIV testing. Moving forward, this can be addressed by training the other staff within the general health system and motivating and allowing them to perform HIV testing in line with the overall approach to integrate the national AIDS control programme into the general health system. This has been done in other countries in Africa, and would be sustainable in the long term.[49,50]

HIV TESTING AMONG PRESUMPTIVE TB PATIENTS IN LOW HIV SETTINGS

Considering the high diagnostic yield of HIV among presumptive TB patients in high HIV-prevalence settings, the national policy making body also requested that similar surveillance

efforts be conducted jointly by the national TB and HIV programmes in moderate and low HIV settings (HIV prevalence <1% among pregnant women and/or <5% among high risk groups) of the country and findings presented before making a national policy decision. Given the heterogeneity of the HIV epidemic in India across states/districts, it was agreed that it was not possible to define a cut-off value of HIV prevalence to decide if PITC among presumptive TB patients was justified. Hence, it was agreed that if the prevalence of HIV among presumptive TB patients was as high as or greater than the HIV positivity among the general clients attending the HIV testing centres, then the strategy of PITC for presumptive TB patients might be justified. To address this knowledge gap, we undertook a study with the aim of assessing HIV testing uptake and HIV positivity among presumptive TB patients in Puducherry, a district with low HIV prevalence in South India. This is presented in Chapter 7 and discussed here.[51]

This was one of the first studies from India examining the effectiveness and feasibility of implementing the PITC strategy for presumptive TB patients in a low HIV prevalence setting under routine programmatic conditions. Overall, the HIV testing uptake was low with less than half of presumptive TB patients getting their HIV status ascertained. HIV prevalence was relatively higher (3.3%) among presumptive TB patients who were tested as compared to antenatal clinic attendees (<1%), TB patients (2%) and clients attending HIV testing centres excluding pregnant women (1.6%). This confirmed the findings from other studies that 'presumptive TB patients' remained an important target group for HIV testing.[51]

At about the same time, this study was replicated in eight low HIV prevalence districts across the country with similar findings.[52] The overall HIV prevalence in low HIV settings was 2.6% (95% CI 2.3%-2.9%) and it ranged from 0.2% to 4.6%.[52] While the overall HIV prevalence was relatively lower compared to high HIV settings, it was higher than the HIV prevalence among antenatal women (which ranged from 0.0% to 0.2% in the same settings). Another independent study published in 2012 from Punjab reported a prevalence of 1.2% among presumptive TB patients.[53] All these study findings were presented to the NTWG which took a policy decision to extend HIV testing to all presumptive TB patients in low HIV settings of India (especially those aged 25-54 years if there were resource constraints). With this, HIV testing among presumptive TB patients became a national policy in India.[52] Similar low levels of HIV prevalence have been reported among presumptive TB patients in the public health centres of the Republic of Korea (where the HIV prevalence was 8.2 per 10,000 in 2000 which decreased to 1.9 per 10,000 in 2013)[54] and Colombian prisoners (HIV prevalence of 2%).[55]

ART ELIGIBILITY AMONG HIV–INFECTED PRESUMPTIVE TB PATIENTS

In the evolution of ART eligibility guidelines, several groups (such as TB patients, antenatal women, children aged less than 5 years, and those living in sero-discordant relationships) were considered high priority and it was recommended that they be started on ART irrespective of CD4 cell counts or WHO staging.[56] A preliminary assessment from India and another study from Zimbabwe had shown that nearly 90% of all HIV-infected presumptive TB patients were

eligible for ART and there was high mortality, if these patients were not started on ART.[47,57] Thus, this was another high priority group which deserved to be started on ART irrespective of CD4 cell counts. However, there was no systematic evidence on this issue from India. So, a study was conducted to assess the proportion of HIV-infected presumptive TB patients who were eligible for ART using the guidelines at that point in time (WHO 2013 ART guidelines).[56] The findings of this study have been detailed in Chapter 8 and are discussed here.[58]

The findings confirmed our hypothesis that nine out of ten HIV-infected presumptive TB patients (without TB) were eligible for ART as per the WHO guidelines at the time.[56] This too was an underestimate as we did not assess all the criteria of ART eligibility at that time. For example, we did not have any information about whether the patients in our study had co-existing Hepatitis-B infection with severe liver disease, if they were pregnant or if they were living in a sero-discordant relationship, all of which were criteria for starting ART at the time of the study.[59] Some studies had indicated that nearly 75% of PLHIV in India were sero-discordant, [60,61] so if we applied this figure to our cohort then nearly all HIV-infected presumptive TB patients would have been eligible for ART. Hence, as a public health approach to ART initiation, we recommended that all HIV-infected presumptive TB patients should be initiated on ART irrespective of the CD4 cell count. This recommendation has little relevance today with WHO recommending since 2015 that all people living with HIV should start on ART irrespective of CD4 cell count or WHO clinical stage.[59] India has also accepted in principle to implement this 2015 recommendation. We also proposed the addition of an extra column in the TB laboratory register to capture ART initiation status, which could be used for monitoring ART uptake. This remains relevant to this day.

METHODOLOGICAL INNOVATION: EFFICIENT, QUALITY–ASSURED DATA CAPTURE IN MULTICENTRE OR

The multicentre study on HIV testing among presumptive patients nested a methodological innovation and this has been described in detail in Chapter 6.62 In this study, we captured data in an innovative manner using the freely available resources for data entry, storage, sharing and troubleshooting using a combination of three open access technologies – EpiData for data capture, Dropbox for sharing files and TeamViewer for providing remote support. While internet connection was essential for success of this model, the system did not require a large bandwidth, since EpiData file sizes are small (1000 records required ~216 kilobytes only!). Since Dropbox has the option of offline access to shared folders, offline data entry was possible which got synced once internet connection was available. This was a major advantage compared to web-based data capture systems, where internet connection is a pre-requisite for data entry. Telephone costs were circumvented by using Skype™ (http://www.skype.com), which was used for periodic video conference calls among the research staff for monitoring the project. The use of TeamViewer software to remotely access the computers at the data entry sites and troubleshoot meant that frequent travels to study sites were not required thus saving travel costs. The use of Dropbox for storing and sharing

files meant that there was automatic backup on the cloud with no threat of data loss due to a computer crash anywhere. Ensuring quality of data during electronic data capture has been one of the most neglected components of operational research. Multicentre studies are additionally challenged with issues about logistics of travel, training, supervision, monitoring and troubleshooting support. Allocating resources to these issues can pose a significant bottleneck for operational research in resource-limited settings. This approach to ensuring quality of data capture in multicentre operational research in resource-constrained settings has been a great lesson. This model has since been adopted and replicated in other settings and other programmes elsewhere, which include a nationwide, multicentre research on tuberculosis in India and a large state-wide tobacco survey in Tamil Nadu, India.[58,63,64]

LESSONS LEARNED, GAPS IN KNOWLEDGE AND FUTURE RESEARCH

EVIDENCE–POLICY LINKAGE

One of the biggest challenges in policy research is to establish a clear linkage between evidence and policy. As described above, we were able to find a clear link between evidence and policy in the form of minutes of the NTWG meetings which clearly documented the evidence presented during the meetings and the policy decisions taken thereof. For example, the minutes of the NTWG meeting that took place on 21st April 2011 clearly documents the findings of the study in chapter 2 and the policy decision made to start ART among all HIV-TB patients irrespective of the CD4 count.[3] Similarly, the minutes of NTWG meetings on 19th July 2012 and 17th December 2012 document the findings of the operational research studies detailed in chapters 2-5 and chapter 7 and the consequent policy decisions.[3,45,52]

GAPS IN KNOWLEDGE AND FUTURE RESEARCH

There were some limitations in the research conducted which could be a topic for future research. First, we studied only the presumptive pulmonary TB patients who attended the government-run sputum microscopy centres. We were not able to assess HIV prevalence among extra-pulmonary presumptive TB patients, or those evaluated at private laboratories outside the national public programme. Although this information was not required to inform the policy question facing national TB and AIDS programmes, this will remain a limitation in the assessment of true HIV prevalence among all presumptive TB patients and needs to be studied in the future. An extensive search for published literature revealed that HIV prevalence was an incidental finding in two studies on extra-pulmonary presumptive TB patients.[65,66] The findings are no different to those involving presumptive pulmonary TB patients. A study from South Africa among patients suspected of having cranial or spinal meningeal tuberculosis reported a HIV prevalence of 81%.[66] Another study from three countries of Africa (Nigeria, Cameroon, South Africa) among patients suspected of tuberculous pericardial effusion reported a prevalence of 50%.[65] These provide evidence justifying offering HIV testing to extra-pulmonary presumptive TB patients too.

Second, the reasons for non-testing needs further study. While there could be multiple reasons in an individual for non-testing of HIV, only one predominant reason was captured and that too from the provider's perspective. In about one-third of patients, the reason for non-testing was not mentioned and this is a serious limitation. Future research involving qualitative methods should be undertaken to understand patients' perspectives for not getting tested for HIV. This is important as HIV testing is the gateway for HIV care and treatment, and it is the first pillar of the UNAIDS 90-90-90 strategy which is the cornerstone of helping to end the AIDS epidemic by 2030.[67,68]

Third, we did not include children in our studies. There are no studies directly examining the HIV prevalence among presumptive TB patients in the paediatric age group. But, there are a few studies where HIV prevalence among paediatric presumptive TB patients was an incidental finding [Mozambique-13.2%; South Africa-17% to 40%; Tanzania-49% to 51%].[69–74] These support the policy of offering HIV testing to children as well.

Finally, our studies did not assess whether the strategy of moving HIV testing upstream to test all presumptive TB patients instead of TB patients alone actually resulted in increased linkage to HIV care and support and reduced mortality among HIV-infected TB patients. This needs further research.

OPERATIONAL RESEARCH CAPACITY BUILDING

All the studies that have been discussed above happened within an operational research capacity building initiative started initially by The International Union Against Tuberculosis and Lung Disease (The Union) and Médecins sans Frontières (MSF) and continued further in partnership with the Special Programme for Research and Training in Tropical Diseases (TDR) at the World Health Organization (WHO/TDR). There were two capacity building initiatives: 1) SORT IT (Structured Operational Research and Training Initiative) courses,[75] which are well known for their outputs with 90% of participants completing the course and publishing their research in scientific journals and 2) the global OR Fellowship programme.[76]

Dr Ajay Kumar was a participant of the SORT IT course in 2010-11 and the research project described in chapter 2 was conducted as part of the training course. Later, Dr Ajay Kumar joined the Union as an OR fellow and led several OR courses in India and co-facilitated many courses in Asia, Africa, Eastern Europe and the South Pacific regions. The studies described in chapters 3, 4 and 7 were conducted by the participants of the OR courses conducted in India under the leadership and direct mentorship of Dr Ajay Kumar. The other studies described in chapters 5, 6 and 8 were undertaken directly by Dr Ajay Kumar in his role as OR fellow. The contribution of the OR fellowship programme in strengthening the scientific output of The Union South-East Asia (USEA) Regional office is described in Chapter 10.[76]

A vital element in assessing the success of operational research (OR) is to measure its impact on policy and/or practice. Several follow-up assessments were done to understand the impact of the research studies conducted as part of the SORT IT courses on policy and/or practice. One such assessment is described in Chapter 9, where we report on the impact

of research papers on policy/practice that resulted from six SORT IT courses initiated between July 2012 and March 2013.[77] In this study, about 55% (45/81) of papers assessed were considered to have contributed to a change in policy and/or practice. Few capacity-building programmes track outputs, although this is fast changing,[78,79] and the SORT IT model creates a benchmark in this area.[80] This is encouraging and can be attributed to several factors including policy-relevance of the research question, engagement of policy makers as co-investigators, ownership of study results especially when programme managers were principal investigators of the research project and other windows of opportunity available to individual researchers by virtue of these individuals being in national/state level committees.

We need to view these results, however, with caution because these were self-reported by the authors of the papers and there is a high likelihood of responder bias. We tried to mitigate this by verifying official policy documents wherever possible and by adopting a conservative stance in our assessments. However, finding documents that provide documentary support of evidence-policy linkage is challenging. The other challenge relates to varied interpretations of the authors as to whether their study impacted policy or not. Some were modest and did not attribute their study to the policy change while others were more aggressive in their attribution. Given the complexities in interpreting policy impact assessment, future assessments should focus beyond self-reporting of data and use more robust and independent verification of the reported change(s) with all concerned stakeholders to enhance the richness and rigour of the assessments. This is difficult to do with international and regional courses, but more feasible with national courses that have been and are being conducted in India, Pakistan, Myanmar, Sierra Leone, Liberia, Kenya and Zimbabwe.

Chapter 10 describes the contribution of the OR fellowship programme in strengthening the scientific output of The Union South-East Asia (USEA) Regional office.[76] This case study testifies to the large research output that resulted from placing two OR fellows in the USEA Office, Delhi, India. Of particular note, in the six years before the fellows joined there was only one published paper from the office while in the first five years since the fellows joined the cumulative number of published papers reached nearly one hundred. Before joining as OR fellows, the two individuals had little engagement in operational research. They learnt and subsequently taught their craft as they developed, with a number of factors facilitating this process such as their own enthusiasm and passion for the subject, a supportive and enabling environment and strong mentorship from the leadership of the Office and the Centre for Operational Research. Selecting the right individuals for the job is an essential determinant of success, but the performance-related contracts that The Union offers to all OR fellows allow a way out if a mistake is made in selection and individuals fail to deliver. There have been similar successes of OR fellowship programmes in Vietnam[81] and Benin.[82]

The SORT IT model has evolved over a period of time with many innovations introduced to the administration, structure and content of the course. These are described in chapters 11 and 12.[83,84] Over the years, we have faced a number of challenges in

implementing these courses, including shortage of time for data analysis, data interpretation and manuscript drafting, and a high mentorship burden on a limited pool of facilitators. We have introduced several changes in the SORT IT model to address these challenges. The key changes included increasing the duration of the modules, increased number of facilitators and standardized milestones for module 2. The increased costs as a result of the increased duration was mitigated to some extent by conducting module 1 and 2 back to back to reduce the costs and travel time. Despite the increased costs and increased time away for faculty as a result of these changes, this has addressed the previous challenges of insufficient time and overburdened mentors. We have continued with this model ever since.

The SORT IT model has evolved further – geographically, methodologically and thematically. Geographically, we have now decentralised the courses from global to regional and national level. There have also been efforts to replicate SORT IT at the institutional level. Methodologically, we have started SORT IT 2.0 in which we encourage participants to undertake a research study that incorporates "mixed-methods" design which answers research questions not only related to the magnitude of the problem but also explores the reasons and possible solutions to the problem. Similarly, pure qualitative research has been experimented with under the SORT IT model and there are also plans to use the SORT IT model to conduct a course on systematic reviews and meta-analysis. Other models such as e-SORT IT and blended versions (partly online and partly face-to-face modules) have been tried, although these are early days to comment about the effectiveness of such approaches. We have also expanded thematically and have now conducted or are conducting SORT IT courses on specific themes such as multidrug resistant tuberculosis in Eastern Europe[85] and the Ebola epidemic in West Africa.[86]

IMPACT OF RESEARCH ON POLICY AND PRACTICE

As discussed above, there are many implications from the studies conducted in this thesis for policy and practice change and these are shown in the **Table** in relation to the research question and the methodology used. The broad principal recommendations included: acceptance of the WHO guidance that all HIV-TB patients should start ART regardless of CD4 count; a national policy decision that all patients with presumptive TB should be HIV tested in both high and low HIV-prevalence settings and that those diagnosed HIV-positive should be referred to HIV treatment and care including ART, irrespective of CD4 count; and that the SORT IT model of operational research be expanded and used to obtain robust local evidence and generate data to further inform policy and practice. The optimization and use of SORT IT in India also helped to promote this model internationally and at the WHO.

CONCLUSION

The body of work contained in this thesis demonstrates the strong role that operational research has played to inform policy in the setting of a national TB and HIV programme in India. Several key national policy decisions were made on the basis of evidence generated in routine programme settings. First, it was decided that ART should be started for all HIV-infected

TB patients in India irrespective of CD4 count and WHO clinical staging. This has increased the proportion of HIV-TB patients receiving ART from 50% in 2009 to 98% in 2016. Second, a national policy decision was taken to offer HIV testing routinely to all presumptive TB patients in India. Although this policy has been implemented nationally, there is no data measuring the extent of HIV testing in this group from routine reports of the national TB and HIV programmes. There is limited data about the reasons for HIV non-testing among presumptive TB patients. Further, the impact of these strategies in reducing morbidity and mortality due to HIV-associated TB is yet to be studied. Future research needs to focus on these aspects. Third, it was recommended that all HIV-infected presumptive TB patients should be started on ART, irrespective of CD4 count and clinical staging. This recommendation though has little relevance today with India deciding to implement 'test and treat' policy.

Although international and national policies have changed since the start and completion of the HIV-TB studies in this thesis, they are still relevant to the larger picture. Moving HIV testing upstream to presumptive TB patients identifies a vulnerable group who are at high risk of HIV infection and without prompt diagnosis and referral to HIV care are at risk of considerable HIV-related morbidity and mortality. Timely ART can prevent this. For those who have yet to develop TB, this disease can be prevented and other HIV-related disease specifically targeted, prevented or treated. For those who are found to have TB, their prognosis can be improved and case fatality decreased. ART also reduces further transmission of HIV to uninfected partners and leads to a reduction in HIV incidence. HIV testing and referral to ART for presumptive TB patients thus addresses the first 90 of UNAIDS 90-90-90 targets (90% of those HIV-infected are identified), the second 90 of UNAIDS 90-90-90 targets (90% of those diagnosed are started on ART) and the last 90 of the Stop TB Partnership (90% of those diagnosed with TB are successfully treated) as well as tackling TB incidence and mortality which are the key indicators for Ending the TB epidemic by 2030.

The conduct of operational research was facilitated and catalysed greatly by the capacity building initiatives driven by The Union which included training public health professionals in the SORT IT model of training and the Global OR Fellowship programme. Based on the lessons learned in the initial cycles of SORT IT courses, the model has been optimized and expanded geographically, thematically and methodologically. Studies have also showcased the impact of research conducted in SORT IT courses on policy and practice and the case study from the USEA office showed what OR fellows could achieve if provided with the right opportunity, support, mentorship and enabling environment. As a result of these initiatives, a great resource pool has been created in India which is being drawn on to facilitate OR courses in wider areas of disease control both in India and worldwide. With the clock ticking, the scale up and implementation of sound OR embedded within TB and HIV/AIDS programmes is essential for meeting the international goals. Controlling the TB epidemic desperately requires new tools (new diagnostics, new treatments and new vaccines), but these have to rapidly be accommodated and embedded into established programmatic settings for them to have any impact on the epidemic. Operational research is the only way of ensuring this will happen in an evidence-based way.

Table 1: Summary of findings of operational research studies conducted between 2010 and 2012 and documented in the PhD thesis and their impact on policy and practice.

Chapter	Name and Citation of the article	Key objective	Methodology	Key findings	Impact on policy and practice
Chapter 2:	Kumar AMV, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, Lal K, Reddy HRR, Naik B, Prasad R, Yaqoob M, Deepak KG, Shastri S, Satyanarayana S, David Harries A, Chauhan LS, Dewan P. Will Adoption of the 2010 WHO ART Guidelines for HIV-Infected TB Patients Increase the Demand for ART Services in India? PLoS ONE. 2011;6(9):e24297.	To evaluate the additional number of patients that would be initiated on ART if India adopted the current 2010 WHO ART guidelines for HIV-infected TB patients	Cross-sectional study involving review of routinely collected data recorded in TB and HIV programme records.	Of 710 HIV-TB patients, 146(21%) HIV-infected TB patients were on ART prior to TB diagnosis. Of the remaining 564, 497(88%) were assessed for ART eligibility; of these, 436(88%) were eligible for ART according to 2006 WHO ART guidelines. As a public health approach to ART, this strongly justified the adoption of the WHO 2010 ART Guidelines.	A national policy decision was made to start all HIV-TB patients on ART irrespective of CD4 count and clinical staging. This has resulted in major improvements in uptake of ART among HIV-TB patients – from 50% in 2009 to 98% in 2016.
Chapter 3:	Naik B, Kumar AMV, Lal K, Doddamani S, Krishnappa M, Inamdar V, Satyanarayana S, Gupta D, Dewan PK. HIV prevalence among persons suspected of tuberculosis: policy implications for India. Journal of Acquired Immune Deficiency Syndromes. 2012;59(4):e72–6.	To assess the prevalence of HIV among patients with presumptive TB in settings with a relatively high HIV prevalence (Mandya district, Karnataka State)	Cross-sectional study involving primary data collection	Of 1668 presumptive TB patients, HIV status was ascertained for 1539 (92%). Among these, 108 (7%) were HIV positive. Of the 108, 43 (40%) were newly diagnosed as HIV (ie, not previously known to have HIV infection).	A policy decision was taken to offer HIV testing routinely to all presumptive TB patients in high HIV settings (states of Karnataka, Andhra Pradesh, Tamil Nadu, Maharashtra, Manipur and Nagaland) in India.
Chapter 4:	Achanta S, Kumar AMV, Nagaraja SB, Jaju J, Shamrao SRM, Uppaluri R, Tekumalla RR, Gupta D, Kumar A, Satyanarayana S, Dewan PK Feasibility and Effectiveness of Provider Initiated HIV Testing and Counseling of TB Suspects in Vizianagaram District, South India. PLoS ONE. 2012;7(7):e41378.	To assess the prevalence of HIV among patients with presumptive TB in settings with a relatively high HIV prevalence (Vizianagaram district, Andhra Pradesh State)	Cross-sectional study involving primary data collection	Of 2918 presumptive TB patients, HIV status was ascertained for 2465(85%). Among these, 246(10%) were HIV-positive. Of the 246, 84(34%) were newly diagnosed as HIV (HIV status not known previously)	A policy decision was taken to offer HIV testing routinely to all presumptive TB patients in high HIV settings (states of Karnataka, Andhra Pradesh, Tamil Nadu, Maharashtra, Manipur and Nagaland) in India.

Chapter 5:	Kumar AMV, Gupta D, Kumar A, Gupta RS, Kanchar A, Rao R, Shastri S, Suryakanth MD, Rangaraju C, Naik B, Guddemane DK, Bhat P, Nair AS, Harries AD, Dewan P. HIV Testing among Patients with Presumptive Tuberculosis: How Do We Implement in a Routine Programmatic Setting? Results of a Large Operational Research from India. PLoS ONE. 2016;11(5):e0156487.	To assess the feasibility and challenges of provider initiated HIV testing for patients with presumptive TB under programmatic settings	Cross-sectional study involving primary data collection	Overall, 115,308 patients with presumptive TB were examined for sputum smear microscopy at 645 microscopy centres state-wide. Of these, HIV status was ascertained for 62,847(55%) among whom 7,559(12%) were HIV-positive, and of these, 3,034(40%) were newly diagnosed. Reasons for non-testing were reported for 37,700(72%) of the 52,461 patients without HIV testing; non-availability of testing services at site of sputum collection was cited by health staff in 54% of respondents. Only 4% of patients opted out of HIV testing.	This operational research demonstrated a feasible model of implementation of offering HIV testing among presumptive TB patients in routine health settings. A policy decision was taken by the national TB and HIV programmes to adopt and scale-up this implementation model to all high HIV settings in India. (states of Karnataka, Andhra Pradesh, Tamil Nadu, Maharashtra, Manipur and Nagaland)
Chapter 6:	Kumar AMV, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, Lauritsen JM, Rieder HL. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. Public Health Action. 2013;3(1):60–2	To describe an innovative and efficient way of coordinating data capture in multicentre operational research using a combination of three open access technologies	Case study (this is a sub-study undertaken as part of the study described in chapter 5)	Data were captured using an innovative model – EpiData for data capture, Dropbox for sharing files and TeamViewer for providing remote support. While internet connection was essential for success of this model, the system did not require a large bandwidth, since EpiData file sizes are small (1000 records required ~216 kilobytes only!). Since Dropbox has the option of offline access to shared folders, offline data entry was possible which got synced once internet connection was available. This was a major advantage compared to web-based data capture systems, where internet connection is a pre-requisite for data entry. Telephone costs were circumvented by using Skype™ (http://www.skype.com), which was used for periodic video conference calls among the research staff for monitoring the project. The use of TeamViewer software to remotely access the computers at the data entry sites and troubleshoot meant that frequent travels to study sites were not required thus saving travel costs. The use of Dropbox for storing and sharing files meant that there was automatic backup on the cloud with no threat of data loss due to a computer crash anywhere.	This model of quality-assured data capture has been used in other studies undertaken subsequently in India which include a nationwide, multicentre research on tuberculosis and a large state-wide tobacco survey in Tamil Nadu, India.

Chapter 7:	Palanivel C, Kumar AMV, Mahalakshmi T, Govindarajan S, Claassens M, Satyanarayana S, Gurumurthy D, Vasudevan K, Purty A, Paulraj AK, Raman K V. Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India. Public Health Action. 2013;3(3):220–3.	To assess the prevalence of HIV among patients with presumptive TB in settings with a relatively low HIV prevalence	Cross-sectional study involving primary data collection	Of 1886 presumptive TB patients, HIV status was ascertained for 842 patients (44.6%) and 28(3.3%) were HIV positive. This was relatively high as compared to antenatal clinic attendees (<1%), TB patients (2%) and clients attending HIV testing centres excluding pregnant women (1.6%)	A national policy decision was taken to extend HIV testing to all presumptive TB patients in low HIV settings of India (especially those aged 25-54 years if there were resource constraints)
Chapter 8:	Kumar AMV, Singarajipura A, Naik B, Guddemane DK, Patel Y, Shastri S, Kumar S, Deshmukh R, Rewari BB, Harries AD. HIV-infected presumptive tuberculosis patients without tuberculosis: how many are eligible for antiretroviral therapy in Karnataka, India? Journal of Epidemiology and Global Health. 2017;7(1):11–9.	To assess the proportion of HIV-infected presumptive TB patients eligible for starting ART as per 2015 WHO ART guidelines	Cross-sectional study involving review of routinely collected data recorded in TB and HIV programme records.	Of 42,585 presumptive TB patients, 28,964(68%) were tested for HIV and 2262(8%) were HIV positive. Of the latter, 377(17%) had active TB. Of 1885 'presumptive TB patients without active TB', 1100(58%) were already receiving ART. Of the remaining 789 who were not receiving ART, 617(79%) were assessed for ART eligibility and of those, 548(89%) were eligible for ART.	This evidence supported a public health approach of starting all 'HIV-infected presumptive TB patients without TB' on ART irrespective of CD4 count in line with global thinking about 'test and treat'.
Chapter 9:	Kumar AMV, Shewade HD, Tripathy JP, Guillerm N, Tayler-Smith K, Berger SD, Bissell K, Reid AJ, Zachariah R, Harries AD. Does research through Structured Operational Research and Training (SORT IT) courses impact policy and practice? Public Health Action. 2016;6(1):44–9.	To document the operational research capacity building initiative undertaken and its evolution and impact on policy and practice	A cross-sectional, mixed-methods study involving email-based, self-administered questionnaires and telephone/skype/in-person responses from first and/or senior co-authors of course papers.	Of 72 participants, 63(88%) completed the course and course outputs included 81 submitted papers, of which 76(94%) were published. Of the 81 papers assessed, 45(55%) contributed to a change in policy and/or practice: these included 29 contributing to government policy/practice change (20 at national, four at sub-national and five at hospital level), 11 to non-government organizational policy change and five reinforcing existing policy. The changes ranged from modifications to monitoring and evaluation tools to redrafting of national guidelines to scaling-up existing policies.	This study provided evidence supporting the potential impact of operational research conducted in SORT IT courses on policy and practice.

Chapter 10:	Kumar AMV, Satyanarayana S, Berger SD, Chadha SS, Singh RJ, Lal P, Tonsing J, Harries AD. Promoting operational research through fellowships: a case study from the South-East Asia Union Office. Public Health Action. 2015;5(1):6–16.	To describe the impact of OR fellowship programme on research outputs of the South-East Asia office of the International Union Against Tuberculosis and Lung disease and lessons learned in the process.	Case study	In June 2009, the first operational research (OR) Fellow in India was appointed on a full-time basis and the second was appointed in February 2012 - both had limited previous experience in OR. From 2009 to 2014, annual research output and capacity building initiatives rose exponentially and included: i) facilitation at 61 operational research training courses / modules; ii) publication of 96 papers, several of which had a lasting impact on national policy and practice; iii) providing technical assistance in promoting operational research; iv) building capacity of medical college professionals to manage data; v) support to programme staff for disseminating their research findings; vi) reviewing 28 scientific papers for national or international peer-reviewed journals; and vii) developing 45 scientific abstracts for presentation at national and international conferences. The reasons for this success are highlighted along with on-going challenges.	This experience from India provides good evidence for promoting similar models elsewhere. Similar case studies have since been documented in Vietnam and Benin.
Chapter 11:	Kumar AMV, Satyanarayana S, Wilson N, Zachariah R, Harries AD. Operational research capacity building in Asia: innovations, successes and challenges of a training course. Public Health Action. 2013;3(2):186–8.	To document the innovations, successes and challenges of implementing a regional SORT IT course in Asia in 2012	Case Study	Many innovations were introduced into the administration, structure and content of the course. 11 of 12 participants successfully completed all pre-defined milestones. The main challenges included shortage of time, especially for data analysis and interpretation, and insufficient numbers of experienced facilitators.	This helped in optimizing the SORT IT model, which has since been adopted globally by WHO/TDR.
Chapter 12:	Kumar AMV, Zachariah R, Satyanarayana S, Reid AJ, Van den Bergh R, Tayler-Smith K, Khogali M, Harries AD. Operational research capacity building using 'The Union/MSF' model: adapting as we go along. BMC Research Notes. 2014;7(1):819	To describe the revised structure of SORT IT course and experience (successes and challenges) of implementing it in Asia in 2013	Case Study	The key changes introduced included extending the duration of the course modules (by a day each in module 1 and 2 and by three days in module 3), increasing the numbers of facilitators and standardizing milestones related to data entry and analysis. We successfully implemented this revised structure in the Asian course held in Nepal in 2013. Eleven of twelve participants successfully completed all the milestones and submitted 13 scientific manuscripts (two participants completed two projects) to international peer-reviewed journals. Though, this posed two challenges – increased costs and increased time away for faculty and participants.	This helped in optimizing the SORT IT model, which has since been adopted globally by WHO/TDR.

TB-Tuberculosis; HIV-Human immunodeficiency virus; ART-antiretroviral treatment; SORT IT-Structured Operational Research Training Initiative; WHO-World Health Organization; WHO/TDR-Special Programme for research and training in tropical diseases; MSF-Medecins Sans Frontieres; The Union-International Union Against Tuberculosis and Lung Disease;

REFERENCES

1. World Health Organization (WHO). Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach: 2010 revision [Internet]. Geneva, Switzerland; 2006 [cited 2017 Aug 17]. Available from: http://www.who.int/hiv/pub/arv/adult/en/index.html
2. Kumar AMVS, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, et al. Will adoption of the 2010 WHO ART guidelines for HIV-infected TB patients increase the demand for ART services in India? PLoS One. 2011 Jan;6(9):e24297.
3. National AIDS Control Organization and Central TB Division. Minutes of meeting of National Technical Working Group on HIV/TB Collaborative Activities at National AIDS Control Organization, New Delhi, on 21/04/2011. New Delhi, India; 2012.
4. Teck R, Ascurra O, Gomani P, Manzi M, Pasulani O, Kusamale J, et al. WHO clinical staging of HIV infection and disease, tuberculosis and eligibility for antiretroviral treatment: relationship to CD4 lymphocyte counts. Int J Tuberc Lung Dis. 2005 Mar;9(3):258–62.
5. Ministry of Health with Family Welfare, Government of India, World Health Organization. Joint Monitoring Mission Revised National Tuberculosis Control Programme (RNTCP), India 2015. New Delhi, India; 2015.
6. World Health Organization (WHO). Global Tuberculosis Report 2017 [Internet]. Geneva, Switzerland; 2017 [cited 2017 Nov 6]. p. 1–262. Available from: http://www.who.int/tb/publications/global_report/en/
7. Central TB Division Directorate General Health Services, Ministry of Health and Family Welfare, Government of India. Revised National TB Control Programme Technical and Operational Guidelines for Tuberculosis Control in India 2016. New Delhi; 2016.
8. World Health Organization. WHO policy on collaborative TB/HIV activities. Guidelines for national programmes and other stakeholders. Geneva; 2012.
9. Porskrog A, Bjerregaard-Andersen M, Oliveira I, Joaquim LC, Camara C, Andersen PL, et al. Enhanced tuberculosis identification through 1-month follow-up of smear-negative tuberculosis suspects. Int J Tuberc Lung Dis. 2011 Apr;15(4):459–64.
10. Deribew A, Negussu N, Kassahun W, Apers L, Colebunders R. Uptake of provider-initiated counselling and testing among tuberculosis suspects, Ethiopia. Int J Tuberc Lung Dis. 2010 Nov;14(11):1442–6.
11. Srikantiah P, Lin R, Walusimbi M, Okwera A, Luzze H, Whalen CC, et al. Elevated HIV seroprevalence and risk behavior among Ugandan TB suspects: implications for HIV testing and prevention. Int J Tuberc Lung Dis. 2007 Feb;11(2):168–74.
12. Odhiambo J, Kizito W, Njoroge A, Wambua N, Nganga L, Mburu M, et al. Provider-initiated HIV testing and counselling for TB patients and suspects in Nairobi, Kenya. Int J Tuberc Lung Dis. 2008 Mar;12(3 Suppl 1):63–8.
13. Munthali L, Mwaungulu JN, Munthali K, Bowie C, Crampin AC. Using tuberculosis suspects to identify patients eligible for antiretroviral treatment. Int J Tuberc Lung Dis. 2006 Feb;10(2):199–202.

14. Dimairo M, MacPherson P, Bandason T, Zezai A, Munyati SS, Butterworth AE, et al. The risk and timing of tuberculosis diagnosed in smear-negative TB suspects: a 12 month cohort study in Harare, Zimbabwe. PLoS One. 2010 Jul;5(7):e11849.
15. Adjei AA, Adiku TK, Ayeh-Kumi PF, Hesse IF. Prevalence of human immunodeficiency virus infection among tuberculosis suspect patients in Accra, Ghana. West Afr J Med. 2006;25(1):38–41.
16. Macpherson P, Dimairo M, Bandason T, Zezai A, Munyati SS, Butterworth AE, et al. Risk factors for mortality in smear-negative tuberculosis suspects: a cohort study in Harare, Zimbabwe. Int J Tuberc Lung Dis. 2011 Oct;15(10):1390–6.
17. Lockman S, Hone N, Kenyon TA, Mwasekaga M, Villauthapillai M, Creek T, et al. Etiology of pulmonary infections in predominantly HIV-infected adults with suspected tuberculosis, Botswana. Int J Tuberc Lung Dis. 2003 Aug;7(8):714–23.
18. Bruchfeld J, Aderaye G, Palme IB, Bjorvatn B, Britton S, Feleke Y, et al. Evaluation of outpatients with suspected pulmonary tuberculosis in a high HIV prevalence setting in Ethiopia: clinical, diagnostic and epidemiological characteristics. Scand J Infect Dis. 2002;34(5):331–7.
19. Hirao S, Yassin MA, Khamofu HG, Lawson L, Cambanis A, Ramsay A, et al. Same-day smears in the diagnosis of tuberculosis. Trop Med Int Health. 2007;12(12):1459–63.
20. Bigwan E, Ohaeri M, David E, Wakjissa FD, Sheyin Z. Some risk factors associated with Acid-alcohol-fast bacilli in patients with suspected pulmonary tuberculosis in jos, central Nigeria. African J Infect Dis. 2014;8(2):22–6.
21. Abebe G, Deribew A, Apers L, Abdissa A, Kiflie Y, Koole O, et al. Evaluation of the 2007 WHO guideline to diagnose smear negative tuberculosis in an urban hospital in Ethiopia. BMC Infect Dis. 2013;13:427.
22. Page-Shipp L, Voss De Lima Y, Clouse K, de Vos J, Evarts L, Bassett J, et al. TB/HIV integration at primary care level: A quantitative assessment at 3 clinics in Johannesburg, South Africa. South Afr J HIV Med. 2012/09/01. 2012;13(3):138–43.
23. Meintjes G, Schoeman H, Morroni C, Wilson D, Maartens G. Patient and provider delay in tuberculosis suspects from communities with a high HIV prevalence in South Africa: a cross-sectional study. BMC Infect Dis. 2008;8:72.
24. Hanrahan CF, Selibas K, Deery CB, Dansey H, Clouse K, Bassett J, et al. Time to treatment and patient outcomes among TB suspects screened by a single point-of-care xpert MTB/RIF at a primary care clinic in Johannesburg, South Africa. PLoS ONE [Electronic Resour. 2013;8(6):e65421.
25. Scott LE, McCarthy K, Gous N, Nduna M, Van Rie A, Sanne I, et al. Comparison of Xpert MTB/RIF with other nucleic acid technologies for diagnosing pulmonary tuberculosis in a high HIV prevalence setting: a prospective study. PLoS Med / Public Libr Sci. 2011;8(7):e1001061.
26. O'Grady J, Bates M, Chilukutu L, Mzyece J, Cheelo B, Chilufya M, et al. Evaluation of the Xpert MTB/RIF assay at a tertiary care referral hospital in a setting where tuberculosis and HIV infection are highly endemic.[Erratum appears in Clin Infect Dis. 2013 Jan;56(2):313]. Clin Infect Dis. 2012;55(9):1171–8.
27. Davis JL, Huang L, Worodria W, Masur H, Cattamanchi A, Huber C, et al. Nucleic acid amplification tests for diagnosis of smear-negative TB in a high HIV-prevalence setting: a prospective cohort study. PLoS ONE [Electronic Resour. 2011;6(1):e16321.

28. Seni J, Kidenya BR, Obassy E, Mirambo M, Burushi V, Mazigo HD, et al. Low sputum smear positive tuberculosis among pulmonary tuberculosis suspects in a tertiary hospital in Mwanza, Tanzania. Tanzan J Health Res. 2012;14(2):1–9.
29. Somi GR, O'Brien RJ, Mfinanga GS, Ipuge YA. Evaluation of the MycoDot test in patients with suspected tuberculosis in a field setting in Tanzania. Int J Tuberc Lung Dis. 1999 Mar;3(3):231–8.
30. Mavhu W, Dauya E, Bandason T, Munyati S, Cowan FM, Hart G, et al. Chronic cough and its association with TB-HIV co-infection: factors affecting help-seeking behaviour in Harare, Zimbabwe. Trop Med Int Health. 2010 May;15(5):574–9.
31. Ayles H, Schaap A, Nota A, Sismanidis C, Tembwe R, De Haas P, et al. Prevalence of tuberculosis, HIV and respiratory symptoms in two Zambian communities: implications for tuberculosis control in the era of HIV. PLoS ONE [Electronic Resour. 2009;4(5):e5602.
32. Bonnet M, Gagnidze L, Varaine F, Ramsay A, Githui W, Guerin PJ. Evaluation of FASTPlaqueTB to diagnose smear-negative tuberculosis in a peripheral clinic in Kenya. Int J Tuberc Lung Dis. 2009 Sep;13(9):1112–8.
33. Rabna P, Andersen A, Wejse C, Oliveira I, Gomes VF, Haaland MB, et al. High mortality risk among individuals assumed to be TB-negative can be predicted using a simple test. Trop Med Int Health. 2009;14(9):986–94.
34. Reither K, Saathoff E, Jung J, Minja LT, Kroidl I, Saad E, et al. Low sensitivity of a urine LAM-ELISA in the diagnosis of pulmonary tuberculosis. BMC Infect Dis. 2009;9:141.
35. Mutetwa R, Boehme C, Dimairo M, Bandason T, Munyati SS, Mangwanya D, et al. Diagnostic accuracy of commercial urinary lipoarabinomannan detection in African tuberculosis suspects and patients. Int J Tuberc Lung Dis. 2009 Oct;13(10):1253–9.
36. Punnotok J, Shaffer N, Naiwatanakul T, Pumprueg U, Subhannachart P, Ittiravivongs A, et al. Human immunodeficiency virus-related tuberculosis and primary drug resistance in Bangkok, Thailand. Int J Tuberc Lung Dis. 2000 Jun;4(6):537–43.
37. Achkar JM, Jenny-Avital E, Yu X, Burger S, Leibert E, Bilder PW, et al. Antibodies against immunodominant antigens of Mycobacterium tuberculosis in subjects with suspected tuberculosis in the United States compared by HIV status. Clin Vaccine Immunol. 2010 Mar;17(3):384–92.
38. Aguiar FS, Almeida LL, Ruffino-Netto A, Kritski AL, Mello FC, Werneck GL. Classification and regression tree (CART) model to predict pulmonary tuberculosis in hospitalized patients. BMC Pulm Med. 2012 Aug 7;12:40.
39. Daley P, Michael JS, Hmar P, Latha A, Chordia P, Mathai D, et al. Blinded evaluation of commercial urinary lipoarabinomannan for active tuberculosis: a pilot study. Int J Tuberc Lung Dis. 2009 Aug;13(8):989–95.
40. Naik B, Kumar Mv A, Lal K, Doddamani S, Krishnappa M, Inamdar V, et al. HIV prevalence among persons suspected of tuberculosis: policy implications for India. J Acquir Immune Defic Syndr. 2012 Apr 1;59(4):e72-6.
41. Achanta S, Kumar AMVA, Nagaraja SB, Jaju J, Shamrao SRM, Uppaluri R, et al. Feasibility and effectiveness of provider initiated HIV testing and counseling of TB suspects in Vizianagaram district, South India. PLoS One. 2012 Jan;7(7):e41378.

42. World Health Organization (WHO). Intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings [Internet]. Geneva, Switzerland; 2011 [cited 2017 Nov 3]. Available from: http://www.who.int/hiv/pub/tb/9789241500708/en/
43. Harries AD. Paying attention to tuberculosis suspects whose sputum smears are negative. Vol. 15, The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease. France; 2011. p. 427–8.
44. Suthar AB, Lawn SD, del Amo J, Getahun H, Dye C, Sculier D, et al. Antiretroviral therapy for prevention of tuberculosis in adults with HIV: a systematic review and meta-analysis. PLoS Med. 2012;9(7):e1001270.
45. National AIDS Control Organization and Central TB Division. Minutes of meeting of National Technical Working Group on HIV/TB Collaborative Activities at National AIDS Control Organization, New Delhi, on 19/07/2012. New Delhi, India; 2012.
46. Magee MJ, Blumberg HM, Broz D, Furner SE, Samson L, Singh S, et al. Prevalence of drug resistant tuberculosis among patients at high-risk for Hiv attending outpatient clinics in Delhi, India. Southeast Asian J Trop Med Public Heal. 2012;43(2):354–63.
47. Kumar AM, Gupta D, Kumar A, Gupta RS, Kanchar A, Rao R, et al. HIV Testing among Patients with Presumptive Tuberculosis: How Do We Implement in a Routine Programmatic Setting? Results of a Large Operational Research from India. PLoS One. 2016;11(5):e0156487.
48. World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision. 2013.
49. Kennedy CE, Yeh PT, Johnson C, Baggaley R. Should trained lay providers perform HIV testing? A systematic review to inform World Health Organization guidelines. AIDS Care. 2017 Dec;29(12):1473–9.
50. Crowley T, Mayers P. Trends in task shifting in HIV treatment in Africa: Effectiveness, challenges and acceptability to the health professions. African J Prim Heal care Fam Med. 2015 Jul 30;7(1).
51. Palanivel C, Kumar AM V, Mahalakshmi T, Govindarajan S, Claassens M, Satyanarayana S, et al. Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India. Public Health Action. 2013 Sep 21;3(3):220–3.
52. National AIDS Control Organization and Central TB Division. Minutes of meeting of National Technical Working Group on HIV/TB Collaborative Activities at National AIDS Control Organization, New Delhi, on 17/12/2011. New Delhi, India; 2012.
53. Kaur P, Sharma P, Aggarwal A. HIV positivity in TB suspects--an observational, non-randomized study. Indian J Tuberc. 2013;60(1):59–60.
54. Kee M, Lee KH, Lee SY, Kang C, Chu C. Trends and Characteristics of HIV Infection among Suspected Tuberculosis Cases in Public Health Centers in Korea: 2001-2013. Osong Public Heal Res Perspect. 2014;5(Suppl):S37-42.
55. Rueda ZV, López L, Vélez LA, Marín D, Giraldo MR, Pulido H, et al. High incidence of tuberculosis, low sensitivity of current diagnostic scheme and prolonged culture positivity in four colombian prisons. A cohort study. PLoS One. 2013;8(11):e80592.

56. World Health Organization (WHO). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach [Internet]. Geneva, Switzerland; 2013 [cited 2017 Nov 3]. Available from: http://www.who.int/hiv/pub/guidelines/arv2013/download/en/
57. Dlodlo RA, Hwalima ZE, Sithole S, Takarinda KC, Tayler-Smith K, Harries AD. Are HIV-positive presumptive tuberculosis patients without tuberculosis getting the care they need in Zimbabwe? Public Health Action. 2015 Dec;5(4):217–21.
58. Kumar AM V, Singarajipura A, Naik B, Guddemane DK, Patel Y, Shastri S, et al. HIV-infected presumptive tuberculosis patients without tuberculosis: How many are eligible for antiretroviral therapy in Karnataka, India? J Epidemiol Glob Health. 2017 Mar;7(1):11–9.
59. World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection Recommendations for a public health approach - Second edition. Geneva 27 Switzerland: World Health Organization; 2016.
60. Saggurti N, Nair S, Malviya A, Decker MR, Silverman JG, Raj A. Male migration/mobility and HIV among married couples: cross-sectional analysis of nationally representative data from India. AIDS Behav. 2012 Aug;16(6):1649–58.
61. Arora P, Nagelkerke N, Sgaier SK, Kumar R, Dhingra N, Jha P. HIV, HSV-2 and syphilis among married couples in India: patterns of discordance and concordance. Sex Transm Infect. 2011;87(6):516–20.
62. Kumar AM V, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, et al. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. Public Health Action. 2013 Mar 21;3(1):60–2.
63. Axshya SAMVAD Study Group, Shewade HD, Chadha SS, Gupta V, Tripathy JP, Satyanarayana S, et al. Data collection using open access technology in multicentre operational research involving patient interviews. Public Health Action. 2017 Mar 21;7(1):74–7.
64. Shewade HD, Vidhubala E, Subramani DP, Lal P, Bhatt N, Sundaramoorthi C, et al. Open access tools for quality-assured and efficient data entry in a large, state-wide tobacco survey in India. Glob Health Action. 2017;10(1):1394763.
65. Ntsekhe M, Wiysonge CS, Gumedze F, Maartens G, Commerford PJ, Volmink JA, et al. HIV infection is associated with a lower incidence of constriction in presumed tuberculous pericarditis: a prospective observational study. PLoS ONE [Electronic Resour. 2008;3(6):e2253.
66. Bhigjee AI, Padayachee R, Paruk H, Hallwirth-Pillay KD, Marais S, Connoly C. Diagnosis of tuberculous meningitis: clinical and laboratory parameters. Int J Infect Dis. 2007;11(4):348–54.
67. United Nations. Transforming Our World: The 2030 Agenda For Sustainable Development Transforming Our World: The 2030 Agenda For Sustainable Development. 2016.
68. The Joint United Nations Programme on HIV/AIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. Geneva; 2014.
69. Lopez-Varela E, Augusto OJ, Gondo K, Garcia-Basteiro AL, Fraile O, Ira T, et al. Incidence of Tuberculosis Among Young Children in Rural Mozambique. Pediatr Infect Dis J. 2015;34(7):686–92.

70. Nicol MP, Workman L, Isaacs W, Munro J, Black F, Eley B, et al. Accuracy of the Xpert MTB/RIF test for the diagnosis of pulmonary tuberculosis in children admitted to hospital in Cape Town, South Africa: a descriptive study. Lancet Infect Dis. 2011;11(11):819–24.
71. Nicol MP, Allen V, Workman L, Isaacs W, Munro J, Pienaar S, et al. Urine lipoarabinomannan testing for diagnosis of pulmonary tuberculosis in children: a prospective study. Lancet Glob Heal. 2014;2(5):e278-84.
72. Zar HJ. Prevention of HIV-associated respiratory illness in children in developing countries: potential benefits. Int J Tuberc Lung Dis. 2003 Sep;7(9):820–7.
73. Rachow A, Clowes P, Saathoff E, Mtafya B, Michael E, Ntinginya EN, et al. Increased and expedited case detection by Xpert MTB/RIF assay in childhood tuberculosis: a prospective cohort study. Clin Infect Dis. 2012;54(10):1388–96.
74. Kroidl I, Clowes P, Reither K, Mtafya B, Rojas-Ponce G, Ntinginya EN, et al. Performance of urine lipoarabinomannan assays for paediatric tuberculosis in Tanzania. Eur Respir J. 2015/06/27. 2015;
75. Ramsay A, Harries AD, Zachariah R, Bissell K, Hinderaker SG, Edginton M, et al. The Structured Operational Research and Training Initiative for public health programmes. Public Health Action. 2014;4(2):79–84.
76. Kumar AM V, Satyanarayana S, Dar Berger S, Chadha SS, Singh RJ, Lal P, et al. Promoting operational research through fellowships: a case study from the South-East Asia Union Office. Public Health Action. 2015 Mar 21;5(1):6–16.
77. Kumar AM V, Shewade HD, Tripathy JP, Guillerm N, Tayler-Smith K, Berger SD, et al. Does research through Structured Operational Research and Training (SORT IT) courses impact policy and practice? Public Health Action. 2016 Mar 21;6(1):44–9.
78. Rusen ID, Harries AD, Zachariah R, Ramsay A. Capacity Building in Operational Research: More than One Way to Slice the Cake. Front public Heal. 2015;3:176.
79. Klinkenberg E, Assefa D, Rusen ID, Dlodlo RA, Shimeles E, Kebede B, et al. The Ethiopian initiative to build sustainable capacity for operational research: overview and lessons learned. Public Health Action. 2014 Dec;4(Suppl 3):S2-7.
80. Melin G, Allinson R, Grudin M, Mostert B, Ploeg M, Sadeski F, et al. Evaluation of the Developing Operational Research Capacity in the Health Sector Project. Final Report. [Internet]. Technopolis Group, Stockholm, Sweden; 2015 [cited 2015 Nov 3]. p. 1–140. Available from: https://www.gov.uk/dfid-research-outputs/evaluation-of-the-developing-operational-research-capacity-in-the-health-sector-project-final-report
81. Hoa NB, Nhung N V, Kumar AM V, Harries AD. The effects of placing an operational research fellow within the Viet Nam National Tuberculosis Programme. Public Health Action. 2016 Dec 21;6(4):273–6.
82. Ade S, Affolabi D, Adjobimey M, Ade G, Anagonou S, Kumar AMV, Harries AD. Operational research within the national tuberculosis control programme in Benin. BMC Res Notes. 2017;10(1):651.
83. Kumar AM V, Zachariah R, Satyanarayana S, Reid AJ, Van den Bergh R, Tayler-Smith K, et al. Operational research capacity building using “The Union/MSF” model: adapting as we go along. BMC Res Notes. 2014 Nov 19;7:819.

84. Kumar A M V, Satyanarayana S, Wilson N, Zachariah R, Harries a D. Operational research capacity building in Asia: innovations, successes and challenges of a training course. Public Health Action. 2013 Jun 21;3(2):186–8.
85. Cox H, Ford N. The scourge of tuberculosis and anti-tuberculosis drug resistance in Eastern Europe. Public Health Action. 2014 Oct;4(Suppl 2):S1-2.
86. Decroo T, Fitzpatrick G, Amone J. What was the effect of the West African Ebola outbreak on health programme performance, and did programmes recover? Public Health Action. 2017 Jun 21;7(Suppl 1):S1–2.

SUMMARY

Tuberculosis (TB) and the Human Immunodeficiency Virus (HIV) are two of the most deadly infectious diseases in the history of humanity. Despite great progress over the years in the care of TB and HIV, they still remain the leading infectious causes of death globally. In 2015, an estimated 10.4 million patients fell ill with TB and about 1.8 million died due to TB. An estimated 1.2 million (11%) new TB cases occurred among people living with HIV (PLHIV) and 400,000 TB related deaths were among PLHIV. There has been great progress with TB and HIV care over the years. It is estimated that TB treatment averted 49 million deaths between 2000 and 2015, and incidence and death rates fell during this period. Similarly, HIV incidence is declining in many parts of the world and access to antiretroviral therapy (ART) has increased several fold. Buoyed by these developments, the global community has pledged to end the TB and AIDS epidemics by 2030 as part of the larger sustainable development goals.

The global TB burden is primarily driven by the large absolute numbers in India. In 2015, an estimated 2.8 million people fell ill with TB in India thus accounting for 27% of the global TB burden. Similarly, about 480,000 people died due to TB in India accounting for one-third of global TB mortality. About 2.1 million people were estimated to be living with HIV in India (prevalence of 0.26%) in 2015 making the country home to the third largest number of PLHIV globally. The HIV epidemic in India is heterogenous and concentrated among high risk groups, but it is showing a declining trend, probably due to prevention and treatment strategies by the National AIDS Control Programme (NACP). With an estimated HIV prevalence of 5% among people with TB, India is home to the second largest number of HIV-infected TB patients in absolute terms (113,000), next only to South Africa (270,000), and accounts for about 10% of the global HIV-TB burden.

The evolution and progress of TB-HIV collaborative activities in India has been show cased as a success story globally, particularly for a country with a concentrated HIV epidemic. As of now, India follows all the recommendations enshrined in the 2012 WHO global policy on TB-HIV collaborative activities, though the extent of implementation varies across the components. The basic mechanisms of collaboration between the national TB and HIV programmes in India are in place at all levels of the health system (national, state and district), and these include joint recording and reporting, joint monitoring and review.

Since this thesis consists of TB-HIV related operational research studies conducted in India during the period 2011-2015, we begin here by providing a brief overview of the evolution of TB-HIV care in India and analyse the situation in 2010 which stimulated and necessitated the conduct of these operational research studies.

TB-HIV collaboration started in India in 2001, in six selected states of the country - Maharashtra, Manipur, Nagaland, Karnataka, Tamil Nadu and Andhra Pradesh. The early activities were primarily joint training of health staff in TB-HIV and cross-referrals. Based on evidence from several operational research studies conducted between 2005 and 2008, a decision was made at national level to implement a differential strategy in the country

- a package of essential TB-HIV interventions (establishing mechanisms of coordination, training of staff, Intensified TB case finding at HIV counselling and testing centres and ART Centres, risk-based, selective referral of TB patients for HIV testing and linkage to care) to be implemented in all states, while an intensified package (routine referral of TB patients for HIV testing, decentralised cotrimoxazole preventive therapy and referral to ART to all HIV-TB patients) was to be implemented in selected states with a higher burden of HIV, improved availability of HIV testing, better treatment infrastructure and services and higher programme management capacity. It was decided in 2009 to scale-up the implementation of "Intensified TB-HIV activities" nationwide and the goal was reached in July 2012.

There were several important challenges in implementation of TB/HIV collaborative activities.

1) **Challenges in setting up mechanisms of collaboration** at all levels of the health system, especially at district level was challenging. Surveillance of HIV prevalence among TB patients and vice versa was not comprehensive. Administrative guidelines for organizing training of staff were not uniform under the NACP and RNTCP and were frequently a source of conflict in programme implementation. The existing recording and reporting systems were not optimal. There was a lack of time and capacity to conduct policy-relevant operational research among the programme staff.
2) **Challenges in reducing the burden of TB among PLHIV:** Intensified TB case finding (ICF) activities were established in all HIV testing and counselling centres across the country with standardized recording and reporting. But the implementation varied and was suboptimal in low-HIV prevalence states. Sputum smear microscopy was still the mainstay of diagnosis at the time despite its known limitations among PLHIV (limited sensitivity, inability to identify drug resistance). The widely acclaimed rapid diagnostic test such as the Xpert MTB/RIF assay was still not widely available in India. Isoniazid preventive therapy (IPT) for PLHIV without TB was not a policy at the time. The implementation of TB infection control in health care and congregate settings was poor.
3) **Challenges in reducing the burden of HIV among TB patients:** There were wide variations in the implementation of HIV testing among TB patients due to variations in availability of HIV testing services and interruptions in supply of HIV testing kits. HIV testing of presumptive TB patients was not a national policy at the time, even though WHO recommended moving HIV testing upstream by testing all patients with presumptive TB (formerly referred to as TB suspects) as a way of early detection of HIV-infected TB patients. While nearly 90% of HIV-infected TB patients received CPT at the time, only about 50% HIV infected TB patients were linked to ART care and support. One of the reasons ascribed to the low proportion of HIV-TB patients on ART was that not all HIV-infected TB patients were eligible for ART. India still followed the WHO 2006 guidelines and had concerns about adopting the WHO 2010 ART guidelines (these specified that all HIV-infected TB patients were eligible for ART irrespective of the CD4-cell count) since there were concerns about the resource implications and the increased workload that such a strategy would impose on the national ART programme. Other barriers to ART linkage were related to long travel times, distances

and financial burdens for patients as ART services were centralised and were provided in selected health facilities only.

To address the challenges described above and to improve the care and management of HIV-infected TB patients in India, several operational research studies were planned and carried out. The three key objectives were:

1) To evaluate the additional number of patients that would be initiated on ART if India adopted the current 2010 WHO ART guidelines of placing all HIV-infected TB patients on ART regardless of CD4 cell count
2) To assess the prevalence of HIV among patients with presumptive TB in different settings with different levels of HIV infection and the proportion eligible for starting ART according to 2015 WHO Guidelines
3) To document the operational research capacity building initiative undertaken in India, its evolution and impact on policy and practice.

We describe six operational research studies (including two multicentre operational research projects) and their findings in this thesis and discuss their overall contribution to changes in policy, practice and the improvement of health outcomes among HIV-infected TB patients in India. A brief summary of what is covered in each chapter is provided below.

OBJECTIVE 1:

In 2010, WHO expanded previously-recommended indications for ART to include all HIV-infected TB patients irrespective of the CD4 count. India, however, still limited ART to TB patients with CD4-cell counts <350/mm3 or with extra-pulmonary TB. We sought to evaluate the additional number of patients that would be initiated on ART if India adopted the current 2010 WHO ART guidelines for HIV-infected TB patients. The findings of this research study are described in **Chapter 2**. This study showed that nine out of ten HIV-TB patients were already eligible for ART as per WHO 2006 guidelines and recommended that, as a public health approach, ART should be provided to all HIV-TB patients irrespective of CD4 count. India adopted the policy of universal ART for HIV-TB patients following this study.

OBJECTIVE 2:

HIV testing of persons referred for tuberculosis diagnosis (patients with presumptive TB) is recommended by WHO but was not a policy in India, where HIV prevalence among TB suspects had never been studied. To fill this knowledge gap, a study was conducted in two districts of South India to assess the prevalence of HIV among patients with presumptive TB and the feasibility of provider initiated HIV testing under programmatic settings. The findings of these studies are reported in **Chapters 3 and 4**. These studies showed that HIV prevalence among presumptive TB patients was as high as that among TB patients.

Based on the findings of the studies described in **Chapters 3 and 4**, a national policy decision was taken to routinely offer HIV testing to patients with presumptive TB in high-burden HIV states of India. However, how this should best be implemented and monitored in routine health care settings in India was not known. An operational research was conducted in Karnataka State (South India, population 64 million and accounting for 10% of India's national HIV burden) to test processes and learn results and challenges of screening presumptive TB patients for HIV within routine health care settings. The findings of this operational research study are described in **Chapter 5**. The processes piloted in this study have now become part of programme guidelines and practice. An innovative process using open-access technologies like EpiData, Dropbox and TeamViewer was used to co-ordinate quality-assured data capture in this multicentre study. This model of data capture is described in detail in **Chapter 6**.

While it became clear that HIV testing among presumptive TB patients was of value in high-HIV burden settings of India, it was not clear if it was of value in low-HIV burden settings. A study was undertaken in Puducherry to answer this question. The findings of this study are described in **Chapter 7**. This study showed HIV testing among presumptive TB patients was worthwhile even in low HIV settings, especially when offered to people aged 25-54 years.

Chapter 8 describes the results of an operational research study conducted in the state of Karnataka to assess the proportion of HIV-infected presumptive TB patients eligible for initiating ART as per the WHO guidelines at the point in time. This study showed that most of the HIV-infected presumptive TB patients were eligible for ART and made a strong case for universal ART in this group.

OBJECTIVE 3:

To catalyse the generation of evidence, we built capacity of several public health professionals in India using the SORT IT (Structured Operational Research Training Initiative) model of capacity building, developed by the International Union Against Tuberculosis and Lung Disease (The Union) and Medecins Sans Frontieres in partnership with the WHO's Special Programme for Research and Training in Tropical Diseases (WHO-TDR). In addition, the defender of this thesis was mentored under a Global OR fellowship programme run by The Union in 2012. The SORT IT model and its adaptations, the OR fellowship programme and the impact of these on policy and practice have been described in a series of original research and viewpoint articles. Most of the papers described in this thesis are a result and outcome of these two initiatives. We describe in **chapters 9-12** the evolution of this model of capacity building and its impact on policy and practice.

In conclusion, the body of work contained in this thesis demonstrates the strong role that operational research has played to inform policy and change practice in the setting of a national TB and HIV programme in India. Several key national policy decisions were made on the basis of evidence generated in routine programme settings which included starting

ART for all HIV-infected TB patients irrespective of ART and offering HIV testing routinely to all presumptive TB patients in India. The conduct of operational research was facilitated and catalysed greatly by the capacity building initiatives driven by The Union which included training public health professionals in the SORT IT model of training and the Global OR Fellowship programme. Studies have also showcased the impact of research conducted in SORT IT courses on policy and practice and the case study from the USEA office showed what OR fellows could achieve if provided with the right opportunity, support, mentorship and enabling environment. As a result of these initiatives, a great resource pool has been created in India which is being drawn on to facilitate OR courses in wider areas of disease control both in India and worldwide.

The full citations of the published studies that make up this thesis are shown below:

Chapter 2: **Kumar AMV**, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, Lal K, Reddy HRR, Naik B, Prasad R, Yaqoob M, Deepak KG, Shastri S, Satyanarayana S, David Harries A, Chauhan LS, Dewan P. Will Adoption of the 2010 WHO ART Guidelines for HIV-Infected TB Patients Increase the Demand for ART Services in India? PLoS ONE. 2011;6(9):e24297.

Chapter 3: Naik B, **Kumar AMV**, Lal K, Doddamani S, Krishnappa M, Inamdar V, Satyanarayana S, Gupta D, Dewan PK. HIV prevalence among persons suspected of tuberculosis: policy implications for India. Journal of Acquired Immune Deficiency Syndromes. 2012;59(4):e72–6.

Chapter 4: Achanta S, **Kumar AMV**, Nagaraja SB, Jaju J, Shamrao SRM, Uppaluri R, Tekumalla RR, Gupta D, Kumar A, Satyanarayana S, Dewan PK Feasibility and Effectiveness of Provider Initiated HIV Testing and Counseling of TB Suspects in Vizianagaram District, South India. PLoS ONE. 2012;7(7):e41378.

Chapter 5: **Kumar AMV**, Gupta D, Kumar A, Gupta RS, Kanchar A, Rao R, Shastri S, Suryakanth MD, Rangaraju C, Naik B, Guddemane DK, Bhat P, Nair AS, Harries AD, Dewan P. HIV Testing among Patients with Presumptive Tuberculosis: How Do We Implement in a Routine Programmatic Setting? Results of a Large Operational Research from India. PLoS ONE. 2016;11(5):e0156487.

Chapter 6: **Kumar AMV**, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, Lauritsen JM, Rieder HL. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. Public Health Action. 2013;3(1):60–2

Chapter 7: Palanivel C, **Kumar AMV**, Mahalakshmi T, Govindarajan S, Claassens M, Satyanarayana S, Gurumurthy D, Vasudevan K, Purty A, Paulraj AK, Raman K V. Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India. Public Health Action. 2013;3(3):220–3.

Chapter 8: **Kumar AMV**, Singarajipura A, Naik B, Guddemane DK, Patel Y, Shastri S, Kumar S, Deshmukh R, Rewari BB, Harries AD. HIV-infected presumptive tuberculosis patients without tuberculosis: how many are eligible for antiretroviral therapy in Karnataka, India? Journal of Epidemiology and Global Health. 2017;7(1):11–9.

Chapter 9: **Kumar AMV**, Shewade HD, Tripathy JP, Guillerm N, Tayler-Smith K, Berger SD, Bissell K, Reid AJ, Zachariah R, Harries AD. Does research through Structured Operational Research and Training (SORT IT) courses impact policy and practice? Public Health Action. 2016;6(1):44–9.

Chapter 10: **Kumar AMV**, Satyanarayana S, Berger SD, Chadha SS, Singh RJ, Lal P, Tonsing J, Harries AD. Promoting operational research through fellowships: a case study from the South-East Asia Union Office. Public Health Action. 2015;5(1):6–16.

Chapter 11: **Kumar AMV**, Satyanarayana S, Wilson N, Zachariah R, Harries AD. Operational research capacity building in Asia: innovations, successes and challenges of a training course. Public Health Action. 2013;3(2):186–8.

Chapter 12: **Kumar AMV**, Zachariah R, Satyanarayana S, Reid AJ, Van den Bergh R, Tayler-Smith K, Khogali M, Harries AD. Operational research capacity building using 'The Union/MSF' model: adapting as we go along. BMC Research Notes. 2014;7(1):819.

SAMENVATTING

Tuberculose (tbc) en het humaan immunodeficiëntievirus (hiv) zijn twee van de dodelijkste infectieziekten in de geschiedenis van de mensheid. Ondanks de grote vooruitgang die in de loop der jaren is geboekt in de tbc- en hiv-zorg vormen zij wereldwijd nog steeds de belangrijkste infectieuze doodsoorzaken. In 2015 raakten er naar schatting 10,4 miljoen mensen besmet met tbc en stierven er ongeveer 1,8 miljoen als gevolg van tbc. Naar schatting deden 1,2 miljoen (11%) nieuwe tbc-gevallen zich voor onder mensen met hiv en er waren 400.000 tbc-gerelateerde sterfgevallen onder mensen met hiv. In de loop der jaren is er grote vooruitgang geboekt op het gebied van tbc- en hiv-zorg. Naar schatting zijn er door de behandeling van tbc tussen 2000 en 2015 49 miljoen sterfgevallen voorkomen en zijn de incidentie en het sterftecijfer in deze periode gedaald. Op dezelfde manier neemt de hiv-incidentie in vele delen van de wereld af en is de toegang tot antiretrovirale therapie (ART) meermaals toegenomen. Ondersteund door deze ontwikkelingen heeft de wereldgemeenschap zich ertoe verbonden om tegen 2030 een einde te maken aan de tbc- en aids-epidemieën als onderdeel van de grotere doelstellingen voor duurzame ontwikkeling.

De wereldwijde tbc-last wordt voornamelijk veroorzaakt door de grote absolute aantallen in India. In 2015 zijn naar schatting 2,8 miljoen mensen in India ziek geworden door tbc, wat 27% is van de wereldwijde tbc-last. Ook stierven in India ongeveer 480.000 mensen als gevolg van tbc, wat een derde van de wereldwijde tbc-sterfte is. In 2015 leefden er in India naar schatting 2,1 miljoen mensen met hiv (prevalentie van 0,26%), waarmee het land op de derde plaats op de ranglijst komt van landen met grote aantallen mensen met hiv. De hiv-epidemie in India is heterogeen en geconcentreerd onder risicogroepen, maar vertoont een dalende trend, die waarschijnlijk ten gevolge ligt aan de preventie- en behandelingsstrategieën van het nationale aidsbestrijdingsprogramma (NACP). Met een geschatte hiv-prevalentie van 5% onder mensen met tbc staat India nummer twee op de ranglijst van landen met grote aantallen hiv-geïnfecteerde tbc-patiënten in absolute termen (113.000), naast Zuid-Afrika (270.000), en is het land verantwoordelijk voor ongeveer 10% van de wereldwijde hiv-tbc-druk.

De evolutie en vooruitgang van de tbc-hiv-samenwerkingsactiviteiten in India vormen wereldwijd een succesverhaal, vooral gezien het feit dat het een land is met een geconcentreerde hiv-epidemie. Vanaf nu volgt India alle aanbevelingen op die zijn vastgelegd in het wereldwijde beleid van de WGO voor 2012 inzake tbc-hiv-samenwerkingsactiviteiten, hoewel de mate van implementatie per onderdeel verschilt. De basismechanismen voor samenwerking tussen de nationale tbc- en hiv-programma's in India zijn van kracht op alle niveaus van het gezondheidssysteem (nationaal niveau, deelstaatsniveau en districtsniveau), en deze omvatten gezamenlijke registratie en rapportage en gezamenlijke monitoring en evaluatie.

Aangezien dit proefschrift zich richt op operationeel onderzoek naar tbc-hiv in India in de periode 2011-2015, beginnen we hier met een kort overzicht van de evolutie van de tbc-

hiv-zorg in India en analyseren we de situatie in 2010 die de uitvoering van dit operationeel onderzoek stimuleerde en noodzakelijk maakte.

De samenwerking in de instellingen in de tbc- en hiv-zorg in India begon in 2001, in zes geselecteerde deelstaten van het land: Maharashtra, Manipur, Nagaland, Karnataka, Tamil Nadu en Andhra Pradesh. De eerste activiteiten betroffen voornamelijk de gezamenlijke opleiding van gezondheidswerkers op het gebied van tbc en hiv en onderlinge consultatie. Gebaseerd op bewijsmateriaal uit verscheidene studies op het gebied van operationeel onderzoek die tussen 2005 en 2008 werden uitgevoerd, werd op nationaal niveau besloten een differentiële strategie te volgen, waarbij een pakket van essentiële tbc-hiv-acties (het van creëren van coördinatiemechanismen, opleiding van personeel, intensievere opsporing van tbc-gevallen in de hiv-advies- en testcentra en de centra voor antiretrovirale therapie (ART), op risico gebaseerde, selectieve verwijzing van tbc-patiënten voor hiv-testen en koppeling aan zorg) wordt uitgevoerd in alle deelstaten, terwijl een geïntensiveerd pakket (routineverwijzing van tbc-patiënten voor hiv-testen, gedecentraliseerde preventieve cotrimoxazoltherapie en verwijzing van alle hiv-tbc-patiënten naar ART-centra) moest worden uitgevoerd in bepaalde deelstaten met een hogere hiv-last, verbeterde beschikbaarheid van hiv-testen, een betere behandelingsinfrastructuur en betere diensten en een hogere programma-managementcapaciteit. In 2009 werd besloten om de implementatie van geïntensiveerde tbc-hiv-activiteiten landelijk op te schalen. Dit doel werd in juli 2012 bereikt.

Er waren verschillende belangrijke uitdagingen bij de uitvoering van de tbc-hiv-samenwerkingsactiviteiten.

1) **De uitdagingen bij het opzetten van samenwerkingsmechanismen** op alle niveaus van het gezondheidssysteem waren enorm, vooral op districtsniveau. Het toezicht op de prevalentie van hiv onder tbc-patiënten en vice versa was niet volledig. De administratieve richtlijnen voor de organisatie van de opleiding van het personeel waren niet uniform onder het NACP en het herziene nationale programma voor tuberculosebestrijding (RNTCP) en vormden vaak een bron van conflicten bij de uitvoering van het programma. De bestaande registratie- en rapportagesystemen waren niet optimaal. Er was gebrek aan tijd en capaciteit om beleidsrelevant operationeel onderzoek uit te voeren onder de programmamedewerkers.
2) **Uitdagingen bij het verminderen van de tbc-last bij mensen met hiv**: In alle hiv-test- en adviescentra in het hele land werden intensief tbc-gevallenonderzoek (ICF) opgezet met gestandaardiseerde registratie en rapportage. Maar de uitvoering varieerde en was suboptimaal in staten met een lage hiv-prevalentie. De sputumuitstrijkmicroscopie was destijds nog steeds de steunpilaar van de diagnose, ondanks de bekende beperkingen onder mensen met hiv (beperkte gevoeligheid, onvermogen om resistentie tegen geneesmiddelen te identificeren). De alom geprezen snelle diagnostische test zoals de Xpert MTB/RIF-test was nog steeds niet op grote schaal beschikbaar in India. Toentertijd maakte preventieve isoniazidtherapie voor mensen met hiv

zonder tbc nog geen deel van het beleid uit. De tbc-besmettingsbeheersing in de gezondheidszorg en instellingen waar veel mensen samenkomen was slecht geregeld.

3) **Uitdagingen bij het verminderen van de hiv-belasting onder tbc-patiënten**: Er waren grote verschillen in de implementatie van hiv-testen onder tbc-patiënten vanwege variaties in de beschikbaarheid van op hiv testende diensten en vertragingen in de levering van hiv-testkits. Het testen op hiv van vermoedelijke tbc-patiënten was toentertijd geen nationaal beleid, alhoewel de WGO wel de aanbeveling deed om alle vermoedelijke tbc-patiënten (die vroeger tbc-verdachten werden genoemd) te testen en zo te komen tot een vroege opsporing van met hiv besmette tbc-patiënten. Terwijl bijna 90% van de met hiv geïnfecteerde tbc-patiënten op dat moment preventieve cotrimoxazole therapie ontving, kreeg slechts ongeveer 50% van de met hiv geïnfecteerde tbc-patiënten ART-zorg en -ondersteuning. Een van de redenen voor het lage aandeel hiv-tbc-patiënten in de ART-zorg was dat niet alle met hiv besmette tbc-patiënten voor ART in aanmerking kwamen. India volgde nog steeds de richtlijnen van de WGO uit 2006 en had moeite met de goedkeuring van de WGO-richtlijnen voor ART uit 2010 (volgens welke alle met hiv geïnfecteerde tbc-patiënten in aanmerking kwamen voor ART, ongeacht het aantal CD4-cellen) omdat er bezorgdheid bestond over de implicaties voor de beschikbare middelen en de toegenomen werklast die een dergelijke strategie met zich mee zou brengen binnen het nationale ART-programma. Andere belemmeringen voor de koppeling met ART hielden verband met de lange reistijden, afstanden en financiële lasten voor patiënten, aangezien ART-diensten werden gecentraliseerd en alleen in bepaalde zorgfaciliteiten werden verleend.

Om de hierboven beschreven uitdagingen aan te pakken en om de zorg voor met hiv geïnfecteerde tbc-patiënten in India te verbeteren, werden verschillende operationele onderzoeken gepland en uitgevoerd. De drie belangrijkste doelstellingen waren:

1) Het evalueren van het extra aantal patiënten waarmee de ART-centra te maken zouden krijgen als India volgens de WGO-richtlijnen voor ART uit 2010 alle met hiv besmette tbc-patiënten ongeacht de CD4-celtelling opnam in het ART-programma;
2) Het beoordelen van de hiv-prevalentie bij vermoedelijke tbc-patiënten in verschillende settings met verschillende niveaus van hiv-infectie en het percentage dat in aanmerking komt voor ART overeenkomstig de WGO-richtsnoeren van 2015;
3) Het documenteren van het initiatief voor capaciteitsopbouw op het gebied van operationeel onderzoek in India, de ontwikkeling ervan en het effect ervan op het beleid en de praktijk.

In dit proefschrift beschrijven we zes operationele onderzoeken (waaronder twee multicentrische projecten) en de bevindingen waartoe ze hebben geleid en bespreken we hun algemene bijdrage aan veranderingen in het beleid en de praktijk en aan de verbetering van de gezondheidsresultaten onder met hiv geïnfecteerde tbc-patiënten in India. Hieronder volgt een korte samenvatting van wat er in elk hoofdstuk wordt behandeld.

DOELSTELLING 1:

In 2010 breidde de WGO eerder aanbevolen indicaties voor ART uit met alle met hiv geïnfecteerde tbc-patiënten, ongeacht de CD4-telling. India beperkte ART echter nog steeds tot tbc-patiënten met CD4-celtellingen <350/mm3 of met extrapulmonale tbc. We wilden het extra aantal patiënten evalueren dat in de ART-zorg terecht zou komen als India de WGO-richtlijnen voor met besmette tbc-patiënten uit 2010 zou implementeren. De bevindingen van dit onderzoek worden beschreven in **hoofdstuk 2**. Deze studie toont aan dat negen van de tien hiv-tbc-patiënten al in aanmerking kwamen voor ART volgens de richtlijnen van de WGO uit 2006 en adviseert dat, als volksgezondheidsbenadering, ART moet worden verstrekt aan alle hiv-tbc-patiënten ongeacht de CD4 telling. Na deze studie heeft India het beleid met betrekking tot ART voor hiv-tbc-patiënten goedgekeurd.

DOELSTELLING 2:

De WGO adviseert om personen die voor tuberculosediagnose (vermoedelijke tbc-patiënten) worden doorverwezen, te testen op hiv, maar dit was geen gangbaar beleid in India, waar de hiv-prevalentie onder vermoedelijke tbc-patiënten nooit was bestudeerd. Om dit kennishiaat op te vullen, werd een studie uitgevoerd in twee districten in Zuid-India om de hiv-prevalentie onder vermoedelijke tbc-patiënten en de haalbaarheid van provider initiated testing (waarbij de hiv-test wordt aangeraden door de zorgverlener in een klinische setting) te beoordelen. De bevindingen van deze studies worden gerapporteerd in **hoofdstuk 3 en 4**. Deze studies toonden aan dat de hiv-prevalentie onder vermoedelijke tbc-patiënten net zo hoog was als onder tbc-patiënten.

Gebaseerd op de bevindingen van de studies die in hoofdstuk 3 en 4 worden beschreven, werd een nationaal beleidsbesluit genomen om de hiv-test aan te bieden aan vermoedelijke tbc-patiënten in deelstaten van India met een hoge hiv-last. Hoe dit het beste zou kunnen worden uitgevoerd en gecontroleerd in routinematige zorgkaders in India wist men echter niet. Er werd operationeel onderzoek uitgevoerd in de deelstaat Karnataka (Zuid-India, 64 miljoen inwoners en verantwoordelijk voor 10% van de nationale hiv-last in India) om processen te testen en de resultaten en uitdagingen van de hiv-screening van vermoedelijke tbc-patiënten binnen de reguliere gezondheidszorg te achterhalen. De bevindingen van dit operationele onderzoek worden beschreven in **hoofdstuk 5**. De processen die in deze studie zijn getest, zijn nu onderdeel geworden van de programmarichtlijnen en de praktijk. Een innovatief proces met behulp van 'open access'-technologieën zoals EpiData, Dropbox en TeamViewer werden gebruikt om het vastleggen van kwaliteitgerelateerde gegevens in deze multicentrische studie te coördineren. Dit model van gegevensvastlegging wordt in detail beschreven in **hoofdstuk 6**.

Terwijl het duidelijk werd dat het testen op hiv van vermoedelijke tbc-patiënten van waarde was in settings met een hoge hiv-last in India, was het niet duidelijk of het ook van waarde was in situaties met een lage hiv-last. Om deze vraag te beantwoorden werd onderzoek verricht in Puducherry. De bevindingen van dit onderzoek worden beschreven in

hoofdstuk 7. Dit onderzoek toont aan dat het testen op hiv van vermoedelijke tbc-patiënten de moeite waard is, zelfs in lage hiv-settings, vooral bij mensen van 25-54 jaar.

Hoofdstuk 8 beschrijft de resultaten van een operationeel onderzoek die in de staat Karnataka is uitgevoerd om het aandeel van met hiv besmette vermoedelijke tbc-patiënten te beoordelen dat in aanmerking komt voor ART volgens de geldende WGO-richtlijnen. Deze studie toont aan dat de meeste vermoedelijke tbc-patiënten die met hiv besmet zijn in aanmerking komen voor ART en pleit nadrukkelijk voor ART voor deze groep.

DOELSTELLING 3:

Om de bewijsgaring te katalyseren hebben we de capaciteit van verschillende gezondheidsprofessionals in India opgebouwd met behulp van het SORT IT (Structured Operational Research Training Initiative) model voor capaciteitsopbouw, ontwikkeld door de Internationale Unie tegen Tuberculosis en Longziekte (de Unie) en Artsen Zonder Grenzen in samenwerking met het speciale programma voor onderzoek en training op het gebied van tropische ziekten van de WGO. Daarnaast werd de verdediger van dit proefschrift begeleid in het kader van een Global OR-fellowship-programma van de Unie in 2012. Het Structured Operational Research and Training (SORT IT) model en de aanpassingen daarin en het OR-fellowshipprogramma en de impact hiervan op het beleid en de praktijk zijn beschreven in een reeks originele onderzoeksartikelen en gezichtspunten. De meeste papers die in dit proefschrift worden beschreven, zijn het resultaat van deze twee initiatieven. In **hoofdstuk 9-12** beschrijven we de evolutie van dit capaciteitsopbouwmodel en de impact ervan op het beleid en de praktijk.

Concluderend kan worden gesteld dat het werk dat in dit proefschrift is vervat, aantoont dat operationeel onderzoek een belangrijke rol heeft gespeeld bij het opstellen van een nationaal tbc- en hiv-programma in India en dat operationeel onderzoek een belangrijke rol heeft gespeeld bij het bepalen van het beleid en het veranderen van de praktijk. Verscheidene zeer belangrijke nationale beleidsbesluiten werden genomen op basis van bewijsmateriaal dat binnen routinematige programmakaders werd verkregen, zoals het besluit om alle met hiv besmette tbc-patiënten in aanmerking te laten komen voor ART en het besluit om hiv-tests aan te bieden aan alle vermoedelijke tbc-patiënten in India. Operationeel onderzoek werd vergemakkelijkt en werd zeer sterk gekatalyseerd door de capaciteitsopbouwende initiatieven die door de Unie werden ontplooid, waaronder de training van gezondheidszorgprofessionals in het gebruik van het SORT IT-model en het Global OR-Fellowshipprogramma. De studies hebben ook het effect van onderzoek aangetoond dat in SORT-IT-cursussen werd uitgevoerd met betrekking tot het beleid en de praktijk. De casestudy van het bureau USEA toont aan wat OR-medewerkers kunnen bereiken met behulp van de juiste kansen, steun, goed mentorschap en een stimulerende omgeving. Als resultaat van deze initiatieven is een grote pool van middelen gecreëerd in India, die wordt aangesproken om OR-cursussen op bredere gebieden van ziektebestrijding zowel in India als wereldwijd te faciliteren.

De volledige citaten van de gepubliceerde studies die deel uitmaken van dit proefschrift zijn hieronder weergegeven.

Chapter 2: **Kumar AMV**, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, Lal K, Reddy HRR, Naik B, Prasad R, Yaqoob M, Deepak KG, Shastri S, Satyanarayana S, David Harries A, Chauhan LS, Dewan P. Will Adoption of the 2010 WHO ART Guidelines for HIV-Infected TB Patients Increase the Demand for ART Services in India? PLoS ONE. 2011;6(9):e24297.

Chapter 3: Naik B, **Kumar AMV**, Lal K, Doddamani S, Krishnappa M, Inamdar V, Satyanarayana S, Gupta D, Dewan PK. HIV prevalence among persons suspected of tuberculosis: policy implications for India. Journal of Acquired Immune Deficiency Syndromes. 2012;59(4):e72–6.

Chapter 4: Achanta S, **Kumar AMV**, Nagaraja SB, Jaju J, Shamrao SRM, Uppaluri R, Tekumalla RR, Gupta D, Kumar A, Satyanarayana S, Dewan PK Feasibility and Effectiveness of Provider Initiated HIV Testing and Counseling of TB Suspects in Vizianagaram District, South India. PLoS ONE. 2012;7(7):e41378.

Chapter 5: **Kumar AMV**, Gupta D, Kumar A, Gupta RS, Kanchar A, Rao R, Shastri S, Suryakanth MD, Rangaraju C, Naik B, Guddemane DK, Bhat P, Nair AS, Harries AD, Dewan P. HIV Testing among Patients with Presumptive Tuberculosis: How Do We Implement in a Routine Programmatic Setting? Results of a Large Operational Research from India. PLoS ONE. 2016;11(5):e0156487.

Chapter 6: **Kumar AMV**, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, Lauritsen JM, Rieder HL. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. Public Health Action. 2013;3(1):60–2

Chapter 7: Palanivel C, **Kumar AMV**, Mahalakshmi T, Govindarajan S, Claassens M, Satyanarayana S, Gurumurthy D, Vasudevan K, Purty A, Paulraj AK, Raman K V. Uptake of HIV testing and HIV positivity among presumptive tuberculosis patients at Puducherry, South India. Public Health Action. 2013;3(3):220–3.

Chapter 8: **Kumar AMV**, Singarajipura A, Naik B, Guddemane DK, Patel Y, Shastri S, Kumar S, Deshmukh R, Rewari BB, Harries AD. HIV-infected presumptive tuberculosis patients without tuberculosis: how many are eligible for antiretroviral therapy in Karnataka, India? Journal of Epidemiology and Global Health. 2017;7(1):11–9.

Chapter 9: **Kumar AMV**, Shewade HD, Tripathy JP, Guillerm N, Tayler-Smith K, Berger SD, Bissell K, Reid AJ, Zachariah R, Harries AD. Does research through Structured Operational Research and Training (SORT IT) courses impact policy and practice? Public Health Action. 2016;6(1):44–9.

Chapter 10: **Kumar AMV**, Satyanarayana S, Berger SD, Chadha SS, Singh RJ, Lal P, Tonsing J, Harries AD. Promoting operational research through fellowships: a case study from the South-East Asia Union Office. Public Health Action. 2015;5(1):6–16.

Chapter 11: **Kumar AMV**, Satyanarayana S, Wilson N, Zachariah R, Harries AD. Operational research capacity building in Asia: innovations, successes and challenges of a training course. Public Health Action. 2013;3(2):186–8.

Chapter 12: **Kumar AMV**, Zachariah R, Satyanarayana S, Reid AJ, Van den Bergh R, Tayler-Smith K, Khogali M, Harries AD. Operational research capacity building using 'The Union/MSF' model: adapting as we go along. BMC Research Notes. 2014;7(1):819.

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ABOUT THE AUTHOR

Dr Ajay Kumar Madhugiri Venkatachalaiah is the Director of Centre for Operational Research of International Union Against Tuberculosis and Lung Disease (The Union). He is a seasoned Public Health Practitioner with 14 years of experience in low- and middle-income settings. He is a medical doctor with a post-graduate specialisation in public health from JIPMER (Jawaharlal Institute of postgraduate medical education and research), a reputed medical institution in India.

Ajay Kumar was born on the 15th of March 1977 in Bangalore (India). Coming from a modest background, he was studious in his school days and topped all the schools in the South Indian Region in the twelfth standard. He pursued his bachelor's course in Medicine (MBBS) in Bangalore Medical College from 1994 to 2000. He then pursued his master's degree in community medicine (MD) from the world-renowned JIPMER in Puducherry (India) from 2002 to 2005 and passed out with a distinction. Following this, he taught community medicine to MBBS and MD students in JIPMER for a brief stint of nine months before joining World Health Organization-India as a consultant for the National Tuberculosis Programme in India (2006-12), particularly in leading the TB-HIV co-ordination activities at national level with an emphasis on the generation of relevant evidence, quick transfer of evidence to national policy, development of operational guidelines, capacity building of national/state-level staff, supervision, monitoring and evaluation.

In February 2012, he joined the International Union Against Tuberculosis and Lung Disease's Centre for Operational Research as an Operational Research Fellow. Over the last six years with The Union, Dr Ajay Kumar has progressively climbed the ranks in public health leadership becoming deputy director of the Centre for Operational Research in 2015 and Director, two years later, in 2017. He has been an author/co-author in over 160 publications in peer-reviewed scientific international journals and has facilitated over 75 national and international courses on operational research, data analysis and paper writing. Several of his research projects, have impacted national policy and practice including the national policy change of routinely offering HIV testing to all presumptive TB patients and screening of all TB patients for Diabetes in India.

CURRICULUM VITAE

NAME AND CONTACT DETAILS

Dr Ajay Kumar Madhugiri Venkatachalaiah

MBBS, MD (Community Medicine) |

Director (Research), International Union Against Tuberculosis and Lung Disease (The Union), 68, boulevard Saint-Michel, 75006, Paris, France

No.11, "Kanakachala Thanmaya", 2nd Cross, Sadahalli Byanna Layout, Guddadahalli Main Road, Hebbal, | Bengaluru 560024 | India

Tel: +91 9036013437 | Fax: +91 11 46 05 44 30 | Skype: ajay.theunion

AKumar@theunion.org; sathyasaakshi@gmail.com | www.theunion.org

Gender: Male

Current Role:

- As Director for the Centre for Operational Research of International Union Against Tuberculosis and Lung Disease (The Union), Paris, France
- Organize and facilitate many national and international courses on operational research and mentor young researchers across the globe (India, Asia, Europe, Africa and South Pacific)

Personal: I am married and live together with my wife, daughter and parents

Date of Birth: 15th March 1977
Place of Birth: Bangalore, India
Citizenship: INDIAN

Names and location of educational institutions attended:	Dates: From:	To:	Degree:	Major subjects:
Jawaharlal Institute of Post-Graduate Medical Education and Research (**JIPMER**), Pondicherry University, Pondicherry, India	April 2002	March 2005	MD Community Medicine (@ Preventive and Social Medicine @Public Health) Passed with Distinction grade of 77.1%	Epidemiology – General and of Specific communicable and Non-communicable diseases, Bio-Statistics, Public Health Administration, Health Planning and Management.
Bangalore Medical College, Bangalore University, Bangalore, Karnataka, India	October 1994	September 2000	MBBS (Bachelor of Medicine and Bachelor of Surgery) Secured an overall aggregate of 69.4%	Medicine, Surgery, Obstetrics and Gynaecology, Pediatrics, Orthopaedics, ENT, Ophthalmology, Pathology, Pharmacology, Preventive and Social Medicine, Forensic Medicine, Anatomy, Physiology and Biochemistry.

EMPLOYMENT HISTORY

Organization :	Key Responsibilities:	Dates: From:	To:
International Union against TB and Lung disease (The Union)	As Director for the Centre for Operational Research of International Union Against Tuberculosis and Lung Disease (The Union), Paris, France, organize and facilitate many national and international courses on operational research and mentor young researchers across the globe (India, Asia, Europe, Africa and South Pacific)	1.2.2012	Till date
WHO (RNTCP National Consultant for TB/HIV co-ordination at CTD)	Provided technical support to Central TB Division (CTD), States and the field consultants contracted by WHO for improving the general quality of RNTCP services across the country, by proactively assisting in operational research, advocacy, policy, training including drafting technical and operational guidelines, monitoring, supervision and evaluation and suggesting solutions to DDG(TB) in consultation with WHO-India.	7.09.2009	31.01.2012

Key Achievements at Central TB Division

- Co-ordinated with several stakeholders and assisted Central TB Division in preparing RNTCP National Strategic Plan for 2012-17 including strategic vision, project implementation plan, budgeting etc. Assisted National AIDS Control Organization in drafting TB/HIV chapter of National AIDS Control Programme-IV (2012-17).
- As part of many technical committees of RNTCP at National level (National Laboratory committee, National OR committee, National TWG for TB/HIV) and successfully advocated with the policy makers in converting evidence to policy.
- Facilitated the National Technical Working Group of TB/HIV collaborative activities in 2010 and 2011 with key decisions to achieve national coverage of Intensified TB/HIV package of services and guide TB/HIV activities in the next five years.
  - Policy decision on PITC among TB suspects in high HIV settings
  - Piloting the feasibility of IPT at HIV care settings
  - Change in ART guidelines as per latest WHO recommendations
  - Priority deployment of new rapid diagnostics to diagnose TB at HIV care settings
  - Expansion of ICF activities to all HIV care settings.
  - Policy on patient support for HIV-infected TB patients to access ART centre.
  - Joint vision of RNTCP and NACP to create a HIV testing service at every DMC
  - Revision of recording and reporting formats to optimize monitoring of TB/HIV collaborative activities.
  - Operational Research of activities to achieve early diagnosis of HIV-infected TB patients and early linkage to care.

- Have developed policy and normative guidance related to TB/HIV (Revised "National Framework for Joint TB/HIV collaborative activities"(October 2009) and all the training modules for various categories of staff-may be accessed from www.tbcindia.nic.in)
- TB-Diabetes collaboration: Facilitated the new initiative on collaboration between TB and Diabetes in association with the Union including conducting National stakeholders meeting and the subsequent protocol development workshop for pilot testing the feasibility of bidirectional screening in 14 sites across the country in 2012.
- Have designed protocols for several operational research and pilot projects at national level, oversee the conduct, capture and analyse data to inform programme policy. Conducted Operational research on ART eligibility among HIV-infected TB patients in the state of Karnataka and contributed to national policy decision of providing ART for all HIV-TB patients irrespective of CD4 count.
- As a faculty, facilitated the national level capacity building course on Operational Research in collaboration with the Union, CDC and CTD; mentored several projects of national importance with key findings now forming the basis of national policy decisions. (HIV testing of TB suspects study in Karnataka and Andhra Pradesh, Reasons for poor uptake of HIV testing among TB patients in West Bengal, Determinants of poor TB treatment outcomes in the state of Karnataka, 2 vs 1 specimens for follow-up cultures/smears among MDR-patients/smear positive TB patients , utility of mid-CP follow-up among Smear positive TB patients, Prevalence of Diabetes Mellitus among Tb patients in Kerala, Association of HIV and MDR-TB etc)
- Facilitated the National consultation on TB/HIV treatment issues at National AIDS Research Institute and assisted Central TB Division chalk out an evidence-based response to the latest revision of WHO TB treatment guidelines; also helped in its dissemination in various national forums and in the form of a publication in International Journal of TB and Lung disease.
- Worked in in close coordination with NACO for planning and implementing all TB/HIV collaborative activities; have been part of the joint trainings conducted by NACO and other partners like UNODC
- National level trainer/facilitator for training Field Consultants at the time of induction
- Have facilitated the analysis and preparation of performance reports (including TB/HIV) at national, state and district levels and have contributed to TB/HIV briefs for WHO /national/state level status reports.

LIST OF PUBLICATIONS

PEER– REVIEWED PUBLICATIONS

1. Kumar AMV. Confidence intervals and test of significance. **Indian Journal of Community Medicine. 2006;31:46.**
2. Kumar AMV, Gupta D, Rewari BB, Bachani D, Mohammed S, Sharma V, Lal K, Reddy HRR, Naik B, Prasad R, Yaqoob M, Deepak KG, Shastri S, Satyanarayana S, David Harries A, Chauhan LS, Dewan P. Will adoption of the 2010 WHO ART guidelines for HIV-infected TB patients increase the demand for ART services in India? Wilkinson RJ, editor. **PLoS ONE. 2011;6(9):e24297.**
3. Sachdeva KS, Satyanarayana S, Dewan PK, Nair SA, Reddy R, Kundu D, Chadha SS, Kumar AM V, Parmar M, Chauhan LS. Source of previous treatment for Re-Treatment TB cases registered under the national TB control programme, India, 2010. Pai M, editor. **PLoS ONE. 2011;6(7):e22061.**
4. Achanta S, Kumar AMV, Nagaraja SB, Jaju J, Shamrao SRM, Uppaluri R, Tekumalla RR, Gupta D, Kumar A, Satyanarayana S, Dewan PK. Feasibility and effectiveness of provider initiated HIV testing and counseling of TB suspects in Vizianagaram district, South India. **PLoS ONE. 2012;7(7):e41378.**
5. Balakrishnan S, Vijayan S, Nair S, Subramoniapillai J, Mrithyunjayan S, Wilson N, Satyanarayana S, Dewan PK, Kumar AMV, Karthickeyan D, Willis M, Harries AD, Nair SA. High Diabetes Prevalence among Tuberculosis Cases in Kerala, India. **PLoS ONE. 2012;7(10):e46502.**
6. Gandhi MP, Kumar AMV, Toshniwal MN, Reddy RHR, Oeltmann JE, Nair SA, Satyanarayana S, Dewan PK, Mannan S. Sputum smear microscopy at two months into continuation-phase: Should it be done in all patients with sputum smear-positive tuberculosis? **PLoS ONE. 2012;7(6):e39296.**
7. Kumar A, Kumar AMV, Gupta D, Kanchar A, Mohammed S, Srinath S, Tripathy S, Rajasekaran S, Chan P-L, Swaminathan S, Dewan PK. Global guidelines for treatment of tuberculosis among persons living with HIV: unresolved issues. **The International Journal of Tuberculosis and Lung Disease. 2012;16(5):573–8.**
8. Kundu D, Kumar AMV, Satyanarayana S, Dewan PK, Achuthan Nair S, Khaparde K, Nayak P, van den Bergh R, Manzi M, Enarson DA, Deshpande MR, Chandraker S. Can Follow-Up Examination of Tuberculosis Patients Be Simplified? A Study in Chhattisgarh, India. da Silva Nunes M, editor. **PLoS ONE. 2012;7(12):e51038.**
9. Nagaraja SB, Kumar AMV, Sachdeva KS, Ramachandran R, Satyanarayana S, Bansal A, Parmar M, Chadha S, Nair S, Kumar AAM V, Hinderaker SG, Edginton M, Dewan PK. Is One Sputum Specimen as Good as Two during Follow-Up Cultures for Monitoring Multi Drug Resistant Tuberculosis Patients in India? Pai M, editor. **PLoS ONE. 2012;7(9):e45554.**
10. Naik B, Kumar AM, Lal K, Doddamani S, Krishnappa M, Inamdar V, Satyanarayana S, Gupta D, Dewan PK. HIV Prevalence Among Persons Suspected of Tuberculosis: Policy Implications for India. **Journal of Acquired Immune Deficiency Syndromes. 2012;59(4):e72–6.**
11. Sachdeva KS, Kumar A, Dewan P, Kumar AMV, Satyanarayana S. New vision for Revised National Tuberculosis Control Programme (RNTCP): Universal access - "reaching the un-reached". **Indian Journal of Medical Research. 2012;135(5):690–4.**

12. Satyanarayana S, Kumar AMV, Sharath BN, Harries AD. Fast-track writing of a scientific paper with 30 authors: how to do it. **Public Health Action. 2012;2(4):186–7.**
13. Achanta S, Tekumalla RR, Jaju J, Purad C, Chepuri R, Samyukta R, Malhotra S, Nagaraja SB, Kumar AMV, Harries AD. Screening tuberculosis patients for diabetes in a tribal area in South India. **Public Health Action. 2013;3(SUPPL.1):S43–7.**
14. Achanta S, Jaju J, Kumar AMV, Nagaraja SB, Shamrao SRM, Bandi SK, Kumar A, Satyanarayana S, Harries AD, Nair SA, Dewan PK, Da Harries A, Nair SA, Dewan PK. Tuberculosis Management Practices by Private Practitioners in Andhra Pradesh, India. **PLoS ONE. 2013;8(8):e71119.**
15. Ananthakrishnan R, Kumar K, Ganesh M, Kumar AMV, Krishnan N, Swaminathan S, Edginton M, K A, Gupta D, Arunagiri K, Gupta D. The Profile and Treatment Outcomes of the Older (Aged 60 Years and Above) Tuberculosis Patients in Tamilnadu , South India. **PLoS ONE. 2013;8(7):e67288.**
16. Bhat PG, Kumar AMV, Naik B, Satyanarayana S, Deepak KG, Nair SA, Suryakanth MD, Heldal E, Enarson DA, Reid AJ. Intensified tuberculosis case finding among malnourished children in nutritional rehabilitation centres of Karnataka, India: Missed opportunities. **PLoS ONE. 2013;8(12):e84255.**
17. Bishnu B, Bhaduri S, Kumar AMV, Click ES, Chadha VK, Satyanarayana S, Nair SA, Gupta D, Ahmed QT, Sarkar S, Paul D, Dewan P. What Are the Reasons for Poor Uptake of HIV Testing among Patients with TB in an Eastern India District? **PLoS ONE. 2013;8(3):e55229.**
18. Dave P, Shah A, Chauhan M, Kumar AMV, Harries AD, Malhotra S, Pujara K, Patel P, Mane M, Thakkar A, Bharaswadkar S, Sharath BN, Achanta S. Screening patients with tuberculosis for diabetes mellitus in Gujarat, India. **Public Health Action. 2013;3(Suppl 1):S29–33.**
19. Deepa D, Achanta S, Jaju J, Rao K, Samyukta R, Claassens M, Kumar AMV, PH V. The Impact of Isoniazid Resistance on the Treatment Outcomes of Smear Positive Re-Treatment Tuberculosis Patients in the State of Andhra Pradesh, India. **PLoS ONE. 2013;8(10):e76189.**
20. Dendup T, Dorji T, Edgnton ME, Kumar AMV, Wangchuk D, Dophu U, Jamtsho T, Rinzin C. Childhood tuberculosis in Bhutan: profile and treatment outcomes. **Public Health Action. 2013;3(1):11–4.**
21. Harries AD, Kumar AMV, Satyanarayana S, Bissell K, Hinderaker SG, Edginton M, Reid AJ, Zachariah R. References for scientific papers: why not standardise to one global style? **Public Health Action. 2013;3(3):255–7.**
22. Harries AD, Satyanarayana S, Kumar AMV, Nagaraja SB, Isaakidis P, Malhotra S, Achanta S, Naik B, Wilson N, Zachariah R, Lönnroth K, Kapur A. Epidemiology and interaction of diabetes mellitus and tuberculosis and challenges for care: a review. **Public Health Action. 2013;3(1):3–9.**
23. India Diabetes Mellitus – Tuberculosis Study Group. Screening of patients with diabetes mellitus for tuberculosis in India. **Tropical Medicine & International Health. 2013;18(5):646–54.**
24. India Tuberculosis-Diabetes Study Group. Screening of patients with tuberculosis for diabetes mellitus in India. **Tropical Medicine & International Health. 2013;18(5):636–45.**
25. Jali M V, Mahishale VK, Hiremath MB, Satyanarayana S, Kumar AMV, Nagaraja SB, Isaakidis P. Diabetes mellitus and smoking among tuberculosis patients in a tertiary care centre in Karnataka, India. **Public Health Action. 2013;3(1):51–3.**

26. Khann S, Mao ET, Rajendra YP, Satyanarayana S, Nagaraja SB, Kumar AMV. Linkage of Presumptive Multidrug Resistant Tuberculosis (MDR-TB) Patients to Diagnostic and Treatment Services in Cambodia. **PLoS ONE. 2013;8(4):e59903.**
27. Kilale AM, Ngowi BJ, Mfinanga GS, Egwaga S, Doulla B, Kumar AMV, Khogali M, van Griensven J, Harries AD, Zachariah R, Hinderaker SG. Are sputum samples of retreatment tuberculosis reaching the reference laboratories? A 9-year audit in Tanzania. **Public Health Action. 2013;3(2):156–9.**
28. Kumar AMV, Naik B, Guddemane DK, Bhat P, Wilson N, Sreenivas AN, Lauritsen JM, Rieder HL. Efficient, quality-assured data capture in operational research through innovative use of open-access technology. **Public Health Action. 2013;3(1):60–2.**
29. Kumar AMV, Satyanarayana S, Wilson N, Zachariah R, Harries AD. Operational research capacity building in Asia: innovations, successes and challenges of a training course. **Public Health Action. 2013;3(2):186–8.**
30. Kumar AMV, Gupta D, Gupta RS, Satyanarayana S, Wilson N, Zachariah R, Lawn SD, Harries AD. HIV testing in people with presumptive tuberculosis: time for implementation. **The Lancet Respiratory Medicine. 2013;1(1):7–9.**
31. Kumar RS, Kumar AMV, Claassens M, Banurekha V V., Gomathi NS, Venkatesan P, Swaminathan S. Number of sputum specimens during treatment follow-up of tuberculosis patients: two or one? **Public Health Action. 2013;3(4):304–7.**
32. Kumpatla S, Sekar A, Achanta S, Sharath BN, Kumar AMV, Harries AD, Viswanathan V. Characteristics of patients with diabetes screened for tuberculosis in a tertiary care hospital in South India. **Public Health Action. 2013;3(1):23–8.**
33. KV N, Duraisamy K, Balakrishnan S, M S, S JS, Sagili KD, Satyanarayana S, Kumar AMV, Enarson DA. Outcome of Tuberculosis Treatment in Patients with Diabetes Mellitus Treated in the Revised National Tuberculosis Control Programme in Malappuram District, Kerala, India. **PLoS ONE. 2013;8(10):e76275.**
34. Mlilo N, Sandy C, Harries AD, Kumar AMV, Masuka N, Nyathi B, Edginton M, Isaakidis P, Manzi M, Siziba N. Does the type of treatment supporter influence tuberculosis treatment outcomes in Zimbabwe? **Public Health Action. 2013;3(2):146–8.**
35. Naik B, Kumar AMV, Satyanarayana S, Suryakant MD, Swamy NM V, Nair S, Isaakidis P, Harries AD. Is screening for diabetes among tuberculosis patients feasible at the field level? **Public health action. 2013;3(Suppl 1):S34-7.**
36. Nair S, Kumari AK, Subramonianpillai J, Shabna DS, Kumar SM, Balakrishnan S, Naik B, Kumar AMV, Isaakidis P, Satyanarayana S. High prevalence of undiagnosed diabetes among tuberculosis patients in peripheral health facilities in Kerala. **Public Health Action. 2013;3(1):38–42.**
37. Nayak P, Kumar AMV, Claassens M, Enarson DA, Satyanarayana S, Kundu D, Khaparde K, Agrawal TK, Dapkekar S, Chandraker S, Nair SA. Comparing Same Day Sputum Microscopy with Conventional Sputum Microscopy for the Diagnosis of Tuberculosis - Chhattisgarh, India. **PLoS ONE. 2013;8(9):e74964.**
38. Palanivel C, Kumar AMV, Mahalakshmi T, Govindarajan S, Claassens M, Satyanarayana S, Gurumurthy D, Vasudevan K, Purty A, Paulraj AK, Raman K V. Uptake of HIV testing and HIV positivity

among presumptive tuberculosis patients at Puducherry, South India. **Public Health Action. 2013;3(3):220–3.**

39. Patel J, Dave P, Satyanarayana S, Kumar AMV, Shah A, Ananthakrishnan R, Ratnu A. Pretreatment sputum smear grade and smear positivity during follow-up of TB patients in Ahmedabad, India. **Public Health Action. 2013;3(4):308–10.**
40. Prakash BC, Ravish KS, Prabhakar B, Ranganath TS, Naik B, Satyanarayana S, Isaakidis P, Kumar AMV. Tuberculosis-diabetes mellitus bidirectional screening at a tertiary care centre, South India. **Public Health Action. 2013;3(1):18–22.**
41. Reza LW, Satyanarayana S, Pandey A, Kumar S, Devendrappa NM, Anand L, Singh G, Kumar AMV, Chadha SS, Wilson N, Sachdeva KS, Nair SA. LED fluorescence microscopy increases the detection of smear-positive pulmonary tuberculosis in medical colleges of India. **Public Health Action. 2013;3(3):240–2.**
42. Reza LW, Satyanarayna S, Enarson DA, Kumar AMV, Sagili K, Kumar S, Prabhakar LA, Devendrappa NM, Pandey A, Wilson N, Chadha S, Thapa B, Sachdeva KS, Kohli MP. LED-Fluorescence Microscopy for Diagnosis of Pulmonary Tuberculosis under Programmatic Conditions in India. **PLoS ONE. 2013;8(10):e75566.**
43. Satyanarayana S, Kumar AMV, Wilson N, Kapur A, Harries AD, Zachariah R. Taking on the diabetes-tuberculosis epidemic in India : paving the way through operational research. **Public Health Action. 2013;3(S1):S1–2.**
44. Shah SK, Kumar AMV, Dogar OF, Khan MA, Qadeer E, Tahseen S, Masood F, Chandio AK, Edginton ME. Xpert(®) MTB/RIF under routine conditions in diagnosing pulmonary tuberculosis: a study in two hospitals in Pakistan. **Public Health Action. 2013;3(1):20–2.**
45. Shastri S, Boregowda PH, Rewari BB, Tanwar S, Shet A, Kumar AMV. Scaling up antiretroviral treatment services in Karnataka, India: impact on CD4 counts of HIV-infected people. **PLoS ONE. 2013;8(8):e72188.**
46. Shastri S, Sathyanarayna S, Nagaraja SB, Kumar AM, Rewari B, Harries AD, Zachariah R. The journey to antiretroviral therapy in Karnataka, India: who was lost on the road? **Journal of the International AIDS Society. 2013;16(1):18502.**
47. Wahome E, Makori L, Gikera M, Wafula J, Chakaya J, Edginton ME, Kumar AMV. Tuberculosis treatment outcomes among hospital workers at a public teaching and national referral hospital in Kenya. **Public Health Action. 2013;3(4):323–7.**
48. Zachariah R, Reid T, Van den Bergh R, Dahmane A, Kosgei RJ, Hinderaker SG, Tayler-Smith K, Manzi M, Kizito W, Khogali M, Kumar AMV, Baruani B, Bishinga A, Kilale AM, Nqobili M, Patten G, Sobry A, Cheti E, Nakanwagi A, Enarson DA, Edginton ME, Upshur R, Harries AD. Applying the ICMJE authorship criteria to operational research in low-income countries: the need to engage programme managers and policy makers. **Tropical Medicine & International Health. 2013;18(8):1025–8.**
49. Bharaswadkar S, Kanchar A, Thakur N, Shah S, Patnaik B, Click ES, Kumar AMV, Dewan PK. Tuberculosis management practices of private practitioners in Pune Municipal Corporation, India. **PLoS ONE. 2014;9(6):e97993.**

50. Bissell K, Viney K, Brostrom R, Gounder S, Khogali M, Kishore K, Kool B, Kumar AMV, Manzi M, Marais B, Marks G, Linh NN, Ram S, Reid S, Roseveare C, Tayler-Smith K, Van den Bergh R, Harries AD. Building operational research capacity in the Pacific. **Public Health Action. 2014;4(1):2–13.**
51. Chang Y-P, Duo L, Kumar AMV, Achanta S, Xue H-M, Satyanarayana S, Ananthakrishnan R, Srivastava S, Qi W, Hu S-Y. Retention and HIV seroconversion among drug users on methadone maintenance treatment in Yunnan, China. **Public Health Action. 2014;4(1):28–34.**
52. Choudhury SR, Malik F, N A, Badiudzzaman M, Masud JHB, Haque T, Kumar AMV, Tamang D, Nagaraja B, Van Den Bergh R. Differences between coronary angiographic profile between smokers and non-smokers in Bangladesh and its implication for follow up. **Journal of National Heart Foundation of Bangladesh. 2014;3(1):15–7.**
53. Ciobanu A, Domente L, Soltan V, Bivol S, Severin L, Plesca V, Van den Bergh R, Kumar AMV, de Colombani P. Do incentives improve tuberculosis treatment outcomes in the Republic of Moldova? **Public Health Action. 2014;4(Suppl 2):S59-63.**
54. Das M, Isaakidis P, Van Den Bergh R, Kumar AMV, Nagaraja SB, Valikayath A, Jha S, Jadhav B, Ladomirska J. HIV, multidrug-resistant TB and depressive symptoms: When three conditions collide. **Global Health Action. 2014;7(1):24912.**
55. Denisiuk O, Smyrnov P, Kumar AMV, Achanta S, Boyko K, Khogali M, Naik B, Zachariah R. Sex, drugs and prisons: HIV prevention strategies for over 190 000 clients in Ukraine. **Public Health Action. 2014;4(2):96–101.**
56. Dodderi SK, Kumar AMV, Naik BR, Kanchar A, Rewari BB, Harries AD. How many people living with HIV will be additionally eligible for antiretroviral treatment in Karnataka State, India as per the world health organization 2013 guidelines? **PLoS ONE. 2014;9(9):e107136.**
57. Duraisamy K, Mrithyunjayan S, Ghosh S, Nair SA, Balakrishnan S, Subramoniapillai J, Oeltmann JE, Moonan PK, Kumar AMV. Does alcohol consumption during multidrug-resistant tuberculosis treatment affect outcome? A population-based study in Kerala, India. **Annals of the American Thoracic Society. 2014;11(5):712–5.**
58. Girin N, Brostrom R, Ram S, McKenzie J, Kumar AM, Roseveare C. Describing the burden of non-communicable disease risk factors among adults with diabetes in Wallis and Futuna. **Public Health Action. 2014;4(Suppl 1):S39-43.**
59. Guillerm N, Tayler-Smith K, Berger SD, Bissell K, Kumar AMV, Ramsay A, Reid AJ, Zachariah R, Harries AD. What happens after participants complete a Union-MSF structured operational research training course? **Public Health Action. 2014;4(2):89–95.**
60. Harries A, Marais B, Kool B, Ram S, Kumar AMV, Gounder S, Viney K, Brostrom R, Roseveare C, Bissell K, Reid A, Zachariah R, Hill P. Mentorship for operational research capacity building: hands-on or hands-off? **Public Health Action. 2014;4(Suppl 1):S56-8.**
61. Harries AD, Bianchi L, Jensen PM, Pantages M, Bissell K, Kumar AMV, Hinderaker SG, Tayler-Smith K, Van den Bergh R, van den Boogaard W, Manzi M, Isaakidis P, Reid AJ, Zachariah R. Public Health Action for public health action. **Public Health Action. 2014;4(3):139–40.**
62. Isaakidis P, Das M, Kumar AMV, Peskett C, Khetarpal M, Bamne A, Adsul B, Manglani M, Sachdeva KS, Parmar M, Kanchar A, Rewari BB, Deshpande A, Rodrigues C, Shetty A, Rebello L, Saranchuk

P. Alarming levels of drug-resistant tuberculosis in HIV-infected patients in metropolitan Mumbai, India. **PLoS ONE. 2014;9(10):e110461.**

63. Khaliaukin A, Kumar AMV, Skrahina A, Hurevich H, Rusovich V, Gadoev J, Falzon D, Khogali M, de Colombani P. Poor treatment outcomes among multidrug-resistant tuberculosis patients in Gomel Region, Republic of Belarus. **Public Health Action. 2014;4(Suppl 2):S24-8.**
64. Kuchukhidze G, Kumar AMV, de Colombani P, Khogali M, Nanava U, Blumberg HM, Kempker RR. Risk factors associated with loss to follow-up among multidrug-resistant tuberculosis patients in Georgia. **Public health action. 2014;4(Suppl 2):S41-6.**
65. Kumar AMV, Satyanarayana S, Wilson NC, Chadha SS, Gupta D, Nair S, Zachariah R, Kapur A, Harries AD. Operational research leading to rapid national policy change: tuberculosis-diabetes collaboration in India. **Public Health Action. 2014;4(2):85–8.**
66. Kumar AMV, Zachariah R, Satyanarayana S, Reid AJ, Van den Bergh R, Tayler-Smith K, Khogali M, Harries AD. Operational research capacity building using "The Union/MSF" model: adapting as we go along. **BMC research notes. 2014;7(1):819.**
67. Kumar RS, Kumar AMV, Claassens M, Banurekha V V., Sekar G, Venkatesan P, Swaminathan S. Are we justified in treating for multidrug-resistant tuberculosis based on positive follow-up smear results? **The International Journal of Tuberculosis and Lung Disease. 2014;18(4):449–53.**
68. Kumar R, Goel S, Harries AD, Lal P, Singh RJ, Kumar AMV, Wilson NC. How good is compliance with smoke-free legislation in India? Results of 38 subnational surveys. **International Health. 2014;6(3):189–95.**
69. Lucenko I, Riekstina V, Perevoscikovs J, Mozgis D, Khogali M, Gadoev J, de Colombani P, Kumar AMV. Treatment outcomes among drug-susceptible tuberculosis patients in Latvia, 2006-2010. **Public Health Action. 2014;4(Suppl 2):S54-8.**
70. Molfino L, Kumar AM, Isaakidis P, Van den Bergh R, Khogali M, Hinderaker SG, Magaia A, Lobo S, Edwards CG, Walter J. High attrition among HIV-infected patients with advanced disease treated in an intermediary referral center in Maputo, Mozambique. **Global Health Action. 2014;7:23758.**
71. Nagaraja SB, Achanta S, Kumar AMV, Satyanarayana S. Extending tuberculosis notification to the private sector in India: Programmatic challenges? **The International Journal of Tuberculosis and Lung Disease. 2014;18(11):1353–6.**
72. Nasa JN, Brostrom R, Ram S, Kumar AMV, Seremai J, Hauma M, Paul IA, Langidrik JR. Screening adult tuberculosis patients for diabetes mellitus in ebeye, republic of the Marshall Islands. **Public Health Action. 2014;4(SUPPL. 1):S50–2.**
73. Nayak P, Kumar AMV, Agrawal TK, Chandraker S, Nair SA. Same-day light-emitting diode fluorescence microscopy for the diagnosis of tuberculosis in Chhattisgarh, India. **The International Journal of Tuberculosis and Lung Disease. 2014;18(6):666–70.**
74. Oladimeji O, Isaakidis P, Obasanya OJ, Eltayeb O, Khogali M, Van Den Bergh R, Kumar AMV, Hinderaker SG, Abdurrahman ST, Lawson L, Cuevas LE. Intensive-phase treatment outcomes among hospitalized multidrug-resistant tuberculosis patients: Results from a nationwide cohort in Nigeria. **PLoS ONE. 2014;9(4):e94393.**

75. Parija D, Patra TK, Kumar AMV, Swain BK, Satyanarayana S, Sreenivas A, Chadha VK, Moonan PK, Oeltmann JE. Impact of awareness drives and community-based active tuberculosis case finding in Odisha, India. **The International Journal of Tuberculosis and Lung Disease. 2014;18(9):1105–7.**
76. Ramsay A, Harries AD, Zachariah R, Bissell K, Hinderaker SG, Edginton M, Enarson DA, Satyanarayana S, Kumar AMV, Hoa NB, Tweya H, Reid AJ, Van den Bergh R, Tayler-Smith K, Manzi M, Khogali M, Kizito W, Ali E, Delaunois P, Reeder JC. The Structured Operational Research and Training Initiative for public health programmes. **Public Health Action. 2014;4(2):79–84.**
77. Rusovich V, Kumar AMV, Skrahina A, Hurevich H, Astrauko A, de Colombani P, Tayler-Smith K, Dara M, Zachariah R. High time to use rapid tests to detect multidrug resistance in sputum smear-negative tuberculosis in Belarus. **Public Health Action. 2014;4(4):243–8.**
78. Shankar D, Kumar AMV, Rewari B, Kumar S, Shastri S, Satyanarayana S, Ananthakrishnan R, Nagaraja SB, Devi M, Bhargava N, Das M, Zachariah R. Retention in pre-antiretroviral treatment care in a district of Karnataka, India: how well are we doing? **Public Health Action. 2014;4(4):210–5.**
79. Shivaramakrishna HR, Frederick A, Shazia A, Murali L, Satyanarayana S, Nair SA, Kumar AM, Moonan PK. Isoniazid preventive treatment in children in two districts of South India: Does practice follow policy? **International Journal of Tuberculosis and Lung Disease. 2014;18(8):919–24.**
80. Tharu MB, Harries AD, Goel S, Srivastava S, Kumar AMV, Adhikari M, Shrestha B, Maharjan B, Khadka H. Screening retreatment tuberculosis patients for drug resistance in mid-west Nepal: how well are we doing? **Public Health Action. 2014;4(1):60–5.**
81. Yirdaw KD, Jerene D, Gashu Z, Edginton ME, Kumar AMV, Letamo Y, Feleke B, Teklu AM, Zewdu S, Weiss B, Ruff A. Beneficial effect of isoniazid preventive therapy and antiretroviral therapy on the incidence of tuberculosis in people living with HIV in Ethiopia. **PLoS ONE. 2014;9(8):e104557.**
82. Zachariah R, Kumar AMV, Reid AJ, den Bergh R, Isaakidis P, Draguez B, Delaunois P, Nagaraja SB, Ramsay A, Reeder JC, Others, Van den Bergh R, Isaakidis P, Draguez B, Delaunois P, Nagaraja SB, Ramsay A, Reeder JC, Denisiuk O, Ali E, Khogali M, Hinderaker SG, Kosgei RJ, van Griensven J, Quaglio GL, Maher D, Billo NE, Terry RF, Harries AD. Open access for operational research publications from low- and middle-income countries: who pays? **Public Health Action. 2014;4(3):141–4.**
83. Zachariah R, Reid T, Van den Bergh R, Kumar AMV, Tayler-Smith K, Khogali M, Hinderaker SG, Upshur R, Harries AD. RE: Applying the ICMJE authorship criteria to operational research in low-income countries: the need to engage programme managers and policy makers by Zachariah et al. (2013) TMIH 18, pp. 1025–1028. **Tropical medicine & International Health. 2014;19(1):129–30.**
84. Zachariah R, Guillerm N, Berger S, Kumar AMV, Satyanarayana S, Bissell K, Edginton M, Hinderaker SG, Tayler-Smith K, Van den Bergh R, Khogali M, Manzi M, Reid AJ, Ramsay A, Reeder JC, Harries AD. Research to policy and practice change: is capacity building in operational research delivering the goods? **Tropical Medicine & International Health. 2014;19(9):1068–75.**
85. Dave P, Vadera B, Kumar AMV, Chinnakali P, Modi B, Solanki R, Patel P, Patel P, Pujara K, Nimavat P, Shah A, Bharaswadkar S, Rade K, Parmar M, Nair SA. Has introduction of rapid drug susceptibility testing at diagnosis impacted treatment outcomes among previously treated tuberculosis patients in Gujarat, India? **PLoS ONE. 2015;10(4):e0121996.**

86. Deshmukh RD, Dhande DJ, Sachdeva KS, Sreenivas A, Kumar AMV, Satyanarayana S, Parmar M, Moonan PK, Lo TQ. Patient and provider reported reasons for lost to follow up in MDRTB treatment: A qualitative study from a drug resistant TB Centre in India. **PLoS ONE. 2015;10(8):e0135802.**
87. Dogra V, Khanna R, Jain A, Kumar AMV, Shewade HD, Majumdar SS. Neonatal mortality in India's rural poor: Findings of a household survey and verbal autopsy study in Rajasthan, Bihar and Odisha. **Journal of Tropical Pediatrics. 2015;61(3):210–4.**
88. Guillerm N, Tayler-Smith K, Dar Berger S, Bissell K, Kumar AMV, Ramsay A, Reid AJ, Zachariah R, Harries AD. Research output after participants complete a Structured Operational Research and Training (SORT IT) course. **Public Health Action. 2015;5(4):266–8.**
89. Harries AD, Kumar AMV, Satyanarayana S, Lin Y, Takarinda KC, Tweya H, Reid AJ, Zachariah R. Communicable and non-communicable diseases: connections, synergies and benefits of integrating care. **Public Health Action. 2015;5(3):156–7.**
90. Harries AD, Kumar AMV, Karpati A, Jahn A, Douglas GP, Gadabu OJ, Chimbwandira F, Zachariah R. Monitoring treatment outcomes in patients with chronic disease: lessons from tuberculosis and HIV/AIDS care and treatment programmes. **Tropical Medicine & International Health. 2015;20(7):961–4.**
91. Harries AD, Kumar AMV, Satyanarayana S, Lin Y, Zachariah R, Lönnroth K, Kapur A. Addressing diabetes mellitus as part of the strategy for ending TB. **Transactions of the Royal Society of Tropical Medicine and Hygiene. 2015;110(3):173–9.**
92. Joshi B, Chinnakali P, Shrestha A, Das M, Kumar AMV, Pant R, Lama R, Sarraf RR, Dumre SP, Harries a D. Impact of intensified case-finding strategies on childhood TB case registration in Nepal. **Public Health Action. 2015;5(2):93–8.**
93. Kumar AMV, Chinnakali P, Shewade H, Gupta V, Nagpal P, Harries AD. Short EpiData course: do participants use the data entry tool two years post-training? **Public Health Action. 2015;5(4):261–5.**
94. Kumar AM, Satyanarayana S, Berger SD, Chadha SS, Singh RJ, Lal P, Tonsing J, Harries AD. Promoting operational research through fellowships: a case study from the South-East Asia Union Office. **Public Health Action. 2015;5(1):6–16.**
95. Moges T, Gedlu E, Isaakidis P, Kumar A, Den R Van, Khogali M, Mekasha A, Hinderaker SG. Infective endocarditis in Ethiopian children: a hospital based review of cases in Addis Ababa. **Pan African Medical Journal. 2015;20:1–10.**
96. N PGD, Kumar AMV, Chinnakali P, Sahu S, M S, As V, Bb R, Swaminathan S. High Loss to Follow-up Among Children on Pre-ART Care Under National AIDS Program in Madurai , South India. **Journal of Acquired Immune Deficiency Syndromes. 2015;69(3):e109–e114.**
97. Owiti P, Zachariah R, Bissell K, Kumar AMV, Diero L, Carter EJ, Gardner A. Integrating tuberculosis and HIV services in rural Kenya: uptake and outcomes. **Public Health Action. 2015;5(1):36–44.**
98. Philip S, Isaakidis P, Sagili KD, Meharunnisa A, Mrithyunjayan S, Kumar AMV. "They know, they agree, but they don't do" - The paradox of tuberculosis case notification by private practitioners in Alappuzha district, Kerala, India. **PLoS ONE. 2015;10(4):e0123286.**

99. Rajapakshe W, Isaakidis P, Sagili KD, Kumar AMV, Samaraweera S, Pallewatta N, Jayakody W, Nissanka A. Screening patients with tuberculosis for diabetes mellitus in Ampara, Sri Lanka. **Public Health Action. 2015;5(2):150–2.**
100. Reddy KK, Ananthakrishnan R, Jacob AG, Das M, Isaakidis P, Kumar AMV. Intensified tuberculosis case finding amongst vulnerable communities in southern India. **Public Health Action. 2015;5(4):246–8.**
101. Satyavani K, Archana S, Kumar AM, Achanta S, Viswanathan V. Sex Differences in Cardiovascular Risk Factors among People with Diabetes in South India. **The Journal of the Association of Physicians of India. 2015;63(12):20–4.**
102. Sawadogo M, Ciza F, Nzeyimana SD, Shingiro A, Ndikumana T, Demeulenaere T, Khogali M, Edginton M, Reid AJ, Kumar AMV, Harries AD. Effect of increased ART-CPT uptake on tuberculosis outcomes and associated factors, Burundi, 2009-2013. **Public Health Action. 2015;5(4):214–6.**
103. Sharath B, Kumar AM, Ranjini R, Anand S, Sundaram H, Singh S, Kumar P. How better is random blinded re-checking results in Revised National TB Control Programme, India? **Indian Journal of Medical Microbiology. 2015;33(4):572–5.**
104. Shewade HD, Govindarajan S, Sharath BN, Tripathy JP, Chinnakali P, Kumar AMV, Muthaiah M, Vivekananda K, Paulraj AK, Roy G. MDR-TB screening in a setting with molecular diagnostic techniques: who got tested, who didn't and why? **Public Health Action. 2015;5(2):132–9.**
105. Teshome W, Belayneh M, Moges M, Endriyas M, Mekonnen E, Ayele S, Misganaw T, Shiferaw M, Chinnakali P, Hinderaker SG, Kumar AMV. Who takes the medicine? Adherence to antiretroviral therapy in Southern Ethiopia. **Patient Preference and Adherence. 2015;9:1531–7.**
106. Thapa B, Reza LW, Kumar AM, Pandey A, Satyanarayana S, Chadha S. Light Emitting Diode Fluorescence Microscopy increased the detection of smear-positives during follow-up of Tuberculosis patients in India: program implications. **BMC Research Notes. 2015;8:596.**
107. Yeole RD, Khillare K, Chadha VK, Lo T, Kumar AMV. Tuberculosis case notification by private practitioners in Pune, India: how well are we doing? **Public Health Action. 2015;5(3):173–9.**
108. Zam K, Kumar AMV, Achanta S, Bhat P, Naik B, Zangpo K, Dorji T, Wangdi Y, Zachariah R. A first country-wide review of Diabetes Mellitus care in Bhutan: time to do better. **BMC Health Services Research. 2015;15(1):389.**
109. Bairy S, Kumar AMV, Raju M, Achanta S, Naik B, Tripathy JP, Zachariah R. Is adjunctive naturopathy associated with improved glycaemic control and a reduction in need for medications among type 2 Diabetes patients? A prospective cohort study from India. **BMC Complementary and Alternative Medicine. 2016;16(1):290.**
110. Bhardwaj RR, Oeltmann JE, Ravichandra C, Chadda VK, Das M, Kumar AMV. Engaging private providers and Ayurvedic practitioners in Bilaspur, India: did it increase TB case detection? **Public Health Action. 2016;6(2):154–6.**
111. Das M, Isaakidis P, Van den Bergh R, Kumar AMV, Sharath BN, Mansoor H, Saranchuk P. Treating all multidrug-resistant tuberculosis patients, not just bacteriologically confirmed cases. **Public Health Action. 2016;6(2):157–157.**

112. Dave PV, Shah AN, Nimavat PB, Modi BB, Pujara KR, Patel P, Mehariya K, Rade KV, Shekar S, Sachdeva KS, Oeltmann JE, Kumar AMV. Direct Observation of Treatment Provided by a Family Member as Compared to Non-Family Member among Children with New Tuberculosis: A Pragmatic, Non-Inferiority, Cluster-Randomized Trial in Gujarat, India. **PLoS ONE. 2016;11(2):e0148488.**
113. Deka DJ, Choudhury B, Talukdar P, Lo TQ, Das B, Nair SA, Moonan PK, Kumar AMV. What a difference a day makes: same-day vs. 2-day sputum smear microscopy for diagnosing tuberculosis. **Public Health Action. 2016;6(4):232–6.**
114. Edla SR, Kumar AMV, Srinivas B, Raju MS, Gupta V. "Integrated Naturopathy and Yoga" reduces blood pressure and the need for medications among a cohort of hypertensive patients in South India: 3-months follow-up study. **Advances in Integrative Medicine. 2016;3(3):90–7.**
115. Fatima R, Qadeer E, Yaqoob A, Ul Haq M, Majumdar SS, Shewade HD, Stevens R, Creswell J, Mahmood N, Kumar AMV. Extending "contact tracing" into the community within a 50-metre radius of an index tuberculosis patient using Xpert MTB/RIF in urban, Pakistan: Did it increase case detection? **PLoS ONE. 2016;11(11):e0165813.**
116. Harries AD, Kumar AMV, Kyaw NTT, Hoa NB, Takarinda KC, Zachariah R. The role of antiretroviral therapy in reducing TB incidence and mortality in high HIV-TB burden countries. **Asian Pacific Journal of Tropical Disease. 2016;6:243–7.**
117. Hoa NB, Nhung N V, Kumar AMV, Harries AD. The effects of placing an operational research fellow within the Viet Nam National Tuberculosis Programme. **Public Health Action. 2016;6(4):273–6.**
118. Huque R, Ahmed F, King R, Walley J, Hicks JP, Elsey H, Nasreen S, Kumar A, Newell JN. Improving the quality of care of children in community clinics: an intervention and evaluation in Bangladesh. **Public Health Action. 2016;6(2):77–82.**
119. Joshi D, Baral SC, Giri S, Kumar AMV. Universal institutional delivery among mothers in a remote mountain district of Nepal: what are the challenges? **Public Health Action. 2016;6(4):267–72.**
120. Kumar AMV, Shewade HD, Tripathy JP, Guillerm N, Tayler-Smith K, Berger SD, Bissell K, Reid AJ, Zachariah R, Harries AD. Does research through Structured Operational Research and Training (SORT IT) courses impact policy and practice? **Public Health Action. 2016;6(1):44–9.**
121. Kumar AM, Gupta D, Kumar A, Gupta RS, Kanchar A, Rao R, Shastri S, Suryakanth MD, Rangaraju C, Naik B, Guddemane DK, Bhat P, Nair AS, Harries AD, Dewan P. HIV testing among patients with presumptive tuberculosis: How do we implement in a routine programmatic setting? Results of a large operational research from India. **PLoS ONE. 2016;11(5):e0156487.**
122. Lienhardt C, Lönnroth K, Menzies D, Balasegaram M, Chakaya J, Cobelens F, Cohn J, Denkinger CM, Evans TG, Källenius G, Kaplan G, Kumar AMV, Matthiessen L, Mgone CS, Mizrahi V, Mukadi Y diul, Nguyen VN, Nordström A, Sizemore CF, Spigelman M, Squire SB, Swaminathan S, Van Helden PD, Zumla A, Weyer K, Weil D, Raviglione M. Translational Research for Tuberculosis Elimination: Priorities, Challenges, and Actions. **PLoS Medicine. 2016;13(3):e1001965.**
123. Minn Oo M, Gupta V, Aung TK, Thu Thu Kyaw N, Nyunt Oo H, Kumar AM. Alarming attrition rates among HIV-infected individuals in pre-antiretroviral therapy care in Myanmar, 2011–2014. **Global Health Action. 2016;9(1):31280.**

124. Pathak RR, Mishra BK, Moonan PK, Nair SA, Kumar AMV, Gandhi MP, Mannan S, Ghosh S. Can Intensified Tuberculosis Case Finding Efforts at Nutrition Rehabilitation Centers Lead to Pediatric Case Detection in Bihar, India? **Journal of tuberculosis research. 2016;4(1):46–54.**
125. Samuel B, Volkmann T, Cornelius S, Mukhopadhay S, MejoJose, Mitra K, Kumar AMV, Oeltmann JE, Parija S, Prabhakaran AO, Moonan PK, Chadha VK. Relationship between Nutritional Support and Tuberculosis Treatment Outcomes in West Bengal, India. **Journal of tuberculosis research. 2016;4(4):213–9.**
126. Senkoro M, Kumar AMV, Chinnakali P, Mfinanga SG, Egwaga S, Kamara V, van Leth F, Hinderaker SG. Population impact of factors associated with prevalent pulmonary tuberculosis in Tanzania. **The International Journal of Tuberculosis and Lung Disease. 2016;20(10):1326–33.**
127. Shewade HD, Govindarajan S, Thekkur P, Palanivel C, Muthaiah M, Kumar AMV, Gupta V, Sharath BN, Tripathy JP, Vivekananda K, Roy G. MDR-TB in Puducherry, India: reduction in attrition and turnaround time in the diagnosis and treatment pathway. **Public Health Action. 2016;6(4):242–6.**
128. Tripathy JP, Prasad BM, Shewade HD, Kumar AMV, Zachariah R, Chadha S, Tonsing J, Harries AD. Cost of hospitalisation for non-communicable diseases in India: are we pro-poor? **Tropical Medicine & International Health. 2016;21(8):1019–28.**
129. Tripathy JP, Goel S, Kumar AMV. Measuring and understanding motivation among community health workers in rural health facilities in India-a mixed method study. **BMC Health Services Research. 2016;16(1):366.**
130. Wambui Charity K, Kumar AMV, Hinderaker SG, Chinnakali P, Pastakia SD, Kamano J. Do diabetes mellitus patients adhere to self-monitoring of blood glucose (SMBG) and is this associated with glycemic control? Experiences from a SMBG program in western Kenya. **Diabetes Research and Clinical Practice. 2016;112:37–43.**
131. Zachariah R, Rust S, Dar Berger S, Guillerm N, Bissell K, Delaunois P, Reid AJ, Kumar AMV, Olliaro PL, Reeder JC, Harries AD, Ramsay A. Building Global Capacity for Conducting Operational Research Using the SORT IT Model: Where and Who? **PLoS ONE. 2016;11(8):e0160837.**
132. Axshya SAMVAD Study Group, Shewade HD, Chadha SS, Gupta V, Tripathy JP, Satyanarayana S, Sagili K, Mohanty S, Bera OP, Pandey P, Rajeswaran P, Jayaraman G, Santhappan A, Bajpai UN, Mamatha AM, Maiser R, Naqvi AJ, Pandurangan S, Nath S, Ghule VH, Das A, Prasad BM, Biswas M, Singh G, Mallick G, Jeyakumar Jaisingh AJ, Rao R, Kumar AMV. Data collection using open access technology in multicentre operational research involving patient interviews. **Public Health Action. 2017;7(1):74–7.**
133. Chawla S, Shringarpure K, Modi B, Sharma R, Rewari BB, Shah AN, Verma PB, Dongre AR, Kumar AMV. Why are HIV-infected people not started on antiretroviral therapy? A mixed-methods study from Gujarat, India. **Public Health Action. 2017;7(3):183–92.**
134. Choun K, Achanta S, Naik B, Tripathy JP, Thai S, Lorent N, Khun KE, van Griensven J, Kumar AMV, Zachariah R. Using mobile phones to ensure that referred tuberculosis patients reach their treatment facilities: a call that makes a difference. **BMC Health Services Research. 2017;17(1):575.**

135. Datta B, Hazarika A, Shewade HD, Ayyagari K, Kumar AMV. Digital chest X-ray through a mobile van: public private partnership to detect sputum negative pulmonary TB. **BMC Research Notes. 2017;10(1):96.**
136. De Plecker E, Zachariah R, Kumar AMV, Trelles M, Caluwaerts S, van den Boogaard W, Manirampa J, Tayler-Smith K, Manzi M, Nanan-N'zeth K, Duchenne B, Ndelema B, Etienne W, Alders P, Veerman R, Van den Bergh R. Emergency obstetric care in a rural district of Burundi: What are the surgical needs? **PLoS ONE. 2017;12(2):e0170882.**
137. Devi NP, Kumar AMV, Chinnakali P, Rajendran M, Valan AS, Rewari BB, Swaminathan S. Loss to follow-up among children in pre-ART care under the National AIDS Programme, Tamil Nadu, South India. **Public Health Action. 2017;7(2):90–4.**
138. Harries AD, Ade S, Hoa NB, Satyanarayana S, Kumar AMV. Use of inhaled corticosteroids for obstructive lung disease following anti-tuberculosis treatment. **The International Journal of Tuberculosis and Lung Disease. 2017;21(7):833–4.**
139. Jeyashree K, Suliankatchi Abdulkader R, Kathirvel S, Chinnakali P, Kumar AM. Profile of and expenditure on morbidity and hospitalizations among elderly-Analysis of a nationally representative sample survey in India. **Archives of Gerontology and Geriatrics. 2017;74:55–61.**
140. Khan BJ, Kumar AMV, Stewart A, Khan NM, Selvaraj K, Fatima R, Samad Z. Alarming rates of attrition among tuberculosis patients in public-private facilities in Lahore, Pakistan. **Public Health Action. 2017;7(2):127–33.**
141. Khurshid A, Hinderaker SG, Heldal E, Fatima R, Ul Haq M, Yaqoob A, Ansari A, Anwar K, Qadeer E, Kumar AMV. Did "Screeners" Increase Pediatric Tuberculosis Case Notification in Sindh, Pakistan? **Journal of Tuberculosis Research. 2017;5(1):81–6.**
142. Kumar AMV, Singarajipura A, Naik B, Guddemane DK, Patel Y, Shastri S, Kumar S, Deshmukh R, Rewari BB, Harries AD. HIV-infected presumptive tuberculosis patients without tuberculosis: How many are eligible for antiretroviral therapy in Karnataka, India? **Journal of Epidemiology and Global Health. 2017;7(1):11–9.**
143. Kyaw NTT, Harries AD, Kumar AMV, Oo MM, Kyaw KWY, Win T, Aung TK, Min AC, Oo HN. High rate of virological failure and low rate of switching to second-line treatment among adolescents and adults living with HIV on firstline ART in Myanmar, 2005-2015. De Socio GV, editor. **PLoS ONE. 2017;12(2):e0171780.**
144. Kyaw NTT, Kumar AMV, Oo MM, Oo HN, Kyaw KWY, Thiha S, Aung TK, Win T, Mon YY, Harries AD. Long-term outcomes of second-line antiretroviral treatment in an adult and adolescent cohort in Myanmar. **Global Health Action. 2017;10(1):1290916.**
145. Mallick G, Shewade HD, Agrawal TK, Kumar AMV, Chadha SS. Enhanced tuberculosis case finding through advocacy and sensitisation meetings in prisons of Central India. **Public Health Action. 2017;7(1):67–70.**
146. Selvaraj K, Kumar AMV, Chawla S, Shringarpure KS, Thekkur P, Palanivel C, Verma PB, Shah AN, Pandya KN, Roy G, Singh Z, Rewari BB, Dongre AR. Are partners of HIV-infected people being tested for HIV? A mixed-methods research from Gujarat, India. **Public Health Action. 2017;7(1):46–54.**

147. Shewade HD, Jeyashree K, Mahajan P, Kumar AMV. National guidelines on screening for diabetes among patients with tuberculosis in India: Need for clarity and change in screening cut off? Diabetes & Metabolic Syndrome: **Clinical Research & Reviews. 2017;pii: S1871-4021(17)30209-6.**
148. Shewade HD, Jeyashree K, Mahajan P, Shah AN, Kirubakaran R, Rao R, Kumar AMV. Effect of glycemic control and type of diabetes treatment on unsuccessful TB treatment outcomes among people with TB-Diabetes: A systematic review. Ray RB, editor. **PLoS ONE. 2017;12(10):e0186697.**
149. Shewade HD, Kokane AM, Singh AR, Verma M, Parmar M, Chauhan A, Chahar SS, Tiwari M, Khan SN, Gupta V, Tripathy JP, Nagar M, Singh SK, Mehra PK, Kumar AMV. High pre-diagnosis attrition among patients with presumptive MDR-TB: an operational research from Bhopal district, India. **BMC Health Services Research. 2017;17(1):249.**
150. Shewade HD, Vidhubala E, Subramani DP, Lal P, Bhatt N, Sundaramoorthi C, Singh RJ, Kumar AMV. Open access tools for quality-assured and efficient data entry in a large, state-wide tobacco survey in India. **Global Health Action. 2017;10(1):1394763.**
151. Singh AR, Kharate A, Bhat P, Kokane AM, Bali S, Sahu S, Verma M, Nagar M, Kumar AMV. Isoniazid preventive therapy among children living with tuberculosis patients: Is it working? A mixed-method study from Bhopal, India. **Journal of Tropical Pediatrics. 2017;63(4):274–85.**
152. Sinha SK, Saxena A, Mishra V, Volkmann T, Kumar AMV, Nair SA, Moonan PK, Oeltmann JE, Chadha VK. Integration and decentralisation of TB-HIV services increases HIV testing of TB cases in Rajasthan, India. **Public Health Action. 2017;7(1):71–3.**
153. Tripathy JP, Bhatnagar A, Shewade HD, Kumar AMV, Zachariah R, Harries AD. Ten tips to improve the visibility and dissemination of research for policy makers and practitioners. **Public Health Action. 2017;7(1):10–4.**
154. Tripathy JP, Shewade HD, Mishra S, Kumar AMV, Harries AD. Cost of hospitalization for childbirth in India: how equitable it is in the post-NRHM era? **BMC Research Notes. 2017;10(1):409.**
155. Waheed Y, Khan MA, Fatima R, Yaqoob A, Mirza A, Qadeer E, Shakeel M, Heldal E, Kumar AMV. Infection control in hospitals managing drug-resistant tuberculosis in Pakistan: how are we doing? **Public Health Action. 2017;7(1):26–31.**
156. Wali A, Kumar AMV, Hinderaker SG, Heldal E, Qadeer E, Fatima R, Ullah A, Safdar N, Yaqoob A, Anwar K, Ul Haq M. Pre-treatment loss to follow-up among smear-positive TB patients in tertiary hospitals, Quetta, Pakistan. **Public Health Action. 2017;7(1):21–5.**

OTHER PUBLICATIONS: TRAINING MANUALS, GUIDELINES, BOOK CHAPTERS, VIDEO LECTURES, OP–EDS

1. National AIDS Control Organization and Central TB Division, Ministry of Health and Family Welfare, Government of India. National Framework for Joint HIV/TB collaborative activities (October 2009) [Internet]. New Delhi, India; 2009 [cited 2017 Nov 8]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4182&lid=2830
2. National AIDS Control Organization and Central TB Division, Ministry of Health and Family Welfare, Government of India. Training Manual on Intensified TB/HIV package For NACP & RNTCP Programme Managers & Supervisors at State and District level [Internet]. New Delhi, India; 2009 [cited 2017 Nov 8]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4190&lid=2831
3. National AIDS Control Organization and Central TB Division, Ministry of Health and Family Welfare, Government of India. Training Manual on Intensified TB/HIV package For Counsellors [Internet]. New Delhi, India; 2009 [cited 2017 Nov 8]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4190&lid=2831
4. National AIDS Control Organization and Central TB Division, Ministry of Health and Family Welfare, Government of India. Training Manual on Intensified TB/HIV package For Medical Officers [Internet]. New Delhi, India; 2009 [cited 2017 Nov 8]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4190&lid=2831
5. National AIDS Control Organization and Central TB Division, Ministry of Health and Family Welfare, Government of India. Training Manual on Intensified TB/HIV package For Para-medical Workers [Internet]. New Delhi, India; 2009 [cited 2017 Nov 8]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4190&lid=2831
6. National AIDS Control Organization and Central TB Division, Directorate General Health Services, Ministry of Health with Family Welfare, Government of India. Training Module for ICTC Counselors on TB/HIV Coordination [Internet]. New Delhi; 2010 [cited 2017 Nov 8]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4190&lid=2831
7. National AIDS Control Organization and Central TB Division, Ministry of Health and Family Welfare, Government of India. TB/HIV Module for ART Centre Staff [Internet]. New Delhi, India; 2010 [cited 2017 Nov 8]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=3&sublinkid=4190&lid=2831
8. Kumar AMV. UNIT 13: Three I's – Reducing the burden of TB among HIV-infected patients. Block 3: Tuberculosis. In: Course manual of Post-Graduate Diploma in HIV Medicine. New Delhi, India: Indira Gandhi National Open University (IGNOU); 2012.
9. Kumar AMV. UNIT 12: National Programme of collaborative TB/HIV activities. Block 3: Tuberculosis. In: Course manual of Post-Graduate Diploma in HIV Medicine. New Delhi, India: Indira Gandhi National Open University (IGNOU); 2012.
10. Central TB Division, Directorate General Health Services, Ministry of Health and Family Welfare, Government of India. Screening of Tuberculosis Patients for Diabetes Mellitus (A training module for staff of Revised National TB Control Programme). New Delhi, India; 2013.

11. Kumar AMV. Operational Research in Tuberculosis care and control. WorldMed School Video [Internet]. WorldMEDSchool, Global Education; 2014 [cited 2017 Nov 7]. Available from: https://www.youtube.com/watch?v=w0nZF6opqKI
12. International Union Against Tuberculosis and Lung Disease, Medecins Sans Frontieres, WHO/TDR. SORT IT – Structured Operational Research and Training IniTiative Videos [Internet]. Paris, France; 2014 [cited 2017 Nov 8]. Available from: https://www.youtube.com/channel/UC9ZRuVhbrxJm5xAjUHwo6Hw
13. Kumar AMV. Taming the double trouble of TB and diabetes | Business Line [Internet]. The Hindu-Buisness Line. 2015 [cited 2017 Nov 6]. p. 1–2. Available from: http://www.thehindubusinessline.com/specials/pulse/taming-the-double-trouble-of-tb-and-diabetes/article7873836.ece
14. Rieder HL, Lauritsen JM, Hoa NB, Kumar AM, Tun ZM. EpiData Software for Operations Research in Tuberculosis Control: A course manual developed by EpiData Promoters in collaboration with the EpiData Association and the International Union Against Tuberculosis and Lung Disease [Internet]. 2015 [cited 2017 Nov 8]. Available from: https://tbrieder.org/epidata/epidata_31/epidata_31.html
15. International Union Against Tuberculosis and Lung Disease, QMed Knowledge Foundation. PubMed Search & Reference Management. Training Manual for Health Care Providers. Paris, France; 2016.
16. International Union Against Tuberculosis and Lung Disease. A training manual for health care providers on geographic information systems using QGIS software. Paris, France; 2018.
17. International Union Against Tuberculosis and Lung Disease, QMed Knowledge Foundation – The Union Short Courses [Internet]. Paris, France; 2014 [cited 2017 Nov 8]. Available from: https://www.youtube.com/channel/UCBlxhIdcSpICfaIytcq8J9g