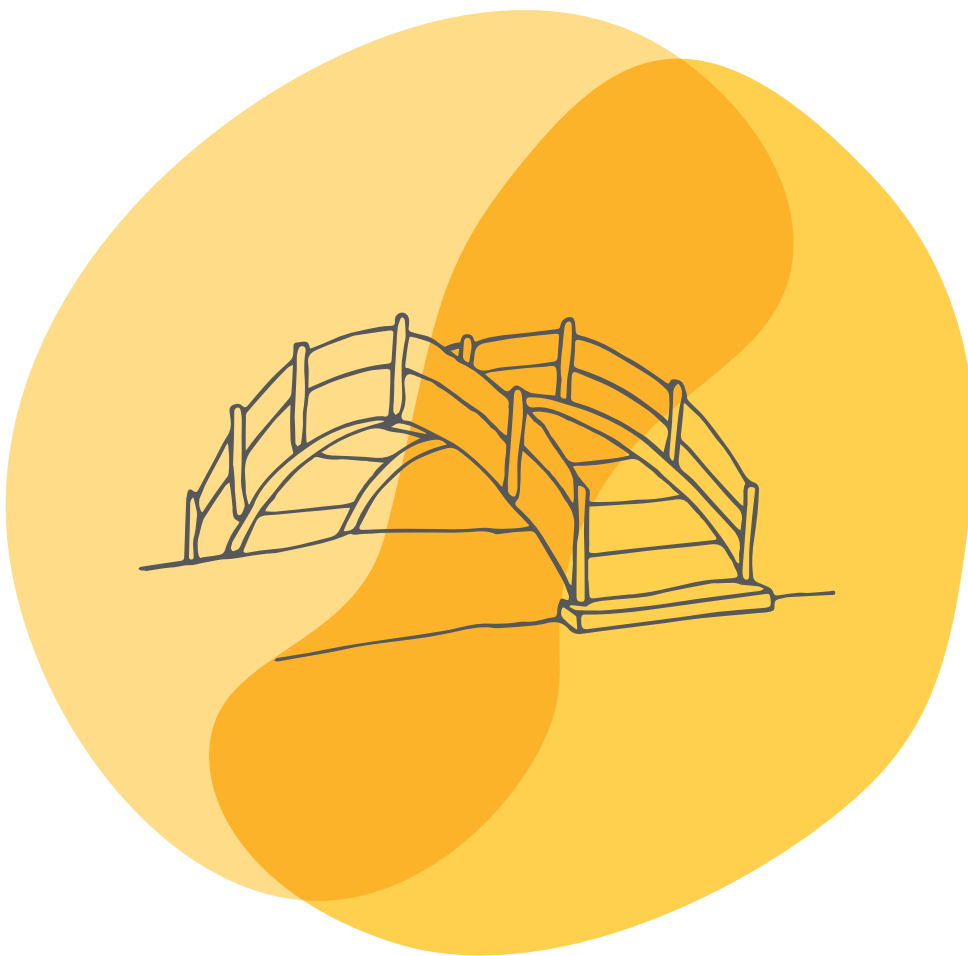


Global policy to local implementation: experiences from active tuberculosis case-finding in high-burden countries



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GLOBAL POLICY TO LOCAL IMPLEMENTATION: EXPERIENCES FROM ACTIVE TUBERCULOSIS CASE-FINDING IN HIGH-BURDEN COUNTRIES

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GLOBAL POLICY TO LOCAL IMPLEMENTATION: EXPERIENCES FROM ACTIVE TUBERCULOSIS CASE-FINDING IN HIGH-BURDEN COUNTRIES THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To my parents Young-Eun and Bernd Biermann

In theory, screening is an admirable method of combating disease
... [but] in practice, there are snags.

– J. M. G. Wilson and G. Jungner, World Health Organization, 1968

POPULAR SCIENCE SUMMARY

Tuberculosis (TB) is a pandemic that has been around for millennia and that remains one of the world's leading infectious killers, especially affecting poor people in low- and middle-income countries. The World Health Organization estimates that 10 million people fall ill with TB every year, out of which about 3 million people are never diagnosed, contributing to suffering and transmission. TB screening outside of health facilities, also known as active case-finding, is one way to help people access TB treatment early to have better health outcomes and stop transmitting the disease to others. Yet, TB screening is not a straight-forward task; there are many different ways to do it, people have varying opinions about its usefulness and risks and there are relatively few scientific studies to back it up, e.g., showing the benefits of TB screening for individuals and communities.

Three areas must be better understood to improve TB screening decision-making and practice. First, it is key to understand the forces that shape policies for TB screening, such as the results of scientific studies, money, politics and decision-makers' preferences. Second, it is crucial to know about the enablers and obstacles for doing TB screening, e.g., resource availability and awareness about TB among people screened, or the lack thereof. Third, it is critical to identify the lessons learnt for how to use these enablers and overcome obstacles. The studies included in this thesis address these three areas by assessing what scientific studies say on these topics, and by bringing out the views of international experts, managers of National TB Programmes from countries with a high TB burden, as well as local leaders, implementers and people with TB.

The results presented in this thesis provide insights into experiences with TB screening, from global policies to local practices. To understand local practices, Nepal and Vietnam served as example countries. Globally, we found that more and more scientific studies on TB screening have been published, especially since 2010, but there are still knowledge gaps, particularly concerning the forces that shape TB screening policies. Based on what international experts described, TB screening has both positive and negative sides, depending on how it is designed and put into practice. The experts cautioned that TB screening policies could be shaped by misleading "power plays", for instance between governments, donors and non-governmental organisations. In contrast to some international experts, National TB Programme managers supported TB screening, but almost all of them also said that money and staff were lacking to do it. They stated that local health care managers were important people for both developing TB screening policies and putting those policies into practice. In Nepal and Vietnam, local leaders, implementers and people with TB described how individuals could "make or break" the TB screening practice, but they also described how screening projects could help make TB screening a reality, e.g., through the provision of money, staff, equipment and training.

Based on these results, TB screening policies and practices can be improved by the following actions: Involve key people, including local health care managers who understand both policy and practice, and use different types of scientific studies as guiding lights. Furthermore, consider positive and negative aspects of TB screening from start to finish to lower, or avoid, negative effects for people screened, as well as communities and health systems. Moreover, increase money and staff in countries with a high TB burden, so that meaningful screening can actually take place. Finally, understand what enables or hinders TB screening, as well as “how-to” strategies, to help decision-makers, practitioners, researchers and donors make better decisions – not so much about whether or not, but when and how to do TB screening outside of health facilities.

If done well, TB screening outside of health facilities can be an important, complementary tool to detect more people with TB early and contribute towards ending the disease. Meanwhile, more money, staff and scientific studies are needed to improve TB screening decision-making and practice.

Popular science summary in عربي, 中文, Deutsch, Español, Français, Русский, Svenska, नेपाली and Tiếng Việt in Appendix 1.

ABSTRACT

Background: Tuberculosis (TB) is one of the world's leading infectious killers. Every year, an estimated 10 million people fall ill with the disease, of whom 2.9 million people are never diagnosed and treated. Thirty low- and middle-income countries account for almost 90% of the global TB burden. The World Health Organization's (WHO) End TB Strategy highlights active case-finding (ACF) as one approach to finding people with TB who are currently being missed by health services. ACF has been shown to find more people with TB at an earlier stage of the disease compared to passive case-finding. Passive case-finding is the standard approach to TB screening, relying on people seeking care when they have TB symptoms. Given the relatively limited evidence on both the epidemiological impact of ACF and optimal implementation strategies, questions remain about what influences ACF policy development and implementation and how these processes can be improved. This thesis aims to contribute to the knowledge base on ACF policy development and implementation in high TB burden countries.

Objectives: To review antecedents, components and influencing factors for ACF policy development and implementation based on the literature. To explore how international experts and National TB Programme (NTP) managers from high TB burden countries perceive ACF policy development and implementation, and to identify facilitators, barriers and "how-to" strategies for ACF implementation in Nepal and Vietnam, which serve as example countries.

Methods: A scoping review of the literature (n=73) was performed, and a frequency and thematic analysis applied. Qualitative semi-structured interviews were conducted with 39 experts from a variety of institutions worldwide. The experts' perceptions were analysed using framework analysis. A mixed methods survey with NTP managers (n=23) was implemented, yielding both quantitative and qualitative data. The data were analysed in parallel and merged in the interpretation of the findings. The survey results were further complemented by a narrative review of national TB strategic plans (n=22). Qualitative semi-structured interviews were conducted with 17 key-informants in Nepal and 39 key-informants in Vietnam. Participants comprised implementers of ACF and people with TB identified through ACF. Thematic analysis was applied, using an implementation science framework.

Results: The results presented in this thesis provide insights into experiences with ACF, from global policies to local implementation. *Study I:* The evidence base for ACF has been growing, especially since 2010. Although much is known about factors influencing ACF implementation (e.g., resources), evidence on what influences ACF policy development (e.g., politics) remains scarce. Articles described the WHO's recent emphasis on ACF as a crucial antecedent of the increasing interest in ACF, especially in high TB burden countries. *Study II:* Experts had a wide range of views on ACF, from ACF being a "waste basket" for resources to it being "common sense" and something that should be done. They described the influence of and "power plays" between donors, governments and non-governmental organisations on ACF policy development and highlighted the need for different types of evidence to inform ACF policy

development and implementation. Experts also stressed the importance of existing systems, processes and experience in influencing ACF implementation, e.g., ACF could build on experience from other screening programmes. *Study III*: Perceived benefits of ACF were linked to its objective of finding people with TB early, while ACF was also perceived as a “double-edged sword” that could cause harm, if inappropriately designed and implemented. *Study IV*: NTP managers unanimously agreed on the need for ACF scale-up in high TB burden countries. This was also reflected in the national TB strategic plans, even though not all documents included explicit aims and targets related to ACF. At the same time, 90% of the NTP managers also described a lack of financial and human resources for ACF. Strategies to increase resources included generating local evidence for advocacy. Managers in districts or regions were the only ones among a list of stakeholders that NTP managers considered crucial for both ACF policy development and implementation. *Studies V and VI*: In Nepal and Vietnam, the main themes revolved around how people (the implementers and people with TB) could “make or break” TB screening, but also how projects could provide a context that is conducive to ACF implementation (e.g., through human resources, equipment and training). Many similar facilitators and barriers for ACF implementation were identified in Nepal and Vietnam, such as the implementers’ dedication, motivation, skills and network. Barriers and facilitators at the societal and organisational levels were more context specific. For instance, in Nepal, poverty and community support were mentioned as critical. In Vietnam, participants elaborated on the importance of commitment and support from various stakeholders for ACF implementation. In both countries, the implementers requested increased incentives and training.

Conclusions: Based on these results, evidence remains limited with regards to factors influencing ACF policy development. Experts have opposing views on ACF policy development and implementation, while NTP managers unanimously agree on the need for ACF scale-up, which is also reflected in the national TB strategic plans. Yet, 90% of the NTP managers state that human and financial resources are currently insufficient, and funds for ACF might have to be sought from alternative domestic and external sources. Benefits and harms of ACF must be considered throughout the screening and diagnostic pathway to avoid possible negative effects for people screened, as well as communities and health systems. Furthermore, the use of different types of evidence and the engagement of stakeholders (e.g., managers in districts and regions) are necessary to mitigate “power plays” that might otherwise mislead ACF policy development and implementation. Most facilitators, barriers and “how-to” strategies for ACF implementation identified in Nepal and Vietnam are similar across contexts, but there are also nuances, e.g., based on the predominant social determinants of TB. ACF projects can provide a context that is conducive to ACF implementation, but implementation success still depends on individuals. Ultimately, if done well, ACF can be an important, complementary tool to contribute towards ending TB, while more resources and evidence are needed to improve ACF policy development and implementation.

LIST OF SCIENTIFIC PAPERS

- I. Biermann O, Lönnroth K, Caws M, Viney K. Factors influencing active tuberculosis case-finding policy development and implementation: a scoping review. *BMJ Open*; 2019;9:e031284.
- II. Biermann O, Atkins S, Lönnroth K, Caws M, Viney K. ‘Power plays plus push’: Experts’ insights into the development and implementation of active tuberculosis case-finding policies globally, a qualitative study. *BMJ Open*. 2020;10:e036285.
- III. Biermann O, Klüppelberg R, Lönnroth K, Viney K, Caws M, Atkins S. ‘A double-edged sword’: The benefits and harms of active case-finding for people with presumptive tuberculosis and communities—A qualitative study based on expert interviews. *PLOS ONE*. 2021;16(3):e0247568.
- IV. Biermann O, Tran PB, Viney K, Caws M, Lönnroth K, Annerstedt KS. Active case-finding policy development, implementation and scale-up in high-burden countries: a mixed methods survey with National Tuberculosis Programme managers and document review. *PLOS ONE*. 2020;15(10):e0240696.
- V. Biermann O, Dixit K, Rai B, Caws M, Lönnroth K, Viney K. Building on facilitators and overcoming barriers to implement active tuberculosis case-finding in Nepal, experiences of community health workers and people with tuberculosis. *BMC Health Services Research*. 2021;21(1):295.
- VI. Biermann O, Tran PB, Forse RJ, Vo LNQ, Codlin AJ, Viney K, Caws M, Lönnroth K. Capitalizing on facilitators and addressing barriers when implementing active tuberculosis case-finding in six districts of Ho Chi Minh City, Vietnam: a qualitative study with key stakeholders. *Submitted*.

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LIST OF ABBREVIATIONS

ACF	Active case-finding
BNMT	Birat Nepal Medical Trust
CAD	Computer-aided detection
CHERRIES	Checklist for Reporting Results for Internet E-Surveys
COREQ	Consolidated criteria for Reporting Qualitative research
CRP	C-Reactive Protein
FIT	Friends for International Tuberculosis Relief
HIV	Human immunodeficiency virus
IMPACT TB	Implementing proven community-based active tuberculosis case-finding interventions
NSP	National strategic plan
NTP	National Tuberculosis Programme
PRISMA-ScR	Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews
TB	Tuberculosis
UN	United Nations
WHO	World Health Organization

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DEFINITIONS

Active tuberculosis case-finding: Active case-finding is synonymous with systematic screening for active tuberculosis, although active case-finding normally implies screening that is implemented outside of health facilities (1).

Contact investigation: Tuberculosis contacts are people who have close contact with patients with infectious tuberculosis. As they are at high risk for infection, tuberculosis contacts should be investigated systematically and actively for tuberculosis infection and disease. Tuberculosis contact investigation contributes to early identification of active tuberculosis, thus decreasing its severity and reducing the transmission of *Mycobacterium tuberculosis* to others. Contact investigation also helps identifying tuberculosis infection to allow preventive measures, such as preventive tuberculosis treatment (2).

High tuberculosis burden country: The World Health Organization defines “high-burden country” as the top 20 in terms of absolute numbers of tuberculosis cases plus the additional 10 countries with the most severe burden in terms of case rates per capita that do not already appear in the “top 20” and that meet a minimum threshold in terms of 10,000 tuberculosis cases per year (3). Vietnam is part of this list of 30 high-burden countries. Nepal is not included on the list of 30 high-burden countries, as it is a relatively small country with a relatively low absolute number of tuberculosis cases. Still, Nepal can be considered a high-burden country given its comparatively high annual incidence rate of tuberculosis.

Implementation: The act of starting to use a plan or system (4).

Passive tuberculosis case-finding: Passive case-finding, also referred to as “standard case detection”, is a patient-initiated pathway to tuberculosis diagnosis involving: 1) a person with active tuberculosis experiencing symptoms that he or she recognises as serious enough to need medical attention; 2) the person having access to and seeking care, and presenting spontaneously at an appropriate health facility; 3) a health worker correctly assessing whether the person fulfils the criteria for suspected tuberculosis; and 4) the successful use of a diagnostic algorithm with sufficient sensitivity and specificity (1).

Policy: A set of ideas or a plan of what to do in particular situations that has been agreed to officially by a group of people, a business organisation, a government, or a political party (5).

Systematic screening for active tuberculosis: Systematic screening for active tuberculosis is the systematic identification of people with suspected active tuberculosis in a predetermined target group, using tests, examinations or other procedures that can be applied rapidly. Among those screened positive, the diagnosis needs to be established by one or several diagnostic tests and additional clinical assessments, which together have high accuracy (1).

Tuberculosis disease: The disease state caused by *Mycobacterium tuberculosis*. It is usually characterised by clinical manifestations, which distinguish it from tuberculosis infection without signs or symptoms (previously referred to as latent tuberculosis infection). Also referred to as active tuberculosis (6).

1 PREFACE

More than a decade ago, I was working on my Bachelor thesis on international health policies and mother-to-child transmission of human immunodeficiency virus in India and South Africa. It puzzled me how one and the same global guideline from the World Health Organization was supposed to work in those very different countries. One of my conclusions was that “political will” was important, but I was still confused and curious to learn more. My interest in health policies was born. For my Master thesis, I found myself in the Ecuadorian rainforest, asking local people about how they perceived a non-governmental organisation and the health care and outreach activities it provided. I learned that the only thing people really cared about was *that* they were provided with care, no matter from where that care was coming.

A few years later, I was based at the World Health Organization Regional Office for Europe. The work focused on how to make better health policies based on the best available evidence. I learned a lot about what was lacking to make evidence-informed policies. Although there were examples of evidence-informed policies in the region, these were rare and fragmented, and bottlenecks seemed to be everywhere: in a country’s health systems, research infrastructure, health information systems, as well as in researchers’ and decision-makers’ capacity. Even when countries had developed policies based on evidence, were these policies actually being implemented?

When I embarked on my PhD journey, one of the first questions I asked my supervisors was whether active case-finding was actually a “proven intervention”, as it had been described in some instances. The answer was complicated. For me, my PhD has been an opportunity to ask questions that had been growing in me over the past years. Active case-finding was an intriguing example to explore gaps (and bridges) from evidence to policy and from policy to implementation. I enjoyed having the opportunity to talk to so many different people, from international experts to National Tuberculosis Programme managers, local leaders, implementers and people with tuberculosis.

Why are health services not reaching people? There are many reasons and active case-finding provides one solution by reaching out. The balancing act of making and implementing policies for active case-finding in high tuberculosis burden countries must be informed by the best available evidence. But policies must also be informed by the “best available stakeholders”; it is their experience that can help shape policies which fit the national or local context and that are thus more meaningful and more likely to be put into practice – only then do we have a real opportunity to build bridges to help improve people’s health.

2 BACKGROUND

2.1 TUBERCULOSIS – A MAJOR GLOBAL HEALTH CHALLENGE

2.1.1 Basic facts

Tuberculosis (TB) is an infectious disease that remains one of the leading causes of death from a single infectious agent and one of the top 10 causes of death worldwide (7). The disease is caused by the bacillus *Mycobacterium tuberculosis*, which is spread by airborne droplets when people with TB expel bacteria into the air, e.g., by coughing. Other symptoms of TB include fever, night sweats and weight loss (7). TB most commonly affects the lungs (pulmonary TB), but can also affect other parts of the body (extrapulmonary TB) (7).

A quarter of the world's population is estimated to be infected with *Mycobacterium tuberculosis*, but not (yet) ill with disease (7). People with TB infection are not infectious but have a lifelong risk of around 5-10% of falling ill with TB and becoming infectious (7). Preventive treatment reduces this risk considerably. The burden of TB can also be reduced by strengthening health systems and addressing determinants of TB, such as poverty, poor living conditions, undernutrition, infection with human immunodeficiency virus (HIV), smoking and diabetes (7–10).

TB is curable and preventable (7). Drug-sensitive TB can be treated with a 6-month regimen consisting of four antimicrobial drugs. This treatment has an efficacy of at least 85% and effectively reduces transmission (7). Meanwhile, drug-resistant TB is much more difficult to treat and poses a threat to the progress made in TB care and prevention worldwide (11). The impact of Bacille Calmette-Guérin vaccination on transmission of *Mycobacterium tuberculosis* is limited at the population level, as it prevents severe forms of TB in children, but does not effectively prevent primary infection or reactivation of TB infection in adults (12). A new and more efficacious vaccine is needed to quickly reduce TB incidence globally, as well as better diagnostic tools and more effective medicines, especially to treat drug-resistant TB (7).

2.1.2 Global commitments

The WHO End TB Strategy (13) was endorsed by Member States at the World Health Assembly in 2014. The United Nations (UN) Sustainable Development Goals were adopted in 2015 (14). Both have included the goal of ending TB. The three pillars of the End TB Strategy are: 1) integrated, patient-centred care and prevention, 2) bold policies and supportive systems and 3) intensified research and innovation. Pillar 1 comprises the component of early diagnosis of TB, including universal drug-susceptibility testing and systematic screening of contacts and high-risk groups. The End TB Strategy aims for a 95% reduction in TB deaths (compared with 2015), a 90% reduction in TB incidence rate (less than 10 TB cases per 100,000 population) and no affected families facing catastrophic costs due to TB by 2035. Yet, TB incidence is estimated to be decreasing at a slow pace of 2% per year only (13).

International attention on TB has been increasing in the recent past. In 2017, the Global Ministerial Conference on Ending TB in the Sustainable Development Era took place in Russia aiming to accelerate the implementation of the End TB Strategy. The conference resulted in the Moscow Declaration to End TB (15). In 2018, the UN held the first-ever General Assembly high-level meeting on TB during which a political declaration was adopted to speed up progress towards the End TB Strategy targets, committing to diagnosing and treating 40 million people with TB between 2018 and 2022. The political declaration also included ambitious targets for the scale-up of TB care and prevention services, as well as commitments on research for new tools, principles of equity and human rights, and targets for the resource needs for implementation and research (16). A follow-up WHO Executive Board meeting focused on ending TB and re-affirmed the targets set for 2022 (17). A 2020 progress report to the General Assembly showed that urgent and more ambitious investments and actions are needed to reach the targets, particularly in the context of COVID-19 (18). The World Health Organization (WHO) stated that building synergies with contact tracing efforts related to the COVID-19 pandemic may help reach the targets set at the UN high-level meeting (7). The next high-level meeting on TB is planned for 2023 (18).

2.1.3 Global burden

In 2019, an estimated 10 million fell ill with TB and 1.4 million died (7). Thirty high-burden countries¹ account for almost 90% of TB cases worldwide (3,7). TB is more common among men than women, and most people with TB are adults who are often poor and face vulnerability, stigma and discrimination (7). Many people with TB are diagnosed only after long delays (19), causing exacerbated suffering, economic hardship and transmission (1).

Almost a third of all TB cases globally (2.9 million) were not diagnosed or reported to the WHO in 2019 (7). This gap reflects a combination of a lack of universal health coverage, underdiagnosis and underreporting of detected TB cases (7). A high number of undiagnosed cases in the community has also been demonstrated by the 33 national TB prevalence surveys conducted between 2007 and 2019 (7).

The impact of the COVID-19 pandemic on TB services has been severe, as human and financial resources have been reallocated from TB to the COVID-19 response, diagnostic machines have been repurposed and health seeking has declined due to lock-downs and precautions against infections risks in health facilities (7). This has caused sharp drops in TB notifications in the high TB burden countries in 2020, and the WHO estimated that a 50% decrease in TB case detection over 3 months could result in 400,000 additional TB deaths in 2020 alone (7).

¹ The 30 high-burden countries, as per WHO definition, include: Angola, Bangladesh, Brazil, Cambodia, China, Congo, Central African Republic, Democratic People's Republic of Korea, Democratic Republic of the Congo, Ethiopia, India, Indonesia, Kenya, Lesotho, Liberia, Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, Russian Federation, Sierra Leone, South Africa, Thailand, the United Republic of Tanzania, Vietnam, Zambia and Zimbabwe (3).

2.2 ACTIVE TUBERCULOSIS CASE-FINDING

2.2.1 What is active case-finding?

Finding the “missing” 2.9 million people with TB and ending the disease will require intensified activity to improve diagnosis and initiation of care for people with TB (20). One strategy for increased TB case detection and early diagnosis is systematic screening which the WHO defines as the systematic identification of people with presumed active TB in a predetermined target group, using tests, examinations or other procedures that can be applied rapidly (1). Active case-finding (ACF) is synonymous with systematic screening, although it usually implies screening outside of health facilities. ACF is mostly provider-initiated. It targets people in risk groups who do not seek health care actively because they: a) do not have or recognise symptoms, b) do not perceive that they have a health problem requiring medical attention or c) face barriers to accessing care (1). ACF has been shown to find more people with TB at an earlier stage of disease, compared to passive case-finding (21,22). Passive case-finding is the standard approach to TB case-finding, relying on people seeking care when they have signs and symptoms of TB (23). The main controversy in the field is about doing ACF versus passive case-finding, even though ACF should complement rather than replace passive case-finding (1). Contact investigation has a stronger evidence base (1,6,24–27) and is thus less controversial, compared to screening in other risk groups. Many countries integrate screening for TB infection into screening for active TB disease, especially in contact investigation. However, this thesis does not focus on TB infection or screening in children. This thesis focuses on different ACF models (including contact investigation and screening for other risk groups outside of health facilities) that aim to detect active TB disease in adults.

2.2.2 A brief history

ACF has been implemented for many decades primarily in high-income countries, starting with mass chest X-ray screening campaigns in the general population in the 1950s and 1960s, then moving towards specific risk populations in recent decades, such as migrants from high-incidence countries and people in prisons (28). In low- and middle-income countries, the interest in ACF has increased, mainly as a response to the sustained case detection gap documented in annual Global TB Reports produced by the WHO (7) and the emergence of the WHO guidelines on systematic screening for active TB in 2013 (1). Generally, TB programs have moved from traditionally vertical approaches and passive case-finding towards being closer to people and communities through community-based solutions and outreach activities to increase TB case detection (29–32).

In 1976, the WHO Expert Committee on TB recommended that countries abandon indiscriminate mobile mass radiography, as evidence showed the inefficiency of population-wide screening in settings that had seen TB rates drop dramatically since the second World War (33). It should be noted that the Expert Committee emphasised that TB screening should still be done in selected risk groups (33,34). The 2013 WHO guidelines on systematic

screening, and the updated version from 2021, also discourage indiscriminate mass screening and strongly recommend ACF only in selected risk groups (1,6).

The global commitments to end TB, as mentioned in section 2.1.2, put ACF back on the global agenda. In line with these commitments, donor organisations such as the Global Fund to Fight AIDS, Tuberculosis and Malaria and the case-finding initiative TB REACH have prioritised ACF. The Global Fund has strategic initiatives that complement country allocations. One such strategic initiative focuses on targeted technical assistance for innovative approaches to finding missing people with TB for the period 2020-2022 (35). TB REACH was established in 2010 and also provides funding for ACF (36). It is a multilateral funding mechanism primarily supported by Global Affairs Canada, with additional funding from the Bill and Melinda Gates Foundation, the United States Agency for International Development and the National Philanthropic Trust (36). Many high TB burden countries receive such international funding to supplement their national TB budgets (7).

2.2.3 Algorithms, tools and the new WHO guidelines

An array of ACF models exist, which apply different screening and diagnostic tools and target different risk groups. Screening tools detect possible TB. Diagnostic tools are required to confirm the presence or absence of TB (1). The accuracy (sensitivity and specificity) and predictive values of the tools and algorithms differ depending on the characteristics of the tools used and the population in which they are used. In many high TB burden countries, sputum-smear microscopy remains the primary diagnostic test, while the gold standard for TB diagnosis is culture (37). Culture requires more resources and a longer waiting time for results (2-6 weeks) compared to sputum-smear microscopy and Xpert® MTB/RIF molecular-test assay (Xpert®; Cepheid, Sunnyvale, USA), which can provide results in less than one day (1). Xpert® MTB/RIF is one of the molecular WHO-approved rapid diagnostic tests for TB (37). For example, an algorithm could include screening for TB symptoms and the use of sputum-smear microscopy or the Xpert® MTB/RIF to confirm TB diagnosis, such as in a project in Nepal (Panel 2, page 20). An algorithm could also be based on the use of chest X-ray for screening and Xpert® MTB/RIF for diagnosis, such as in an example from Vietnam (Panel 3, page 22).

On 22 March 2021, WHO published updated guidelines and an updated operational handbook on systematic screening for active TB (6,38). The new guidelines include four strong and four conditional recommendations for systematic screening. Accordingly, screening is strongly recommended in household and close contacts of people with TB, people living with HIV, miners exposed to silica dust and prisoners (6). Screening is conditionally recommended among subpopulations with structural risk factors for TB², people with an untreated fibrotic

² Structural risk factors include urban poor communities, homeless communities, communities in remote or isolated areas, indigenous populations, migrants, refugees, internally displaced persons and other vulnerable or marginalised groups with limited access to health care (6).

lesion seen on a chest X-ray and people with individual risk factor for TB³ who are either seeking health care or who are already in care in settings where TB prevalence is 0.1% or higher (6). WHO also conditionally recommends screening among the general population in areas with an estimated TB prevalence of 0.5% or higher (6); the threshold for community-wide screening was at a prevalence of 1% in the 2013 WHO guidelines (1).

The updated WHO guidelines and the related operational handbook (6,38) reflect new evidence and new screening tools that have emerged since the first guidelines were published in 2013. As such, the new guidelines highlight the preference for chest X-ray over symptom checklists as a screening tool for ACF in adults and children at higher risk (e.g., people living with HIV), as many people with TB disease do not have symptoms and can thus only be identified for required diagnostic confirmation tests through chest X-ray screening (39–41). The new guidelines also recommend the use of computer-aided detection (CAD) software for the automated interpretation of chest X-rays for screening and triage of TB (6). Studies used to inform the guidelines showed that the performance of CAD was similar to the interpretation of digital chest X-rays by a human reader, though the context for implementation should be assessed as the performance may vary accordingly (6). Furthermore, the new guidelines introduce the use of C-Reactive Protein (CRP) for TB screening among people living with HIV. CRP is an indicator for inflammation that can be measured using point-of-care tests performed on blood collected via finger-prick (6). In people living with HIV who are newly in care and not yet on antiretroviral treatment, the accuracy of symptom screening is low and CRP could offer a significant improvement in accuracy (6). Finally, the new guidelines also introduce the use of molecular WHO-approved rapid diagnostic tests for TB (e.g., Xpert® MTB/RIF) also as a first screening test (not just a test to confirm diagnosis), based on improved accuracy and effectiveness in people living with HIV and other risk populations (6).

2.2.4 Benefits and harms

As for any screening intervention, the potential benefits and harms of ACF must be assessed in any given context (1,6). Documented benefits of ACF for the individual include reduced diagnostic delays (13,14,33,42,43) and decreased economic impact for people with TB (43–47). In addition, screening of household and close contacts can improve case notification (i.e., registration with the National TB Programme, NTP) (25) and case detection (i.e., microbiological confirmation) (48). Yet, the evidence on improved detection and notification through screening in the general population is inconsistent (49–51). Moreover, direct evidence of individual benefit from improved treatment success from ACF in the general population remains limited (6).

³ Individual risk factors comprise diabetes mellitus, previous TB, chronic lung disease, smoking, alcohol use disorder, substance use disorder, malnourishment, pregnancy, immunocompromising conditions (organ transplant, renal failure, dialysis) and health care workers (6).

At the community level, there is some evidence on the impact of ACF on TB prevalence and transmission. A trial of contact screening in South Africa and Zambia showed evidence that TB prevalence may be reduced after four years of contact investigation (even though not statistically significant) (48). An observational study in China reported that three rounds of door-to-door symptom screening followed by chest X-ray were associated with reductions in the absolute number of people with TB detected (52). A cluster-randomised trial in Vietnam demonstrated that door-to-door sputum collection followed by Xpert® MTB/RIF testing (annually for three years) reduced TB prevalence (53). However, there is currently no evidence that population-wide ACF with less sensitive screening algorithms is effective at reducing TB prevalence or transmission (6). Moreover, a systematic review published in March 2021 concluded that ACF might only be effective in changing TB epidemiology, if delivered with high coverage and intensity; single rounds of ACF, even if well-implemented, will not have a lasting epidemiological effect (54).

While empirical evidence on the benefits of ACF is still relatively weak, evidence on the harms is even weaker. Harms associated with ACF comprise unintended negative effects of being correctly diagnosed, e.g., stigma and discrimination (38,42,55), and the harms caused by false-positive or false-negative diagnoses (38,56). Balancing the potential benefits and harms of ACF is vital for everyone, particularly for certain groups of people such as migrants who may risk deportation if TB is diagnosed (38,56), employees who lack legal protection (38,56,57) and people who may not have requested to participate in ACF in the first place (33).

2.2.5 Screening principles

In 1968, Wilson and Jungner described ten principles of early disease detection, starting a debate on how best to tackle perennial challenges related to screening policymaking (58) (Panel 1). These principles are still valid to date for all types of screening, from non-communicable diseases such as cancer to infectious diseases such as TB. At the same time, the authors did not expect the principles to stay unchanged over time, but rather hoped that their publication would spark reflection and deliberation: “If anywhere we have appeared dogmatic, we hope this may serve to stimulate discussion, since, in the end, real development depends on an exchange of views” (58). Indeed, infectious disease screening requires further considerations, as its inherent benefits extend beyond the individual and include community-level benefits, such as reducing transmission.

For ACF, most of the screening principles are fulfilled, while some are conditional and have to be locally assessed (33), such as the availability of facilities for diagnosis and treatment (principle 3), the cost of case-finding (principle 9), which depends on the risk group, algorithm and local TB epidemiology, and the principle that case-finding should be a continuing process and not a “once and for all” project (principle 10).

Panel 1. Principles of early disease detection by Wilson and Jungner (58)

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognised disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage of the disease.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a “once and for all” project.

2.2.6 Putting active case-finding into practice

According to the WHO, implementing ACF requires six steps: 1) assessing the situation; 2) setting goals and specific objectives; 3) identifying and prioritising risk groups; 4) choosing algorithms for screening and diagnosis; 5) planning, budgeting and implementing and 6) monitoring, evaluating and modifying the programme (38). NTPs are often responsible for these steps, as their responsibilities include the delivery of high-quality and effective diagnostic, treatment and preventive services (59,60). NTPs are usually housed within national ministries of health, though their activities are implemented at different levels of the health system (60). Prioritising ACF can be challenging, as ACF may “compete” with improving passive case-finding or other interventions within TB control that NTPs are responsible for, as well as other health interventions that ministries of health may prioritise. In addition, many different stakeholders can be involved in ACF implementation, e.g., non-governmental organisations that screen and provide social support for vulnerable groups (56).

The implementation considerations include the additional human and financial resources needed for ACF, including the ability to accommodate the extra TB cases that may be identified through screening (56). The implementers, such as community health workers, are the ones putting ACF into practice (61–63). In some settings, these implementers may receive an incentive or a salary. A systematic review showed the importance of considering the local context when planning incentives to implement and maintain them over time, e.g., health system arrangement, environmental conditions, baseline health conditions, social norms and the existence of sufficient resources (64).

2.3 ABOUT NEPAL

In this thesis, Nepal and Vietnam served as examples of countries with a high TB burden. The country contexts, health systems, indicators and determinants of health, as well as TB and ACF in the two countries are described in sections 2.3 and 2.4.

2.3.1 Country context

The Federal Democratic Republic of Nepal is located in South Asia, bordering China and India. Nepal has rapidly reduced poverty but remains one of the slowest-growing economies in Asia (65). In 2020, the country transitioned from being a low-income country to a lower middle-income country (66). Nepal had a population of 28.6 million in 2019 (66). Eighty-six percent of the population are Hindu, and the population is further divided into many ethnic groups (67). The literacy rate among adults ≥ 15 years was 57% in 2012 (68) and the country ranked 110 on the gender inequality index in 2019 (69).

Geographically, Nepal consists of the Upper Himalaya, the Middle Hills and Lower Himalaya and the Terai Region. The latter refers to the plains of Nepal, stretching from the far-west to the far-east. With its sub-tropical climate and fertile land, the Terai Region is where the majority of the food grains are produced for the country's population (70).

In line with the federal restructuring of the country according to the new Constitution promulgated in 2015, Nepal has been divided into seven provinces each of which is planned to have its own TB control programme in the future (71). Positive impacts of the restructuring include the local elections that took place for the first time in 20 years in 2017 (72). While federalism is hoped to have further positive effects in terms of local resource usage, bottom-up planning and reduced bureaucracy in decision-making, challenges include the lack of clarity in authority and power across the different layers of the government (73).

2.3.2 Health system

The health system is characterised by insufficient health structures and human resources (74–76). As such, the National Health Policy of Nepal (2014) aims to improve access to quality and equitable health services (77). The Policy also intends to provide basic healthcare services free of charge and to provide other services through social health insurance (77). These aims are also reflected in the Nepal Health Sector Strategy 2015-2020 (78). Currently, out-of-pocket expenditure is still a major barrier to accessing health services (79), especially as many people rely on the private sector when seeking health care (73). In the 1980s, the Female Community Health Volunteers programme was established in Nepal; the approximately 50,000 Female Community Health Volunteers have been described as the backbone of healthcare in Nepal (80). Moreover, a large number of non-governmental organisations are active in Nepal, further backing up the health sector, as well as sectors like agriculture and education (81).

2.3.3 Indicators and determinants of health

Health indicators have been improving in Nepal over the past decades. For example, infant and child mortality decreased from 46 to 32 and 54 to 39 per 1,000 live births respectively between 2011-2016 (67,82). Life expectancy at birth was 73 years for women and 69 years for men in 2019 (68). Despite the progress on some health indicators, non-communicable diseases and injuries due to road accidents have been on the rise (78), and the Nepal Demographic and Health Survey (2016) showed that health gains were not distributed equitably within and across provinces (67).

Based on data from the 2016 Demographic and Health Survey, 95% of all households have access to an improved source of drinking water and 62% of households have an improved toilet facility that is not shared with other households (67). Forty-eight percent of households are food secure and 42% of children aged 12-23 months were covered by all vaccines as per the national immunisation programme (67). In addition, the increasing population and urbanisation have posed challenges to the country (83,84). For instance, the mortality rates due to air pollution and exposure to unsafe water, sanitation and hygiene services were 194 and 20 per 100,000 population respectively (compared to regional estimates of 164 and 15 per 100,000 population) in 2016 (85). In the same year, the prevalence of tobacco use among adults aged ≥ 15 was 27% among men and 6% among women (67).

2.3.4 Tuberculosis and active case-finding in Nepal

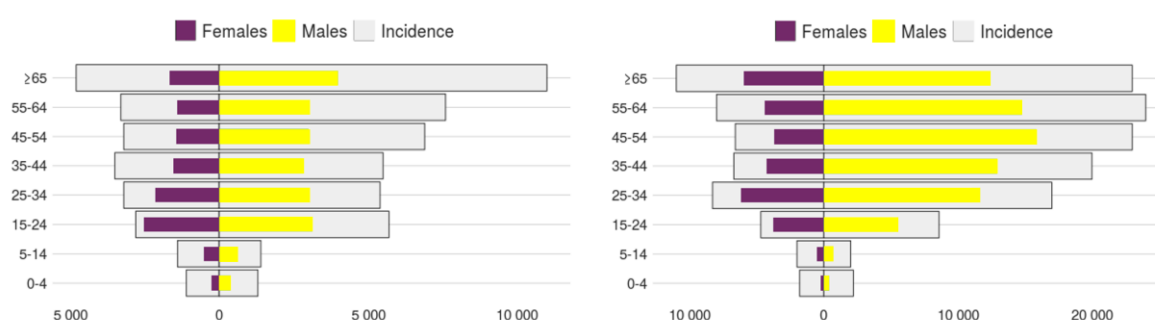
Nepal has seen no decrease in TB related indicators in the past few years. In 2018, the national TB prevalence survey showed an annual incidence of 245 TB cases per 100,000 population, which was almost 1.6 times higher than previously estimated (86). More than 70% of TB cases identified during the TB prevalence survey had no TB symptoms (86) and would have thus been unlikely to seek healthcare. Furthermore, it is estimated that 30-50% of incident TB cases are not notified (87). Determinants of delayed TB diagnoses in Nepal include patient income and occupation (88), smoking (89), as well as long distances to health centers, road conditions and costs associated with travelling, awareness about TB and the availability of personnel and equipment (90).

Nepal's National Strategic Plan (NSP) for Tuberculosis Prevention, Care and Control 2016-2021 envisions a TB-free Nepal by 2050 (71). The NSP aims at reducing TB incidence by 20% by 2021 compared to 2015 and identifying an additional 20,000 patients with TB. In 2019, the incidence rate had decreased by 2.5% compared to 2015 (91). The TB incidence and notified cases in Nepal and Vietnam are shown in Figure 1. The National Tuberculosis Centre (serving as a focal point of the NTP) and the Ministry of Health led the development of the NSP, and consulted a wide variety of stakeholders in that process, e.g., regional and district TB and Leprosy coordinators; district public health officers; representatives from governmental, non-governmental and private organisations; medical college staff; technical and financial experts; social scientists; service providers; Female Community Health Volunteers; TB patients and

their families; as well as community partners and representatives (71). The NSP comprises evaluation reports of the NTP and references the WHO End TB Strategy (71).

One ACF-related objective of the NSP is to increase case notifications, through the examination of close/household contacts of index TB cases and a variety of other risk groups such as people living with HIV or persons with diabetes mellitus, malnourished children, women, marginalised populations and the poor (71). An estimated 10,000 TB patients are out of reach of the NTP, unless ACF is applied. Regarding operational considerations linked to ACF, the NSP emphasises a lack of institutionalisation of screening programs for those at risk of developing TB disease, and a lack of effective mechanisms to identify the risk groups. Furthermore, the NSP describes how a significant number of presumptive TB cases are diagnosed in the private sector (71). The quality of care for TB patients provided by private practitioners has been described as poor (92), while the potential for public-private partnerships to improve service provision and TB notifications in Nepal has been emphasised (93,94). Another consideration is that the NTP remains heavily dependent on external funding; the implementation of the NSP is estimated to cost 105 million USD, but potential funding sources have been identified for only 59.4 million USD (71).

Figure 1. Tuberculosis incidence and notified cases by age group and sex in Nepal (left) and Vietnam (right), 2019 (adapted from the World Health Organization (95,96))



Many ACF projects have been implemented in Nepal, the first projects dating back to 1982 (97). In the past decade, different ACF models have been implemented in the country, e.g., one ACF project among people living with HIV showed that a peer-led approach to ACF resulted in a high participation rate and the identification of people with TB (98). Eight ACF projects in Nepal have been funded by TB REACH, a case-finding initiative sponsored largely by Global Affairs Canada and coordinated by the Stop TB Partnership (www.stoptb.org). For example, one TB REACH project in Nepal focused on people living with HIV, household contacts and urban slum dwellers, resulting in a substantial yield of TB cases (99).

2.4 ABOUT VIETNAM

2.4.1 Country context

The Socialist Republic of Vietnam is located in South-East Asia, bordering China, Laos and Cambodia. After the Vietnam war from 1955-1975, the country has shifted from a centrally planned to a market economy, which transformed Vietnam into a lower middle-income country in 2009 (100). Between 2002 and 2018, the gross domestic product per capita increased by 2.7 times reaching over 2,700 USD, lifting 45 million people out of poverty. Although, 86% of the population remain poor, many belonging to ethnic minorities (100). In 2019, the country had a population of 96.2 million (100). Buddhism is the largest of the major world religions in the country (101). The literacy rate among adults ≥ 15 years was 93% in 2012 (102) and the country ranked 65 on the gender inequality index in 2019 (69).

Vietnam's geography is characterised by a long coastline of 3,260 kilometres. Three quarters of the country are covered by hills and mountains, while one fourth is covered by deltas with fertile land, i.e., the Red River Delta in the north and the Mekong Delta in southern Vietnam (103). The capital city is Hanoi and the largest city is Ho Chi Minh City (former Saigon) (100).

2.4.2 Health system

The health system is divided into central, provincial, district and commune levels. The national Ministry of Health owns hospitals at the central level. Provincial governments, such as People's Committees, own hospitals at provincial, district and commune levels, and are responsible for the allocation of financial and human resources (104). The government has managed healthcare provision through a system called *Direction of Healthcare Activities*, which ensures that healthcare facilities at higher administrative levels support their lower level counterparts and this has facilitated the scale-up of medical technologies across the country (104). The Communist Party of Vietnam and the government launched the *Doi Moi* policy (1986), which established the socialist-oriented market economy including a private healthcare system. User fees were established in state health facilities (105). The transition to the *Doi Moi* policy negatively affected access to healthcare (106–109), drove patients to provincial and national hospitals which became overcrowded (106,108) and 80% of health expenditures were out-of-pocket expenses (110). National health reforms have been implemented since the 1990s (106,108) and plans for reforming the organisational structure of healthcare are underway, as described by the master plan for Vietnam's health system development to 2025 (111).

In Vietnam, private health facilities account for about 32% of outpatient services and 6% of inpatient services provided (112). In 1997, a health insurance system was introduced and 87% of the population are covered by universal health coverage (100). Human resources are currently insufficient to meet practical needs (111) and the available human resources are distributed inequitably across the country (113,114), e.g., leading to shortages of healthcare workers in mountainous and remote areas (115), such as the North West, the Central Highlands and the Mekong Delta regions (111).

2.4.3 Indicators and determinants of health

Today, Vietnam has one of the most rapidly aging populations in the world (100,116). In line with the societal and demographic changes the country has been undergoing, health problems have been shifting from infectious diseases and problems related to maternal and child health to non-communicable diseases such as stroke, ischaemic heart disease and lung cancer (117). However, TB remains one of the top 10 causes of death in the country (117). Many health indicators have improved, e.g., from 1993 to 2017, infant mortality rates decreased from 33 to 17 per 1,000 live births (100). Life expectancy at birth was 78 years for women and 70 years for men in 2019 (102). Yet, disparities remain in core health indicators between rural and urban populations, across regions and among population groups (111).

Between 1993 and 2016, the proportion of the population with access to electricity increased from 14% to 99%. Access to clean water in rural areas increased from 17% to 70% within the same time frame (100). In 2015, 78% of the population had access to improved sanitation, and 96% of children were immunised with three doses of diphtheria-tetanus-pertussis vaccine (118). At the same time, the growth of the economy and the population, as well as urbanisation have led to pollution and road injuries which have significantly impacted health (100,119). Lifestyle factors such as diet and nutrition, physical inactivity, the harmful use of alcohol and tobacco use contribute significantly to death and disability in Vietnam (119). For example, the smoking prevalence among adults aged ≥ 15 was 45.3% among men and 1.1% among women according to the Global Adult Tobacco Survey 2015 (120).

2.4.4 Tuberculosis and active case-finding in Vietnam

Vietnam has slowly but steadily reduced the national TB burden, but it remains a high TB burden country. In Vietnam, the estimated prevalence of TB among adults was 322 per 100,000 population, based on a recent national TB prevalence survey conducted in 2017-2018 (121). In 2019, the estimated gap between incident and notified TB cases in Vietnam was 65,495 (39%) (122). Contributing factors to the TB detection and notification gap in Vietnam are limited awareness of TB, lack of access to health care (123) and stigma (124).

The Vietnamese National TB Strategic Plan until 2020 emphasises the role of ACF for TB elimination (125), while the government passed legislation to end TB by 2030 (126). In the past decade, different ACF models have been implemented in the country (125), including two trials mentioned earlier (25,53). Vietnam's NSP covers the period 2015-2020, striving for a TB-free Vietnam, reducing the prevalence rate to less than 20 cases per 100,000 population by 2030 (125). The NSP is based on national and international guidance and policy documents, recent external program reviews, the WHO re-evaluation of TB burden in Vietnam and scientific publications. Apart from the National TB Program, the Vice Minister of Health, national and international partners (including the Vietnam Stop TB Partnership and the London School of Hygiene and Tropical Medicine) were involved in the development of the NSP (125).

The NSP includes ACF in remote and congregate settings, and a wide range of risk groups, including contacts, people in prisons, miners, elderly, homeless, young adults, migrants, factory

workers, communities, multidrug-resistant TB patients, young males, smokers, intravenous drug users and people living with HIV. The NSP explicitly aims at screening 95% of people living with HIV for TB per year (125). The NSP also includes an analysis of the NTP's strengths and weaknesses in terms of providing access to early diagnosis, emphasising the conduct of ACF in provinces with low case-finding rates and among people in prisons and health workers as strengths, and the lack of screening of adult household contacts as a weakness (125). To increase the sensitivity for ACF, the NSP describes the aim of intensifying the use of X-ray in combination with CAD and Xpert® MTB/RIF testing. In terms of operational considerations for ACF, the NSP emphasises the need to develop funding mechanisms to cover incentives for local health workers to work at commune health stations and in outreach activities. The essential role of health workers to identify presumptive TB cases is highlighted, as well as the crucial role of community mobilisation targeting the most affected populations (125).

2.5 EVIDENCE-INFORMED POLICIES AND PRACTICE

2.5.1 Global commitments

The achievement of equitable and universal access to health care is more likely to be achieved through evidence-informed health policies and practice (127–129). The interest in using research evidence in policymaking has been growing globally. The WHO published the World Report on Knowledge for Better Health in 2004 which comprised a chapter on linking research to action (130). In the same year, the Ministerial Summit on Health Research took place in Mexico, issuing a statement on the importance of research for improved health and strengthened health systems (131). In 2005, the 58th World Health Assembly passed a resolution urging member states “to establish or strengthen mechanisms to transfer knowledge in support of evidence-based public health and health-care delivery systems, and evidence-based health-related policies” (132). The importance of evidence-informed policy and practice was also reflected in the Bamako Statement issued by the Ministers of Health and other Ministerial representatives of 53 countries in 2008 (133).

2.5.2 Evidence use and the policy cycle

Evidence is vital for clarifying the issues being addressed at all stages of the policy cycle, from priority setting, to policy development, implementation and evaluation (134). Gaps may exist between the original objectives of a policy and the way the policy is being implemented. Research can still play an important role in helping to address implementation issues (135). Challenges include difficulties in identifying and categorising evidence use (136). Moreover, one piece of evidence may have several meanings depending on values and interpretation, which in turn affect the framing, presentation and acceptance of evidence (137). Such methodological diversity tends to be more acceptable in health policy, compared to medicine (138).

2.5.3 Factors influencing policy and practice

Evidence is only one of many factors influencing policy and practice (139). To better understand, inform and improve policy processes, it is therefore crucial to unpack those influencing factors which include context, stakeholders and power (140–142). The interaction with and among stakeholders has been described as the key influencing facilitator for evidence-informed policymaking (139). Examples of such an interaction include policy dialogues, which convene key stakeholders to deliberate on a priority topic. Policy dialogues support the integration of research evidence with stakeholders' experience to inform future policy decisions (143,144). Policy dialogues can contribute to integrating research evidence and other factors that influence policy and practice such as values, interests, and stakeholders' political goals. Making policies "fit" complex and dynamic contexts in health has been described as critical for implementation (145). This is particularly valuable in a complex policy area such as ACF.

Policy processes are not linear but nuanced and negotiated (64,65), while there remains strong support for the view that research evidence should inform more of policymaking (146,147). The solutions for evidence-informed policy and practice include a mix of appropriate evidence, key stakeholders, processes and structures (138).

2.6 RATIONALE

To inform ACF policy development and implementation in high TB burden countries, evidence is needed, e.g., on the impact of ACF in different risk groups, impact on equity, the performance of algorithms and tools, cost and cost effectiveness of different ACF models and implementation strategies (148). Due to gaps in our understanding of ACF, related policy development and implementation processes are likely to rely on key stakeholders' experience, values and preferences about which we know little. Key stakeholders for ACF include experts, politicians, policymakers, NTP managers, donors, implementers of ACF, people with TB identified through ACF and affected communities. The studies in this thesis contribute to the evidence base for ACF, from global policy to local implementation, by exploring some of the key stakeholders' experiences from ACF in high TB burden countries.

3 AIM AND RESEARCH QUESTIONS

The overarching aim of this thesis is to contribute to the knowledge base on ACF policy development and implementation, with a focus on high TB burden countries and the perspectives of different stakeholders. The following research questions are addressed:

- What is the state of knowledge on antecedents, components and influencing factors for ACF policy development and implementation globally (Study I)?
- What do experts perceive as factors influencing ACF policy development and implementation? What are their views on evidence use in these processes (Study II)?
- How do experts perceive the benefits and harms of ACF for people with TB and for communities worldwide (Study III)?
- What are the NTP managers' attitudes related to ACF policy development, implementation and scale-up in the 30 high TB burden countries? How do national TB strategic plans in the high-burden countries reflect ACF (Study IV)?
- What do people with TB and implementers of ACF perceive as facilitators, barriers and “how-to” strategies for implementing ACF in Nepal (Study V)?
- What do local leaders, people with TB and implementers of ACF perceive as facilitators, barriers and “how-to” strategies for implementing ACF in Vietnam (Study VI)?

4 METHODS

4.1 OVERVIEW OF THE METHODS USED

This thesis used qualitative and mixed methods approaches as well as a scoping review to identify factors influencing ACF policy development and its implementation in high TB burden countries. The scoping review (Study I) set the scene and informed the subsequent studies. We reported the scoping review using the Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) checklist (149). Studies II, IV, V and VI were exploratory qualitative studies based on semi-structured interviews. Studies II and III focused on the views of experts. Studies V and VI were centred around the perspectives of key-informants, including implementers of ACF and people with TB who had been identified through ACF in Nepal (Study V) and Vietnam (Study VI). Study VI also included interviews with local leaders. Studies V and VI involved project collaboration and field work, which are described in section 4.6. In all qualitative studies, we used information power to guide the sample size, implying that the more information relevant to the study a sample holds, the fewer participants would be needed (150). All qualitative studies were reported using the Consolidated criteria for Reporting Qualitative research (COREQ) checklist (151). Study IV was a mixed methods study with an embedded design; the cross-sectional survey with the NTP managers yielded quantitative and qualitative data, which we reported using the Checklist for Reporting Results for Internet E-Surveys (CHERRIES) (152). A review of national TB strategic plans complemented the results. Table 1 provides an overview of the studies.

Table 1. Overview of the studies forming the thesis and how they link to each other

#	Con-text	Focus	ACF target group	Study type, data sources and methods	Link to other studies in this thesis
I	Global	ACF policy development and implementation	Any	Scoping review using MEDLINE, Web of Science, Cochrane Database of Systematic Reviews and the WHO Library; frequency and thematic analyses	Informed all subsequent studies
II				Qualitative study based on expert interviews (n=39); framework analysis	Informed Study IV and served as comparison
III					
IV	High TB burden countries			Mixed methods study based on cross-sectional survey with NTP managers (n=23) and document review of national TB strategic plans (n=22); descriptive statistics, content analysis and document review	Informed Studies V and VI and served as comparison
V	Nepal	ACF implementation	Household contacts in urban, semi-urban and hard-to-reach areas	Qualitative study based on key-informants (n=17) (people with TB and implementers); thematic analysis	Compared to each other and concretised and complemented findings from Studies I-IV
VI	Vietnam		Household and close contacts, neighbours, people living in slums and boarding homes	Qualitative study based on key-informants (n=39) (people with TB, implementers, leaders); thematic analysis	

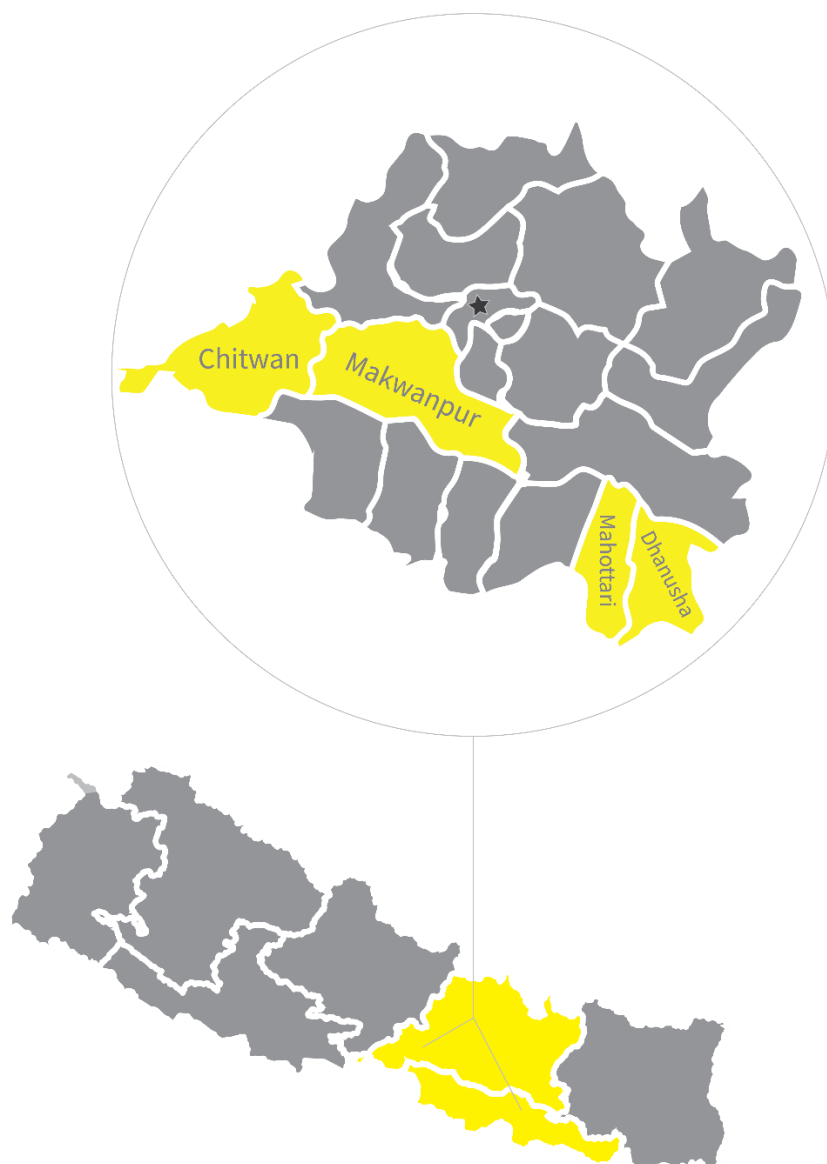
ACF = active case-finding, TB = tuberculosis, NTP = National Tuberculosis Programme, WHO = World Health Organization

4.2 STUDY SETTINGS

Studies I, II and III had a global focus, drawing on literature (Study I) and expert informants (Studies II and III). The articles included in Study I were from all WHO regions, but primarily Africa (22%), Europe (23%) and the Western Pacific region (12%). In Studies II and III, 62% (n=24) of the 39 participants were from high-income countries, 5% (n=2) were from upper middle-income countries and 33% (n=13) were from lower middle-income countries. Study IV involved NTP managers from 23 of the 30 high TB burden countries.

Study V was conducted in Nepal, in collaboration with the Birat Nepal Medical Trust (BNMT). BNMT is a national non-government organisation that implemented the ACF model as part of the IMPACT TB project (Implementing proven community-based active TB case-finding intervention) in four districts of the country that have a high prevalence of poverty and TB: Chitwan, Makwanpur, Mahottari and Dhanusha (76) (Figure 2). Makwanpur is a hilly district with a limited road network, while the other districts are on the lowland plains (the Terai). The districts are challenged by pockets of high urban population density, poor health indicators and high rates of illiteracy (67). The ACF model used is described in Panel 2. Section 4.5 provides information about the IMPACT TB project.

Figure 2. IMPACT TB implementation districts in Nepal



This map has been created for the purpose of indicating the approximate location of the IMPACT TB districts Chitwan and Makwanpur (Province 3), Mahottari and Dhanusha (Province 2). The country and state borders may not be accurate.

Panel 2. Active case-finding as part of IMPACT TB in Nepal

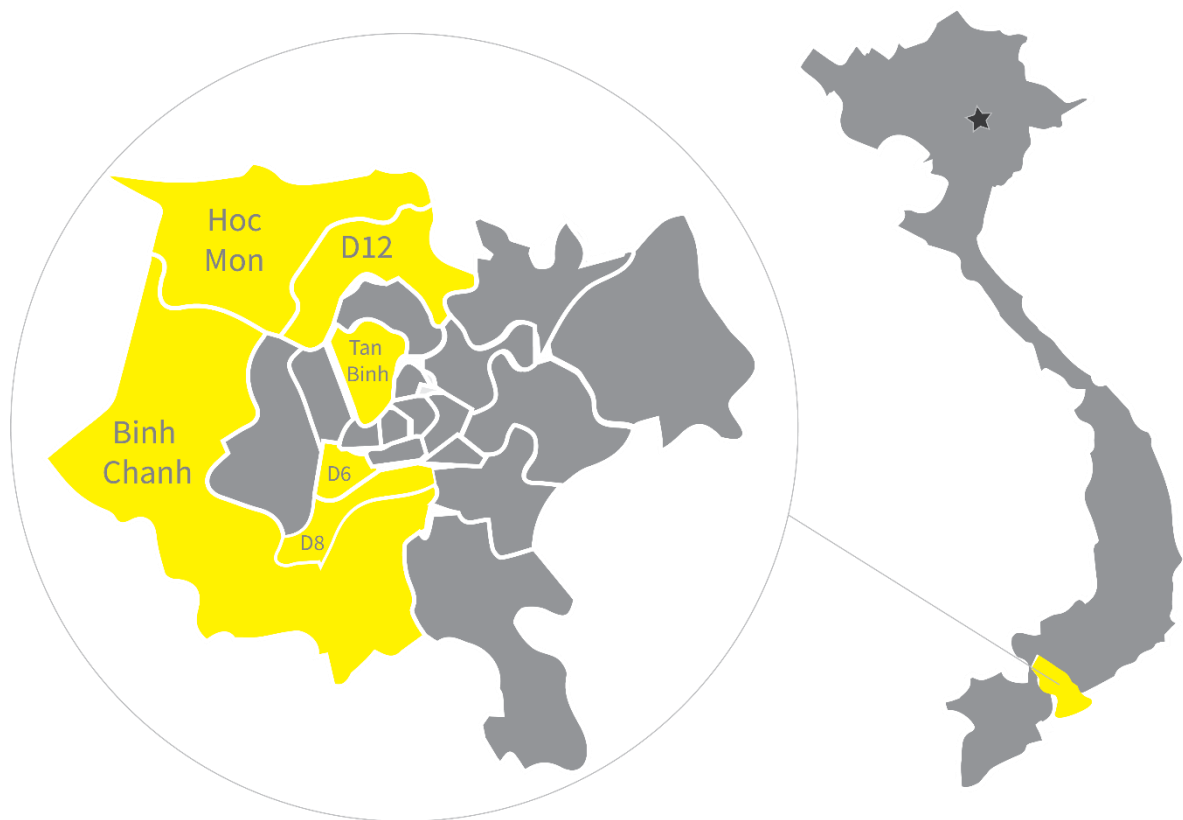
In Nepal, the ACF model was implemented by Female Community Health Volunteers (from the network appointed by the government) supplemented by additional community volunteers and Community Mobilizers (both appointed by BNMT). Staff appointed by BNMT were recruited from the local community by IMPACT TB District Program Coordinators in close collaboration with the local health office (jointly referred to as “implementers”). In urban, semi-urban and hard-to-reach areas, implementers screened household contacts of index TB patients (TB patients notified at health posts, primary health care centers or district hospitals and recorded in a TB register). They used a simple standardised oral symptom screening questionnaire (8 questions), transported sputum samples from anyone who was positive for one or more symptoms to local laboratories, supported people who were diagnosed with TB to enrol in TB treatment and conducted follow-up visits. In Makwanpur and Mahottari, sputum smear microscopy was used for TB diagnosis, while the Xpert® MTB/RIF was used in Dhanusha and Chitwan.

Implementers received incentives for visiting a TB patient and listing his or her contacts (Rs 225, approx. USD 1.90), for each sputum sample collected and transported to the local laboratory (Rs 180, approx. USD 1.50) and for each person identified with TB (Rs 200, approx. USD 1.70). Community Mobilizers supervised and monitored the work of the community volunteers and Female Community Health Volunteers and received an additional stipend to cover transportation costs. The overall coordination of stakeholders in the district, oversight of ACF implementation, planning and reporting was managed by District Program Coordinators. The Community Mobilizers and District Program Coordinators received salaries of Rs 10,000 (approx. USD 86) and Rs 63,000 (approx. USD 536) respectively.

The ACF model generated a substantial yield of TB cases (n=1,193), TB notifications increased by 13% (235) and TB-related patient costs were significantly reduced (44).

Study VI was performed in Vietnam, in collaboration with the non-governmental organisation Friends for International TB Relief (FIT). FIT implemented the IMPACT TB ACF model in six districts of Ho Chi Minh City (Figure 3); employees implemented ACF in Hoc Mon, Tan Binh and District 12, while volunteers implemented the same ACF interventions in Binh Chanh, Districts 6 and 8. These districts constituted an estimated population of 2.7 million people and reported 4,159 All forms TB notifications (149). The districts were selected for IMPACT TB given comparable patient burden and demographics, such as similarly high rates of domestic migrants and temporary residents (30-50%). Panel 3 outlines the ACF model used.

Figure 3. IMPACT TB implementation districts in Vietnam



This map has been created for the purpose of indicating the approximate location of the IMPACT TB districts in Ho Chi Minh City, Vietnam (Hoc Mon, Tan Bin, District 12, Binh Chanh, District 6 and District 8). The country and state borders may not be accurate.

Panel 3. Active case-finding as part of IMPACT TB in Vietnam

In Vietnam, the implementers were identified and recruited by district authorities among retired health staff, civil society members, community volunteers and former TB patients who had been living in the district for at least five years (236). Employees were considered as full-time staff, receiving a salary of 136 USD/month, while volunteers worked part-time and received a stipend of 23 USD/month. All implementers had the same responsibilities within the project, participated in capacity-building activities and received performance-based incentives (236).

The implementers screened household and other close contacts of index TB patients (TB patients notified by the District TB Units). ACF also included persons from risk groups, such as the neighbours of a TB patient (237), people living in slums and boarding homes. All participants had verbal screens for symptoms and a history of TB, which were recorded into a custom-built app installed on a tablet (236). Household contacts were referred for a chest X-ray irrespective of whether they had TB symptoms due to the high rate of asymptomatic TB patients in Vietnam (39,121). All other persons (without confirmed household contact) were only referred for a chest X-ray if they reported any symptom suggestive of TB. People referred for a chest X-ray received a transport voucher and a free chest X-ray at the District TB Unit or community screening events held during weekends. Those with an abnormal chest X-ray were then tested using Xpert® MTB/RIF. Sputum smear microscopy was used for those who had a normal chest X-ray but displayed any symptoms suggestive of TB and those who did not get a chest X-ray.

Implementers transported sputum samples for people who were unable to reach the laboratories. Symptomatic persons with negative sputum test results underwent clinical evaluation by the District TB Unit and the Pham Ngoc Thach Hospital, in line with the national policy. If diagnosed with TB, implementers assisted patients with drug-susceptible TB to access TB treatment, including support to provide proof of residency, if needed, and patient counselling and psychosocial support. Site coordinators assisted the District TB Units with data collection and reporting. Patients with drug-resistant TB were referred to Pham Ngoc Thach Hospital for further evaluation and treatment (236).

The ACF model generated a substantial yield of TB cases (354 per 100,000 population), while TB notifications in the project's intervention area increased by 12.3% (236).

4.3 STUDY DESIGN AND METHODS

4.3.1 Scoping review (Study I)

Study I used a scoping review to identify the antecedents, components and influencing factors for ACF policy development and implementation. Frequency and thematic analyses were used to capture the wide range of research on the topic. We searched MEDLINE, Web of Science, the Cochrane Database of Systematic Reviews and the WHO Library from 1968 until January 2018. The search strategy was developed in collaboration with a medical librarian from Karolinska Institutet and further refined through discussion with the co-authors. The search strategy for MEDLINE is available in Appendix 2. The results of the literature search were imported into Rayyan (<http://rayyan.qcri.org>).

The scoping review included studies describing or analysing ACF policy development and implementation. Facilitators and barriers linked to access or treatment were included if there was a clear link to ACF. Furthermore, the review included studies analysing the use of evidence in ACF policy development and implementation. Studies of any design, conducted in any setting or country, and those published in the English language were eligible for inclusion. We excluded studies focusing only on TB infection, passive case-finding and childhood TB, and studies about effectiveness, yield, accuracy and impact without descriptions of how this evidence has/could influence policy.

I initially reviewed 5,573 titles to remove duplicates, and those studies not focusing on TB. Co-author Kerri Viney and I independently reviewed 2,943 titles and abstracts, and then 271 full-text articles for inclusion. Disagreements were resolved through discussion, based on the inclusion/exclusion criteria. Finally, 73 articles fulfilled our eligibility criteria. I charted relevant data on study design, country, target population for ACF, benefits of ACF, risks of ACF, ACF antecedents, ACF policy development and implementation, lessons learned, future perspectives and future research. Kerri Viney verified this step by charting data from a random sample of studies for comparison. Differences in data-charting were resolved by discussion. All co-authors were consulted at various stages of the scoping review to provide input on the search, data extraction and charting and the interpretation of the results.

The research questions for Studies II-VI were informed by the results of this scoping review, e.g., filling gaps in the knowledge on ACF policy development, and verifying and complementing knowledge on ACF implementation.

4.3.2 Expert interviews (Studies II and III)

Studies II and III used the qualitative method of semi-structured expert interviews (153) to understand the views of experts on the factors that influence ACF policy development and implementation and the use of evidence in these processes (Study II), as well as the perceived benefits and harms for people with TB and communities globally (Study III). Framework analysis, as described by Gale et al. (154), was chosen as it aims at generating policy and practice-oriented findings.

The participants were purposively sampled to include stakeholders involved in ACF policy development and implementation. The initial list of participants was compiled based on the knowledge of networks of experts. We discussed, expanded and verified this list with two independent experts in the field. We contacted 50 individuals via email of who 11 declined participation (seven of whom were women). The 39 participants were based at international (n=16), non-governmental (n=2) and non-profit organisations (n=2), donors (n=4), government institutions (n=2), international societies (n=2), think tanks (n=1), universities (n=6), research institutions (n=3) and one independent consultant (n=1). We developed and piloted the interview guide and revised it by focusing more on the main topics of interest (Appendix 3).

The data were collected between February and May 2018. Twenty-eight interviews were conducted via telephone. Eleven interviews were carried out in person during a field visit to Nepal, WHO meetings and at an international organisation. The participants were asked about their experience in developing and/or implementing ACF policies, factors that influenced these policy processes, the use of evidence and the perceived benefits and harms of ACF. The relatively large number of participants was deemed necessary given the broad aim of the study and that all participants had extremely relevant experience related to different aspects of ACF policy development and implementation. The sample allowed capturing opinions from the diverse range of experts involved in ACF policy development and implementation, but also led to the decision to present parts of the results in what became Study III, to do justice to the breadth and depth of the findings.

I transcribed 10 of the audio-recorded interviews verbatim; the remaining ones were transcribed by a professional company. For both Studies II and III, data were analysed abductively, i.e., identifying themes a priori and allowing for additional themes to emerge from the data. For Study II, I coded all interviews, developed the analytical framework, charted the data into a framework matrix and interpreted the data by writing memos for each study theme. I gained regular input from the co-authors of the study. For Study III, I co-supervised co-author Raina Klüppelberg in using framework analysis and provided input throughout.

4.3.3 Mixed methods survey and document review (Study IV)

This study was designed and conducted to understand the attitudes of the NTP managers related to ACF policy development, implementation and scale-up in the 30 high TB burden countries. The study used a mixed methods approach with an embedded design, i.e., a cross-sectional survey that yielded both quantitative and qualitative data, enhancing each other. This approach allowed us to quantify and compare findings across the high TB burden countries, while also seeking depth and nuances. We analysed the data using descriptive statistics. The qualitative answers were analysed using content analysis, as described by Graneheim et al. (155). The analysis was further complemented by the document review, which included a sample of national TB strategic plans from the high TB burden countries. The document review provided additional information on whether or not and how ACF was reflected in the national TB strategic plans.

NTP managers from all 30 high TB burden countries were contacted via email. In total, 23 NTP managers agreed to participate in the survey (participation rate: 77%). Seventeen NTP managers took part themselves, whereas six appointed one of their team members to participate on their behalf. In this thesis, I refer to “the NTP managers”, meaning all 23 respondents from Bangladesh, Brazil, Cambodia, China, Congo, Democratic Republic of the Congo, Ethiopia, Indonesia, Kenya, Lesotho, Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, South Africa, Tanzania, Thailand, Vietnam, Zambia and Zimbabwe.

The questionnaire included sections on the general views on ACF, national ACF policies, evidence use, contextual factors, scale-up, monitoring and evaluation and lessons learned. Question formats included Likert scales, lists, yes/no questions and open-ended questions (without probing questions) (Appendix 4). Five-point Likert scales investigated: 1) agreement with statements about the potential benefits and risks of ACF, 2) degree of influence of contextual factors on ACF policies and 3) frequency of use of different types of evidence in ACF policy. The NTP managers also confirmed which stakeholders were involved in ACF policy development and implementation, using a list of 14 types of stakeholders. We developed and piloted the survey questionnaire and condensed it to be more feasible to implement.

The data were collected between March and October 2018. As we implemented all surveys through structured interviews, I refer to them as “interviews” in the subsequent text. Ten interviews were conducted in person during international conferences, five at a WHO meeting and eight on the telephone/Skype, depending on the participants’ preferences. The interviews were voice-recorded. Co-author Phuong Tran or I transcribed the responses verbatim and shared the transcripts with the NTP managers for their information and review. Five NTP managers replied after having received the filled-in survey; one included additional information. If the NTP managers did not respond within four weeks, the survey was considered complete. Phuong Tran entered all responses into REDCap (Research Electronic Data Capture), a secure, web-based platform (156).

Using STATA 15 (StataCorp LLC), we computed descriptive statistics (frequencies, mean, median and proportions). Additional indicators were added to investigate any patterns in the responses: e.g., 1) country income level, 2) region (157), and 3) proportion of NTP budget consisting of domestic funding, 4) international funding and 5) being unfunded (158). The content analysis focused on the manifest content and generated meaning units, codes and categories.

For the document review, we identified 18 national TB strategic plans through an online search, while an additional four strategic plans were shared with us by staff from the Stop TB Partnership and WHO. Strategic plans from the following 22 countries were included: Angola, Bangladesh, Brazil, Cambodia, Ethiopia, India, Indonesia, Kenya, Liberia, Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, Sierra Leone, South Africa, Tanzania, Vietnam, Zambia and Zimbabwe. Eighteen of these countries overlap with the countries that were represented in the survey. We developed a data extraction table, which we filled with data on the development of the national TB strategic plan, background and aims,

targets, operational and ethical considerations, budget estimates and funding sources. We added insights from the document review where appropriate throughout the analysis to further complement the findings.

4.3.4 Key-informant interviews in Nepal (Study V)

Studies V and VI used the qualitative methods of semi-structured key-informant interviews to identify facilitators, barriers and “how-to” strategies linked to the implementation of the IMPACT TB ACF model in four districts of Nepal (Study V) and six districts of Ho Chi Minh City, Vietnam (Study VI). Thematic analysis was chosen, as described by Braun et al. (159), as it allows patterns of meaning in the data to be identified and interpreted. Furthermore, the implementation science framework “Barriers to and incentives for change at different levels of healthcare” (160) was applied to classify the data and facilitate comparisons between Studies V and VI. The framework is displayed in Panel 4. The framework describes how barriers and facilitators can be identified, categorised and used for the development of a tailored intervention strategy. It categorises facilitators and barriers into levels: the innovation (in our case ACF), the individual professional, the patient, the social context, the organisational context, and the economic and political context.

Panel 4. Barriers to and incentives for change at different levels of healthcare – framework by Richard Grol and Michel Wensing (160)

Level	Barriers/incentives
Innovation	Advantages in practice, feasibility, credibility, accessibility, attractiveness
Individual professional	Awareness, knowledge, attitude, motivation to change, behavioural routines
Patient	Knowledge, skills, attitude, compliance
Social context	Opinion of colleagues, culture of the network, collaboration, leadership
Organisational context	Organisation of care processes, staff, capacities, resources, structures
Economic and political context	Financial arrangements, regulations, policies

In Nepal, participants were purposively sampled and included two different stakeholder groups: (1) people diagnosed with TB, identified through ACF and (2) implementers of ACF. The people with TB had to be on TB treatment or have recently completed it to be approached for an interview. The implementers were chosen among those with the longest working

experience within IMPACT TB. The implementers also had to be available during the days of the interviews while many were travelling as part of the sample collection program. In collaboration with the IMPACT TB District Program Coordinators and Community Mobilizers in the districts, co-authors Kritika Dixit and Bhola Rai recruited the participants. All invited participants agreed to be interviewed, amounting to nine interviews with implementers and eight interviews with people with TB (n=17). We developed and piloted interview guide, revising it in terms of the order and clarity of the questions (Appendix 5). The interview guide was translated into Nepali and translated back into English. Being bilingual in English and Nepali, Kritika Dixit and Bhola Rai ensured the quality of the translations.

The data were collected by Kritika Dixit and Bhola Rai in June 2019. The interviews were conducted in hotels, health facilities, homes of people with TB and the BNMT regional office in Hetauda, depending on the preference of the participant. The interviews covered questions on the perceived facilitators and barriers of implementing/participating in ACF, and suggestions for how to improve ACF implementation. To ensure the quality of the data collection, Kritika Dixit, Bhola Rai and I travelled to the four IMPACT TB districts together during the period of data collection and held debriefings after each interview. I also got to observe the majority of the interviews, giving me a better understanding of the context and interactions. The audio-recorded interviews were transcribed verbatim and translated into English by an independent public health professional fluent in both languages.

We conducted a data-driven thematic analysis (159), employing a realist approach considering the whole data set and reporting experiences, meanings and the reality of the participants. Choosing a realist approach meant that we focused on the manifest rather than the latent content of the interviews. I took the following steps in analysing the data: 1) coding, 2) developing a list of codes that reflected the facilitators and barriers for ACF implementation, 3) checking the codes across the data set and adding new codes, 4) reviewing and structuring the data based on the implementation science framework, 5) creating categories from observed patterns of meaning in the data and the theoretical understanding gained during the previous step, 6) mapping the findings onto the framework and 7) identifying themes that captured the meaning and association between the categories. Throughout these analysis steps, I gained regular input from the co-authors of the study.

4.3.5 Key-informant interviews in Vietnam (Study VI)

In Vietnam, participants were purposively sampled and included three different stakeholder groups: (1) people with TB identified through ACF, (2) implementers of ACF and (3) local leaders. Local leaders included District TB Unit leaders from the six IMPACT TB districts; representatives of the NTP, as well as from the Centre for Community Development and from international organisations based in Vietnam. We compiled an initial list of the types of participants to be included in the study. IMPACT TB coordinators in the different districts suggested volunteers and employees to be interviewed (stakeholder group 1). The implementers suggested TB patients (stakeholder group 2) who had to be on TB treatment or had completed it. Co-author Luan Vo suggested participants for stakeholder group 3. A local

research assistant (Linh Hoang) and co-author Phuong Tran contacted 41 potential participants, out of whom 12 implementers, 12 people with TB and 15 local leaders agreed to participate (n=39). Two persons declined participation due to lack of time or interest.

Using the interview guide from Study V as a starting point, I discussed the interview questions with the co-authors, and we were able to further improve the questions by making them clearer language-wise and more specific to each stakeholder group (Appendix 6). As in Study V, the questions were designed to elicit information about the facilitators, barriers and “how-to” strategies for ACF implementation. The interview guide for stakeholder group 3 comprised an additional section about ACF data. The interview guides were translated into Vietnamese and translated back into English. Phuong Tran ensured the quality of the translations, being bilingual in English and Vietnamese. The first interviews were conducted as pilot interviews (two with each stakeholder group) after which the interview guides were revised, e.g., for stakeholder groups 1 and 2, questions were added on people refusing ACF participation.

Data were collected between October and December 2019. Phuong Tran and Linh Hoang conducted the 39 semi-structured key-informant interviews. The 36 face-to-face interviews were conducted at participants’ homes, workplaces, international conferences, health stations or District TB Units, depending on the participants’ preferences. Three interviews (stakeholder group 3) were conducted via telephone. The audio-recorded interviews were transcribed verbatim and translated into English by a professional translator. As in Study V, we conducted a data-driven thematic analysis (159) in NVivo 11, employing a realist approach considering the whole data set and reporting experiences, meanings and the reality of the participants. For the data analysis, we followed the same steps as in Study V.

4.4 ETHICAL CONSIDERATIONS

Study I did not require ethical approval as it was based on published articles. Studies II-IV were approved by the Swedish Ethical Review Authority in Stockholm (#2017/2281-31/2). For Study V, ethical permission was granted by the Nepal Health Research Council, Nepal (#3046), and the Liverpool School Tropical Medicine Research Ethics Committee, United Kingdom (#19-002). For Study VI, ethical approval was received from Pham Ngoc Thach Hospital Institutional Review Board, Vietnam (#1773/HDDD-PNT).

Even though Study I did not require ethical approval, an important issue to consider for reviews is whether the included studies were conducted in an ethical manner (161). We worked under the assumption that the ethical aspects of the studies had been assessed during peer review and that the studies were approved by a research ethics committee. Studies II-VI applied qualitative or mixed methods approaches, with the aim of identifying the views of participants on factors influencing ACF policy development and implementation. Some topics were potentially sensitive, e.g., when participants expressed their views on barriers for ACF, such as challenges in collaborating with others or lacking resources.

I prepared clear, written information sheets for the participants, encouraging them to ask questions before and after the interview. Information about the studies was available in English

(Studies II-IV), Nepali (Study V) and Vietnamese (VI). I also emphasised to the participants that they could terminate the interview at any time without giving a reason, although none did. Before starting an interview, I always sought the participants' written informed consent. In case of illiterate participants in Nepal, information was provided verbally and consent was sought by thumb print. The participants in Studies V and VI were potentially more vulnerable (e.g., implementers and people with TB) than participants in Studies II-IV (e.g., experts). In the information sheet, I therefore indicated that their decision not to participate would not have any repercussions for the work they did/the care they received.

I respected my participants' time and effort and tried to make their participation as comfortable and convenient as possible. For example, I adjusted the length of the interviews in Studies II and III to how much time experts were happy to offer me (from 15 to 80 minutes) and implemented the survey for Study IV where and when convenient for the National TB Program managers (during coffee breaks at a WHO meeting or via telephone). In Studies IV and V, we adjusted to the participants' schedules and interviewed them where convenient for them, e.g., at their homes or in private rooms in health facilities. Moreover, the participants received a monetary incentive to compensate for their time: Rs 500 (approx. USD 4.28) in Nepal and 300,000 VND (approx. 13 USD) in Vietnam.

To guarantee the participants' privacy and confidentiality to the highest degree possible, their information was anonymised. In Studies I and II, there was a risk for experts to be recognised by the way they expressed themselves. I was therefore cautious in reporting the data and in picking quotes for the manuscripts. In Study IV, I reported the data referring to the high TB burden countries overall, without pinpointing any individual country. In Studies V and VI, I protected participants' privacy and confidentiality (especially of the people with TB who may experience stigma due to their disease) by interviewing participants in private locations. However, since project staff were asked to help identify eligible participants, it was not possible to keep a request to participate fully confidential. Yet, I anonymised all transcripts, so that my co-authors (some of whom were project staff) did not know which participants said what.

4.5 PROJECT COLLABORATION AND FIELDWORK OBSERVATIONS

The thesis project was developed as part of the EU-Horizon 2020-funded project IMPACT TB (reference number: 733174, website: <http://impacttbproject.org/>). Between 2017-2019, IMPACT TB was implemented in Nepal and Vietnam. The project evaluated different human resource strategies (incentivised volunteers versus salaried employees) in Vietnam, and the use of different diagnostic testing strategies (smear microscopy versus Xpert® MTB/RIF) in Nepal. IMPACT TB also assessed the health economic impact and social returns on investment of ACF under the different models and modelled transmission patterns in relation to the long-term epidemiological impact. An overview of the IMPACT TB project is included in Appendix 7.

Karolinska Institutet led IMPACT TB's Work Package 6 "From research to policy: networking and translational activities". The Work Package included workshops and dissemination

meetings with global and local stakeholders, as well as the preparation of policy briefs and the organisation of policy dialogues in both countries. In addition, the Work Package entailed liaising with the WHO's Global TB Programme and the WHO Regional Offices for the Western Pacific and South-East Asia.

Being part of the IMPACT TB consortium was a privilege. On the one hand, the consortium gave me the opportunity to collaborate with and learn from a wide variety of researchers from all over the world who had diverse backgrounds. On the other hand, the broad network of the consortium, in particular through Work Package 6, provided valuable links between the research done as part of IMPACT TB and policy and practice. The studies included in this thesis complement the work of IMPACT TB.

From March to July 2019, I was based at the BNMT office in Kathmandu, Nepal, to work on Study V. Most importantly, I shared my day-to-day work and life with colleagues at BNMT, learning about Nepal's country context through our daily interactions and conversations. To be better able to analyse and interpret the data, I tried to immerse myself in the country and its culture, including by learning the Nepali language and by travelling to the four study districts with Kritika Dixit and Bhola Rai (co-authors) for the data collection.

From August to December 2019, I was based at the FIT offices in Vietnam for the data collection for Study VI. I spent two months in the FIT office in Hanoi where the NTP is located, and three months in the FIT office in Ho Chi Minh City where ACF was being implemented as part of IMPACT TB. I learned much about the context by being based in the country and sharing my everyday life with colleagues at FIT. I spent considerable time in preparing the data collection process together with Phuong Tran (co-author) and Linh Hoang (local research assistant). Due to local government regulations, it was not possible for me to join Phuong Tran and Linh Hoang for the interviews. Yet, we still collaborated closely, e.g., through weekly debriefings to discuss topics that had emerged during the interviews.

4.6 PHOTOS FROM ACTIVE CASE-FINDING ACTIVITIES



Nepal: Implementers screen people with presumptive tuberculosis for symptoms (photos on top and on the bottom right). Implementer collects sputum sample (photo on the bottom left). © Birat Nepal Medical Trust



Vietnam: Medical doctor at a District Tuberculosis Unit examining a chest X-ray for signs of tuberculosis (photo on top left). Person with presumptive tuberculosis participates in screening event in the community (photo on top right). Implementers screen people with presumptive tuberculosis for symptoms using tablets.
 © Friends for International TB Relief

5 RESULTS

The following sections shed light on the main results: the perceived benefits and harms of ACF; stakeholders and evidence that influence ACF policy development; facilitators, barriers and the “how-to” of ACF implementation; and ACF scale-up and sustainability.

5.1 PERCEIVED BENEFITS AND HARMS OF ACTIVE CASE-FINDING

Main results

- ACF could be a “double-edged sword” and cause harms, if inappropriately designed and implemented (Study III).
- Benefits of ACF are often perceived to be linked to its inherent aim of early detection and treatment of TB, while harms are often believed to be associated with inappropriate implementation (Study III).
- Benefits and harms of ACF must be considered throughout the screening and diagnostic pathway to reap the potential benefits and mitigate harms (Study III).
- Views on the potential harms of ACF are more heterogenous compared to views on the potential benefits (Study IV).
- Perceived benefits of ACF serve as facilitators for ACF implementation, e.g., access to healthcare, free testing and treatment, as well as support for TB patients through ACF (Studies V and VI).

We explored experts’ views on the benefits and harms of ACF for people with presumptive TB and communities (Study III). Most of the perceived benefits of ACF could be linked to its objective of finding and treating persons with TB early (Theme 1). Meanwhile, ACF was also perceived as a “double-edged sword” and could cause harms if inappropriately designed and implemented (Theme 2). On the one hand, the perceived benefits of ACF included reaching vulnerable populations, reducing patient costs, helping raise awareness for TB among individuals and engaging communities as well as reducing TB transmission. On the other hand, the perceived harms of ACF comprised increasing stigma and discrimination, causing false-positive diagnoses, as well as triggering other unintended negative consequences related to screening, such as the deportation of migrants once confirmed to have TB.

“[ACF] has two sides: If it is well designed, it can increase your case detection (...), reduce delays and it can reduce probably disease burden and patient cost. But if it is (...) poorly implemented, it can cause a lot of problems (...). So, it’s a double-edged sword – this is a lesson learned.” (Interviewee #11, international organisation, high-income country, Study III)

Study IV described the attitudes of the NTP managers related to ACF policy development, implementation and scale-up, including the perceived benefits and harms of ACF. Many potential benefits of ACF were highlighted, including early detection, reduced transmission, reduced future health system costs, positive social and economic consequences and improved treatment outcomes. Other potential benefits of ACF that were mentioned included better health system performance (e.g., increased access and care-seeking, increased human resource capacity and synergies), epidemiological impact (e.g., reduced TB mortality) and health educational benefits through increased knowledge and awareness.

“Improving knowledge about TB among patients and the community I think is the most important component of the programme.” (NTP manager #22, Study IV)

The potential harms of ACF that the NTP managers were asked about comprised increased health system costs, increased worry about health among households screened, increased risk of stigma and discrimination, increased health system costs, increased patient costs and an increased risk of false-positive diagnoses (Study IV). Overall, the NTP managers’ views on the potential harms of ACF were more heterogeneous compared to their views on the potential benefits. For example, more than half of the NTP managers neither agreed nor disagreed that ACF leads to increased false-positive diagnoses of TB; they emphasised that the risk of a false-positive diagnosis depended on the diagnostic test used. The NTP managers acknowledged the risk that ACF may cause increased health system costs in the short-term, but also recognised the possibility of decreasing costs in the long-term.

Studies V and VI aimed to identify the facilitators and barriers for ACF implementation in Nepal and Vietnam as described by key stakeholders. Facilitators of ACF implementation in both countries included: access to healthcare through ACF, free testing and treatment and support for TB patients. These facilitators were also inherent benefits of ACF. In Nepal, early detection of TB and economic benefits (e.g., through early diagnosis or by saving travel costs) further helped increase participation in ACF. For example, a few participants in Nepal expressed that without ACF people with TB would have kept “roaming” around in search of a diagnosis, costing them time and money, while their health status would deteriorate.

“If (the volunteer) would not have come, I would have kept roaming, would take medicines and tablets, would be cured or not. No one knew, but when (the volunteer) came he knew about my problems and did my check-up (ACF).” (Interviewee #11, person with TB, Study V)

Participants in Vietnam elaborated on the benefits of mobile chest X-ray to provide access to health care; ACF participants could avoid travelling long distances, saved money and time and received a monetary incentive for chest X-ray testing.

“In this program, I spent no money, and I was offered money for fuel and free medicines, it was in a nearby place and took little time. It’s not just me, everyone likes those things.” (Interviewee #13, person with TB, Study VI)

5.2 STAKEHOLDERS AND EVIDENCE THAT INFLUENCE ACTIVE CASE-FINDING POLICY DEVELOPMENT

Main results

- Articles described the WHO's recent emphasis on ACF as a critical antecedent of the increasing interest in ACF, especially in high-burden countries. ACF policy development processes are not well described in the literature (Study I).
- Governments, the WHO, donors and non-governmental organizations strongly influence ACF policy development (Study II).
- Managers in districts or regions are key stakeholders for ACF policy development and implementation (Study IV).
- Different types of evidence are needed for different levels of ACF policymaking (e.g. global versus local policies) (Study II).
- All NTP managers applied the WHO guidelines and the majority also used expert knowledge and personal experience for ACF policy development and implementation. International scientific evidence was mostly used when national evidence was limited (Study IV).

Study I found that ACF policy development processes were not well described in the literature. Only two articles reported facilitators and/or barriers for ACF policy development: politics (162,163) and laws (163). Welshman (162) describes how, in the mid-1950s, the Ministry of Health in the United Kingdom subverted pressure from stakeholders who were in favour of compulsory ACF at ports of entry; the Ministry “argued that the problem [of TB in migrants] was a minor one” so a policy was not developed. Furthermore, laws such as the 1958 Commonwealth Migration Act were described, which made screening compulsory, and thus influenced ACF policy development in the United Kingdom (163).

Study II aimed to explore the views of experts on the factors influencing ACF policy development. According to the experts, many different stakeholders influence ACF policy development, specifically governments, non-governmental organisations and donors. For example, TB REACH was said to have “*brought this concept of ACF to the country*” (Interviewee #2, international organisation, low-income country, Study II), while the Global Fund “*hold[s] every power to change things and not to change things*” regarding ACF policy development (Interviewee #7, non-governmental organisation, low-income country, Study II). Likewise, experts pointed out that the donors’ influence was linked to the WHO’s influence, as donors request countries to adopt the WHO guidelines to be eligible for funding.

The 2013 WHO guidelines on systematic screening were perceived positively by many experts, e.g., as a reference document when planning ACF activities as well as to put ACF on the agenda (Study II). Negative perceptions included the guidelines being vague, lacking information about the “how-to” of ACF and being unduly negative in terms of mentioning the risk of

increasing false-positive diagnoses through ACF. One interview pointed out that in a middle-income country *“you’ve got really serious domestic universities providing the formal policy evidence. (...) They are really driving their own decisions. WHO is really not consulted very much, if at all.”* (Interviewee #15, funding organisation, high-income country Study II). Some participants lamented that the WHO can be paralysed by the need to use the strongest evidence available and suggested that the organisation should consider more programmatic, less scientifically rigorous data. In addition, participants pointed out that the WHO recommendations should be based on what *should* be done, not on what *can* be done. For example, a country (not the WHO) has to be the one to decide about the ability to pay for the use of Xpert® MTB/RIF.

Experts in Study II emphasised the need to generate different types of evidence to inform ACF policy development (from effectiveness and health economic evaluations to implementation and operational research). An interviewee pointed out the importance of distinguishing clearly where the decisions are being made; be it at the community, district or national level.

“I think this is very important, i.e., what types of evidence you would need to make decisions at various levels (...). What evidence is enough evidence at what level to take the decision.” (Interviewee #7, non-governmental organisation, low-income country, Study II).

The NTP managers described key stakeholders and types of evidence that had influenced ACF policy development; key stakeholders included international organisations, policymakers in the national government and managers in districts or regions. Furthermore, the NTP managers described the need for people with TB to be at the centre of the discussion when developing ACF policies, while they would seldom directly influence policy development processes.

“What we are trying to do is providing them a service they haven't demanded or didn't know they will get, what we need to think about is their expectation, their fear, and take those onboard when we design the policy.” (NTP manager #13, Study IV).

In terms of the evidence use in ACF policy development and implementation, all NTP managers used the WHO guidelines. They described using them as a reference document, but also underscored the need for contextualisation. The use of expert knowledge and personal experience in ACF policy development and implementation ranked second and third respectively. International scientific evidence was only used when local data and evidence were limited and to learn from other countries experiences or when in doubt about the WHO guidelines. National scientific evidence was especially important for implementation.

Study IV also showed that written ACF policies exist in 91% (n=21/23) of the countries, typically as part of an NSP. In line with that, the majority of the NTP managers (87%, n=20/23) said that ACF contributes to the achievement of the goals outlined in their NSP. The document review supported this and showed that 86% (n=19/22) of the NSPs stated aims directly related to ACF. Yet, only six NSPs (27%) outlined concrete targets for the number of people screened and three NSPs (14%) specified targets for the number of people tested.

5.3 FACILITATORS, BARRIERS AND THE “HOW-TO” OF ACTIVE CASE-FINDING IMPLEMENTATION

Main results

- Facilitators and barriers for ACF implementation are well described in the literature; the scoping review identified 43 studies on the topic, describing mostly factors at the levels of health systems, communities and individuals (Study I).
- Available systems, processes and experience within a given health system facilitate ACF implementation, e.g., from other screening programmes (Study II).
- ACF implementation is influenced by “power plays” between different stakeholders, especially government actors and donors (Study II).
- The priorities of donor organisations influence ACF implementation in high TB burden countries according to 86% of the NPT managers (Study IV).
- ACF implementation is influenced by individual-level factors, such as willingness to participate in ACF, trust and knowledge and awareness about TB (Study IV).
- Many similar facilitators, barriers and “how-to” strategies for ACF implementation were identified in Nepal and Vietnam, but there were also nuances. For instance, individual level factors such as poverty and community support were important factors in Nepal, while commitment and support from various stakeholders were highlighted to be key in Vietnam (Studies V and VI).
- The main themes identified in both Nepal and Vietnam revolved around how people could “make or break” ACF implementation, but also how projects could provide a conducive organisational and social context for implementing ACF (Studies V and VI).

Study I found that ACF implementation processes are widely researched. In total 43, articles reported barriers and/or facilitators for ACF implementation. Most articles mentioned factors at the level of the health system, as well as the individual and community level. Regarding the health system, articles mentioned: availability of financial resources, existing systems and structures, availability of diagnostic tests, staff experience and motivation, collaboration between different actors and implementation of a person-centred approach. In terms of the individual and community level, articles brought up themes such as: stigma and discrimination, individual characteristics and socio-cultural factors and knowledge and awareness.

As part of Study II, experts elaborated on available systems, processes and experience within a given health system, donor and government stakeholders, as well as the motivation and incentives for health workers as major factors influencing ACF implementation. First, existing systems, processes and experience were said to be central because *“if you start from scratch, it [ACF] is much more difficult than if there are already things to which you can link”* (Interviewee #17, international organisation, high-income country, Study II). For instance,

ACF implementation could build upon experience from existing screening programmes (e.g., cervical cancer screening) or activities for vulnerable populations (e.g., needle exchange programmes). Second, ACF implementation was said to depend on “*power plays plus push*” between stakeholders. For example, in a country with no written ACF policy, ACF was still being implemented because the NTP manager was respected and able to push for it (Interviewee #29, international organisation, lower middle-income country, Study II). Third, the motivation of the implementers was described as a significant enabler for ACF implementation. For example, the implementers could be strongly motivated by their desire to help people, by understanding the benefit of ACF for communities, by receiving feedback on the outcomes of their work or by feeling a sense of ownership of the ACF process. Financial and non-financial incentives (e.g., salaries, transportation allowances, provision of motorbikes or mobile airtime) were said to have a significant role in motivating the implementers, while incentives should be in line with what a country could adopt later, they are often difficult or impossible for governments to sustain, an interviewee said.

As part of Study IV, the NTP managers rated how much ACF implementation was influenced by the country and health system contexts, donors’ priorities, and factors at the level of the individual. Country-level factors, such as geography, climate and culture, influenced ACF implementation to a high degree according to 45% (n=10/22) of the NTP managers. Sixty-eight percent (n=15/22) of the NTP managers said that health system factors influenced ACF implementation to a high degree, including buy-in at sub-national levels, financial and human resources. Many NSPs documented the need to expand human resources, as well as to improve their training, coordination, engagement and supervision. Priorities of donor organisations influenced ACF implementation according to 86% (n=20/22) of the NTP managers. Finally, all NTP managers stated that factors at the level of the individual would influence ACF implementation to at least some degree, e.g., in terms of trust and willingness to participate in ACF, as well as knowledge and awareness of TB.

Many similar facilitators, barriers and “how-to” strategies for ACF implementation were identified in Nepal and Vietnam (Studies V and VI). Table 2 merges some of the main results that were mentioned in both Studies V and VI. Those facilitators and barriers that were more context-specific are not included in the table. For instance, in Nepal, poverty and community support were key factors influencing ACF implementation. Meanwhile, in Vietnam, participants elaborated on the importance of commitment and support from various stakeholders for ACF implementation.

Table 2. Building on facilitators and overcoming barriers for active case-finding implementation in Nepal and Vietnam (adapted from Studies V and VI)

Level	Facilitators and barriers	Examples of how to build on facilitators and overcome barriers
Individual professional	Dedication and motivation	Implementers showed persistence and strong willingness to help others and adapted their schedules based on the availability of people with TB
	Experience and skills	Implementers used communication, persuasion and interpersonal skills, were familiar with the local context and shared experience with each other
	Having a network	Implementers used their networks and relationships (e.g., from working as teachers or social workers) to find their way around in communities and to approach people with presumed TB
Patient	Limited participation	Implementers used their experience and skills (see above) and addressed stigma, discrimination, fear and mistrust (see next row) to convince people to participate in ACF
	Stigma, discrimination and fear	Implementers contacted patients on the telephone instead of visiting them at home, invited whole communities instead of selected groups for ACF and took sputum samples privately
	Trust and mistrust	Implementers communicated clearly and truthfully, were friendly and kind and applied experience and skills (see above) to gain trust
Social context	Knowledge and awareness about TB	Implementers spread knowledge and awareness about TB among persons with presumed TB and communities; suggestions were made to further increase knowledge and awareness, e.g., in schools, via radio, television, online media, gatherings and street drama
Organisational context	Training for implementers	IMPACT TB included capacity-building for implementers; suggestions were made to provide more training on TB
	Incentives for implementers	IMPACT TB provided monetary incentives; suggestions were made to increase monetary incentives
	Collaboration and engagement	IMPACT TB and implementers collaborated with politicians, public health offices, village elders and laboratory personnel (Study V), and District TB Units, health stations, committees, local leaders and residential groups (Study VI)

ACF = active case-finding, TB = tuberculosis

The main themes identified in Studies V and VI revolved around how people “make or break” ACF implementation, but also how projects such as IMPACT TB could provide a conducive organisational and social context for implementing ACF. In terms of people influencing ACF implementation, the studies highlighted the important roles of people with (presumed) TB as well as implementers. In Nepal, a theme was that trust in the implementers was fundamental for implementing ACF (Study V). In Vietnam, themes included that the implementers capitalised on their strengths to facilitate ACF implementation, e.g., experience, skills and communication, and that the implementers were in a position to address patient-level barriers to ACF implementation, e.g., stigma, discrimination and mistrust (Study VI).

“I usually don’t believe in others’ words, but [the employee] is different. She said if I didn’t believe, she would drive me there and gave me some money to go home. [...] Then she drove me to the exam address. After finishing the exam, that’s when I began to trust her.” (Interviewee #32, patient, Study VI)

In terms of providing a conducive organisational and social context, themes from Study V in Nepal comprised: ACF addressed social determinants of TB by providing timely access to free healthcare; knowledge and awareness about TB among people with TB, communities and implementers were the “oil” in the ACF “machine”; community engagement and support had a powerful influence on ACF implementation; and improved working conditions and better collaboration with key stakeholders could further facilitate ACF. A theme from Study VI in Vietnam was: IMPACT TB provided a conducive social and organisational context for ACF implementation, however areas for improvement include communication and awareness-raising, preparation and logistics, data systems and processes and incentives.

“Support comes from all sides. There is support from the lab. We have support from volunteers also. Now volunteers are working in the field; they are doing hard work. We have supported them, and they have also supported us.” (Interviewee #3, Community Mobilizer, Study V)

5.4 ACTIVE CASE-FINDING SCALE-UP AND SUSTAINABILITY

Main results

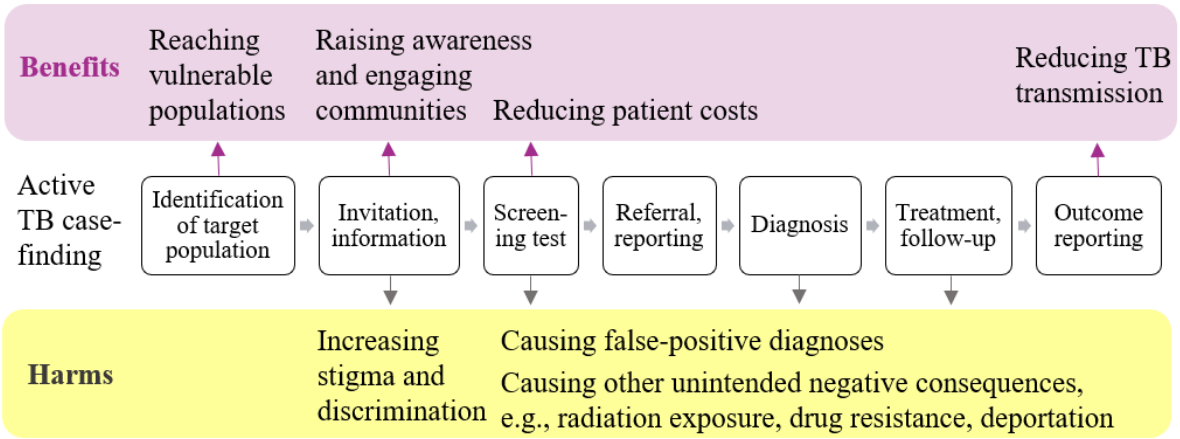
- The building blocks of ACF are well-described in the literature, so are the components of the wider health system on which ACF depends (Study I).
- ACF policy development and implementation require increased stakeholder engagement and ownership, as well as the use of diverse evidence (Study II).
- For ACF to be sustainable, governments and NTPs must take a leadership role in ACF, moving away from donor dependence (Study II).
- While NTP managers unanimously agreed on the need for ACF scale-up, most of them stated that human and financial resources were currently lacking (Study IV).
- NTPs may not have allocated funding for ACF implementation and funds might have to be sought from alternative domestic and external sources.
- Strategies for increasing financial resources included: generation of evidence to show impact, advocacy for domestic funding, diversification of funding sources, and the development and exploration of new funding mechanisms (Study IV).
- Implementation and scale-up of ACF require increasing the knowledge and awareness among people with presumed TB and communities, and providing implementers with more training on TB and increased monetary incentives (Studies V and VI).

In Study II, experts stressed the need to broaden stakeholder engagement and to increase the ownership of ACF policy development and implementation by involving not only governmental decision-makers but the local leaders and community members. At the same time, experts also emphasised the importance of using diverse evidence to inform ACF policy development and implementation to mitigate the “power plays” and “push” between stakeholders that might otherwise disrupt and mislead these policy processes. Ultimately, the sustainability of ACF was a cross-cutting theme; experts highlighted that the interest in and leadership for ACF through the government and the NTP are important for the sustainability of ACF. Experts also pointed out that ACF cannot be sustainable if it depends on donor funding and that it should instead be integrated in routine programming.

“It [ACF] is difficult to sustain. Most of the activities that have been done for ACF have been project-based. (...) So, the Global Fund comes and says: ‘Here is a pot of money for ACF for the next three years.’ (...) And then USAID comes (...). Or TB REACH (...). And people do it. But that’s not a sustainable way of doing this and this should be part and parcel of routine programming.” (Interviewee #35, international organisation, high-income country, Study II)

As part of Study III, we mapped the categories on the perceived benefits and harms of ACF along the screening and diagnostic pathway, dividing the categories according to perceived benefits and harms (Figure 4). We thereby captured the importance of considering the benefits and harms at different stages of ACF to reap the potential benefits and mitigate potential harms.

Figure 4. Considering benefits and harms of active case-finding throughout the screening and diagnostic pathway



This figure shows the seven-step screening and diagnostic pathway (adapted from the World Health Organization Regional Office for Europe (164)) for active tuberculosis case-finding from the identification of a target population to outcome reporting. The categories on the perceived benefits and harms of active case-finding are mapped along the pathway.

The NTP managers unanimously agreed on the need for ACF scale-up in high TB burden countries (Study IV). This was reflected in the national TB strategic plans reviewed, even though not all documents included explicit aims and targets related to ACF. At the same time, 91% (n=20/22) of the NTP managers stated that financial resources for ACF were insufficient, and 89% (n=17/19) of the NTP managers furthermore said that human resources for ACF were inadequate. When asked about strategies for increasing financial resources, the NTP managers underlined the generation of evidence to show impact, advocacy for domestic funding, diversification of funding sources, and the development and/or exploration of new funding mechanisms.

Through Studies V and VI, we elicited “how-to” strategies of ACF, which are important for ACF implementation and scale-up (Table 2). In particular, participants from both Nepal and Vietnam emphasised the need to further increase the knowledge and awareness among people with presumed TB and communities, e.g., through campaigns in schools, via radio, television, online media, gatherings and street drama; to provide the implementers with more training on TB; and to increase monetary incentives.

6 DISCUSSION

6.1 THE DOUBLE-EDGED SWORD

This thesis revealed that the perceived benefits of ACF were often linked to its aim of early detection and treatment of TB, although ACF could also be a “double-edged sword” and cause harms, if inappropriately designed and implemented (Study III). The views on the potential harms of ACF were more heterogenous compared to views on the potential benefits (Study IV). Perceived benefits of ACF facilitated ACF implementation (Studies V and VI).

Many of the perceived benefits of ACF that have been articulated in Studies III, IV, V and VI are in line with the available evidence in the field. First, the perceived benefit that ACF reaches vulnerable populations is supported by studies that show reduced delays in seeking healthcare (13,14,33,42,43) and improved TB case detection and notification (25,48). In addition, a study from Ethiopia showed that poor and rural ACF participants appreciated the opportunity of being screened and receiving the results from within their home communities (165). Second, the perceived benefits were related to reduced costs which is in line with recent studies that have confirmed that ACF reduces patient costs (43–47), which seems particularly important given that on average 49% of all people with TB face catastrophic costs when accessing TB care (7). Third, the perceived benefit of ACF in reducing TB transmission and prevalence is supported by modelling studies (166–171) and a recently published trial (53).

However, empirical evidence remains weak, especially for the perceived harms, but also for some of the perceived benefits of ACF mentioned in Studies III, IV, V and VI. The perceived harm that ACF leads to unintended negative consequences such as increased stigma and discrimination has been discussed in the literature, but it has not been demonstrated that ACF leads to such unintended negative consequences to a higher extent than does passive case-finding (42,55). Increased or decreased stigma and discrimination can generally be difficult to attribute to ACF through a single intervention. In addition, false-positive diagnoses were highlighted as a potential harm (Studies III and IV), which is in line with the evidence from modelling studies based on test accuracy data and prevalence surveys (1), while little is known about the actual proportion of false positive yield from ACF. Finally, participants noted that ACF can help raise awareness of TB among individuals and engage communities (Studies III, IV, V and VI), for which there is only limited evidence (172).

That said, participants described some potential benefits and harms of ACF for which there may not yet be a strong evidence base, and some of these factors may not be actual but only perceived benefits and harms. This suggests that even *potential* benefits and harms can influence decisions related to ACF. Notably, a systematic review has shown that lay people and health personnel tend to overestimate the benefits of screening for health conditions and underestimate the harms (173). Both actual and potential benefits and harms of ACF should be considered not only when planning ACF but throughout the screening and diagnostic pathway (Study III).

Considering the benefits and harms also means conducting ACF ethically. In particular, people with TB who are identified through ACF must be linked to treatment and care, which echoes Wilson and Jungner who stated that the ability to treat the condition adequately when discovered is “perhaps the most important” of all screening criteria (58). At the same time, the principle that there should be an accepted treatment for patients with recognised disease can become tricky to implement in infectious disease screening. In the case of COVID-19, screening may be justified in certain contexts to reduce transmission (174), even though no treatment may be offered to people who screen positive, and individual harm may occur through isolation and travel restrictions. Thus, although the value of the principles by Wilson and Jungner remains undisputed, their use depends on the disease screened for, and requires stakeholder engagement and debate locally.

The WHO has stressed ethical principles which can help decision-making in the context of infectious disease outbreaks (175). The principles include justice, beneficence, utility, respect for persons, liberty, reciprocity and solidarity. The WHO also emphasises that governments need sufficient authority through public health law to respond effectively to infectious diseases, while also protecting individuals’ human rights (175). For example, certain public health interventions (e.g., travel restrictions) depend on having a clear legal basis for government action, as well as a system to monitor and evaluate such measures. The ethical conduct of ACF also includes confidentiality and privacy considerations and informed consent. The necessity of informed consent has been signalled by the WHO (1,175), although informed consent does not remove responsibility for any harm caused through screening (176). The understanding and promotion of informed consent may be facilitated by training health workers in communicating the potential benefits and harms of screening (164).

Making judgements on the benefits and harms of ACF may be challenging, as they may be difficult to quantify (e.g., increased discrimination) or compare (e.g., reduced transmission versus false-positive results). Evaluating the potential benefits and harms of ACF may be even more challenging in high TB burden settings, as many low- and middle-income countries do not have established processes for the development of screening policies in place (177). Contextual considerations may help ensure that ACF is well-designed and implemented.

6.2 EVIDENCE-INFORMED ACTIVE CASE-FINDING POLICY DEVELOPMENT

This thesis demonstrated that ACF policy development processes are not well described in the literature. The WHO’s emphasis on ACF over the past decade has been portrayed as a critical antecedent of the increasing interest in ACF, especially in high TB burden countries (Study I). Governments, the WHO, donors and non-governmental organisations strongly influenced ACF policy development (Study II), as well as managers in districts or regions (Study IV). Different types of evidence were needed for different levels of ACF policymaking (e.g., global versus local policies) (Study II). All NTP managers applied the 2013 WHO guidelines and the majority also used expert knowledge and personal experience for ACF policy development and implementation. International scientific evidence was mostly used when national evidence was limited (Study IV).

The evidence base for evidence-informed ACF policy development must be strengthened and include a wide range of research, while the need for systems and processes for research production and use must not be forgotten. A variety of evidence is needed and used in developing ACF policies (Studies II and IV) and ACF-related projects themselves offer opportunities for generating evidence that can inform future practice (Study II). The NTP managers stressed the importance of local evidence to inform local policymaking, but also to advocate for increased resources for ACF (Study IV). The investment in local evidence has been stressed as important for ending TB (178). In line with that, the World Health Report on research for universal health coverage in 2013 stated that “all nations should become consumers and producers of research knowledge” (179). Still, local research infrastructure and research capacity may be limited, especially in low- and lower middle-income countries (130,180) and research capacity must be built (181). Yet, even with weak research systems and processes and an imperfect evidence base, decisions still have to be made. This has also been a dilemma during the COVID-19 pandemic where policymakers have been torn between waiting for better data and evidence and making decisions, e.g., on travel restrictions and school closure, as well as whom, when and where to screen for COVID-19. The pandemic has also shown that myriad factors influence policymaking, including politics, culture and resources, as well as stakeholders’ preferences. Transparent and systematic processes are key for evidence-informed policymaking (127), no matter if for TB or COVID-19 screening. The fact that most NTP managers in the high TB burden countries had research experience and many countries seemed to have institutionalised processes for ACF policy development in place, such as regularly convening working groups and committees (Study IV), are critical indicators that could facilitate evidence-informed policymaking (182,183).

Successful ACF policy development and implementation also necessitate stakeholder engagement (Study II). Stakeholder engagement is an inclusive process essential for achieving legitimate decisions, which are accepted by the population and conducive to effective implementation (184). At the global level, the WHO engages external experts in their guideline development process. One could argue that the WHO has been more inclusive in the 2020 update of the guidelines on systematic screening compared to the 2013 guidelines, especially in terms of including countries at different income levels. In 2013, the Guideline Development Group consisted of 21 members, 62% of whom were women and 38% were men, while 71% of the group were from high-income countries, 19% from upper middle-income countries and 10% from lower middle-income countries (1). In 2020, the Guideline Development Group consisted of 20 members, 50% of whom were women and men respectively. Forty-five percent of the group members were from high-income countries, 30% from upper middle-income countries and 25% from lower middle-income countries (185). Stakeholder engagement is also key at the national level. According to the NTP managers, the “top three” stakeholders perceived to be influencing ACF policy development at the national level were international organisations, policymakers in the national government and managers in districts or regions (Study IV). Managers in districts or regions were the only “top” stakeholder named in both ACF policy development and implementation. The involvement of these managers in ACF

policy processes may increase the ownership and relevance of policies (186), and thus increase the likelihood for implementation.

The WHO guidelines for systematic screening for active TB (1) played an important role in ACF policy development nationally. All NTP managers used the WHO guidelines, while they stressed the importance of contextualisation (Study IV). Experts highlighted the need for the guidelines to not only describe the “what” but the “how” of systematic screening (Study II). The WHO guidelines may easily be adopted but not adapted to national contexts. Consideration of the local context is particularly crucial for interpreting the conditional recommendations the guidelines entail, which is also pointed out again in the new WHO guidelines and the related operational handbook (6,38). National key stakeholders mentioned above, as well as the Global Fund and TB REACH who are involved in ACF in many high TB burden countries, can provide guidance in interpreting the guidelines. Yet, countries should guarantee that these interpretations and adaptations are based on the local epidemiology, health system capacity, resources, feasibility, effects and economic impact, etc. Considering the local context is paramount in order not to move away from the guidelines’ original intention and get distracted by donors’ targets, which may only be reached through massive ACF, as experts indicated in Study II. Ensuring continuous monitoring and evaluation is therefore essential (186).

6.3 PUTTING ACTIVE CASE-FINDING INTO PRACTICE

This thesis has also provided insight into putting ACF into practice. Study I has shown that facilitators and barriers for ACF implementation are well described in the literature, especially factors at the levels of health systems, communities and individuals (Study I). Studies V and VI add to that existing evidence base, while main themes revolved around how people could “make or break” ACF implementation, and how projects such as IMPACT TB could provide a conducive organisational and social context for implementing ACF. Experts emphasised how available systems, processes and experience within a given health system as well as “power plays” between different stakeholders influence ACF implementation (Study II). All NTP managers highlighted that ACF implementation was influenced by individual-level factors, such as a willingness to participate in ACF, trust as well as knowledge and awareness about TB, whereas 86% of them also stressed the influence of donor priorities (Study IV).

A direct comparison between Nepal (Study V) and Vietnam (Study VI) showed that, despite the contextual differences, there were many similarities with regards to the facilitators and barriers for ACF implementation but also subtle differences. In both countries, the implementers capitalised on their own strengths (e.g., motivation and skills) to address the barriers at the “patient level”, such as stigma, discrimination and mistrust. It is also crucial to consider that they are frequently vulnerable populations themselves, who are often poor and dependent on project-based salaries and/or incentives (187). Increased capacity, knowledge and empowerment of the implementers that accompany ACF implementation should be considered as a positive impact of ACF and be reinforced. Moreover, factors at the “social context level” were more context-specific and included poverty and community support in Nepal (Study V), and engagement, commitment and support among stakeholders in Vietnam

(Study VI). At the “organisational context level”, factors such as distance, weather conditions and transportation were important in Nepal (Study V), less so in Vietnam where ACF was conducted in an urban area only (Study VI). In both Nepal and Vietnam, participants appreciated and requested increased incentives and training.

The facilitators and barriers identified in Studies IV, V and VI are in line with the available literature in the field. For example, our results showed that the implementers’ experience, skills and motivation influence ACF implementation, which other studies have also described (188–192). As such, a qualitative study conducted in Uganda described the provision of patient support as a crucial facilitator for TB contact investigation (188). A study from Ethiopia emphasised that within community-based approaches for addressing TB, context-embedded strategies are needed to support, sustain and motivate implementers who play a key role in linking health systems and communities (193). In addition, many studies also pinpoint stigma and discrimination as barriers for ACF (194–196), as well as the related fear (197–200). In Vietnam (Study VI) the importance of collaboration and engagement of actors, such as District TB Units, health stations and implementers was emphasised, as has also been found in settings such as Uganda (188), Cambodia (199), Thailand and Myanmar (201). Mistrust of people with TB and their families has previously been reported as a major barrier for ACF implementation (202) and for accessing TB treatment (203) in Nepal, as demonstrated by Study V. Finally, in line with Study IV, a major barrier for ACF implementation is the lack of human and financial resources (199,202,204–206). The lack of resources is also reflected in the World TB Report 2020 (7); only six of the high TB burden countries had a national TB budget consisting of more than 80% domestic resources, while ten countries had aspirational budgets that remained 50% unfunded. Most high TB burden countries depended on international funding such as the Global Fund, covering between 10-90% of national TB budgets (7).

Studies II, V and VI also identified “how-to” strategies of ACF implementation. Such strategies included close collaboration between implementers and staff from District TB Units to overcome challenges with preparation and logistics, and the use of their networks and relationships to easily navigate the districts and to approach people with presumptive TB (Study VI). While these are fundamental concepts, concrete locally adapted steps should be conceived in detail, e.g., how to foster close collaboration and how to support implementers that may not have local networks. Studies from Nigeria (207) and India (208) are among the few studies that also elaborate on the “how-to” of ACF implementation: Shamenewadi and colleagues (208) mentioned involving local leaders, training implementers in counselling TB patients and supporting patients financially for ACF implementation. Though it is difficult to weigh facilitators and barriers against one another, Studies V and VI showed that, apart from overcoming barriers, capitalising on facilitators was decisive in implementing ACF successfully. In fact, focusing on facilitators, rather than on barriers only, may encourage individuals, communities and policymakers to be proactive rather than reactive towards the threats posed by TB (209). In addition, experts stressed the importance of community engagement to enhance the implementation of ACF (Study II). Available evidence also shows the importance of community engagement and support for ACF implementation, e.g., through

collaboration with respected community leaders (i.e., chiefs, civic leaders, village elders and counsellors) (210,211). In addition, familiarity with the community (204) and community buy-in (199) as well as community appreciation and respect through the engagement of the implementers have been described as important (212,213).

Studies I and V in particular also brought to light the importance of the social determinants of TB for ACF implementation. Study I showed that social determinants such as the educational level (48,188), employment status (189,214) and access to care (215) of the target population often act as barriers or facilitators for implementing ACF. Furthermore, Study V brought to light determinants such as social class (caste), gender, education and income, as well as living and working conditions, as influencing factors for ACF implementation. Reviews have specified a large range of determinants that influence people's vulnerability to TB, which are also likely relevant to consider when implementing ACF. These determinants include individual, household and community level factors (e.g., poverty, poor nutrition, livelihoods, gender and illness conceptualisation) (216), as well as environmental and institutional factors (e.g., migration and increasing drug resistance) (209). Importantly, many of those determinants not only mattered for people with TB, but for the implementers (Study V). While social determinants influence ACF implementation, ACF also helps address some of the social determinants (e.g., access to care). Yet, even when designing services to be more accessible, target populations may still not come forward, take the next step of referral to complete the diagnostic pathway or adhere to treatment due to socioeconomic barriers. ACF should not be designed as a short cut to reaching the poor, but in conjunction with addressing the underlying determinants. For instance, people with TB could be provided with socioeconomic and psychological support (217,218).

Knowledge of both facilitators and barriers, and how to address them is essential for planning and implementing effective ACF. Involving multiple stakeholders in developing strategies on how to utilise facilitators (e.g., providing economic benefits) and overcome barriers (e.g., addressing stigma to increase participation in ACF) could further optimise ACF implementation and scale-up. Finally, the similarity of our results compared to available evidence suggests possibilities for cross-learning, not only with regards to what the facilitators and barriers for ACF are, but in terms of strategies on how to address these factors.

6.4 SUSTAINABLE ACTIVE CASE-FINDING

This thesis demonstrated that the building blocks of ACF, as well as the components of the wider health system that ACF depends on, are multifaceted and well-described in the literature (Study I). Sustainable ACF requires the government, including the ministry of health and NTP, to take a leadership role in ACF, moving away from donor dependence (Study II). The benefits and harms of ACF must be considered throughout the screening and diagnostic pathway to reap the potential benefits and mitigate the potential harms (Study III). The NTP managers unanimously agreed on the need for ACF scale-up, while human and financial resource constraints must be overcome (Study IV). ACF requires increasing the knowledge and

awareness among people with presumed TB and communities and providing the implementers with more training on TB and increased monetary incentives (Studies V and VI).

ACF should be integrated into a given health system for it to be sustainable, and it is paramount to link to and build on existing structures (e.g., infrastructure) and processes (e.g., supportive supervision) (Study II). The need for embedding ACF into health systems has been previously described, e.g., using available systems for outreach and health promotion (33), laboratory networks (205), free-of-charge services (219) and previous implementation experience (220). The integration of implementers into the health system has also been emphasised (204,221). Collaboration between various actors has been described as key for sustainable ACF implementation, e.g., between public health practitioners and clinicians (222), district TB teams and government health staff (223), health care staff and implementers (199,204), HIV and TB sectors (30), with laboratory staff (204) and with community organisations (30,224). The fact that experts highlighted the need for health system integration, which seems to be relevant for any health intervention, may indicate that such integration might not always occur in ACF. “Integration” may describe a variety of organisational arrangements across different settings (225), while in many low-income countries, interventions often operate through a complex patchwork of arrangements, rather than through stand-alone or integrated approaches (226).

In Study III, NTP managers mentioned strategies to overcome resource constraints for ACF, which appear necessary to implement and scale up ACF. Strategies included the diversification of funding sources and the generation of local evidence to inform the resource allocation for ACF. In terms of diversified funding, Study III showed that some countries already have a diverse funding base, including the government, national health insurances, the private sector, etc. Even out-of-pocket payments were explained as a funding source for ACF implementation, while ACF should rather be seen as a strategy to decrease patient cost (204,205,219). Adding to the strategies that the NTP managers described, ACF could be anchored more strongly in the countries’ NSPs, i.e., as part of a holistic approach where ACF complements other efforts, including passive case-finding, and with concrete targets.

Lastly, key stakeholders mentioned in Studies II and IV, such as governments, NTPs, the WHO and donors, should contribute to the long-term thinking and action related to ACF and towards ending TB. Only a mix of appropriate evidence, key stakeholders, processes and structures can be a solution for evidence-informed ACF policy development and implementation (138).

6.5 METHODOLOGICAL CONSIDERATIONS

The overall aim of this thesis was to contribute to the knowledge base on ACF policy development and implementation, with a focus on high TB burden countries and the perspectives of different stakeholders. To reach this aim, a variety of methods were applied that require different methodological considerations, i.e., a review method (Study I), qualitative methods (Studies II, III, VI and V) and mixed methods (Study IV).

6.5.1 Review method

The scoping review (Study I) allowed us to assess the state of knowledge on antecedents, components and influencing factors for ACF policy development and implementation globally, but there were also limitations in terms of comprehensiveness and strengths of the conclusions.

First, evidence selection bias is likely present, as the scoping review did not identify all available data on the topic (227). This can partly arise from publication bias, but also from several limitations in our search. For example, the review was limited in that we only searched MEDLINE, Web of Science, the Cochrane Database of Systematic Reviews and the WHO Library for eligible studies. We did so for reasons of feasibility. Meanwhile, we acknowledge that searching additional databases, the grey literature (e.g., TB REACH reports from high TB burden countries and meeting reports from the WHO), literature in other languages than English (e.g., French and Portuguese), references of included studies, as well as contacting authors for more information may have yielded further insights.

Second, we may have gained deeper insights had two reviewers been involved in the full data extraction. However, the data extraction was planned jointly with all team members and my data extraction was verified by co-author Kerri Viney who reviewed a random selection of the data. We discussed any questions within the team and also sought advice from the Joanna Briggs Institute, which provides guidance on scoping reviews.

Third, scoping reviews do not necessitate risk of bias assessments and quality appraisals of the included studies (149), which limits the strengths of the conclusions that can be drawn. Furthermore, the variety in study designs, country contexts and definitions of ACF made synthesising the data challenging; studies could only be compared and contrasted at a low level of detail. Moreover, the reporting of ACF policy development and implementation varied in completeness across the included studies. Consequently, our data are limited by the details described in the literature, e.g., most papers described steps to implementation, but did not provide details on non-response or unsuccessful practices.

6.5.2 Qualitative methods

Data collection

The experts interviews in Studies II and III enabled us to elicit views on factors influencing ACF policy development and implementation, and the use of evidence in these processes (Study II), as well as on the perceived benefits and harms for people with TB and communities globally (Study III). The use of Focus Group Discussions may have been interesting to further explore controversial aspects of the topics, while some experts may have felt uncomfortable to express their views in a group setting. Moreover, the conduct of Focus Group Discussions would have not been feasible given that the experts were based across the globe. At the time of the study (2018), we had not considered the possibility of conducting Focus Group Discussions via Zoom, a collaborative, cloud-based videoconferencing service. However, as people around the world have become more accustomed to virtual discussions during the COVID-19

pandemic, Zoom or similar services, may offer new possibilities for research. Careful consideration would have to be given to possible security issues, privacy breaches, technical challenges and feasibility, as well as limitations to using and responding to body language (228), but these are the present realities for all of life due to the pandemic.

Key-informant interviews with implementers of ACF and people with TB identified through ACF (and local leaders in Study VI) let us identify facilitators, barriers and “how-to” strategies linked to the implementation of the IMPACT TB ACF model in four districts of Nepal (Study V) and six districts of Ho Chi Minh City, Vietnam (Study VI). As described above, Focus Group Discussions may have offered an alternative or an addition to the interviews conducted. While Focus Group Discussions could have provided opportunities for discussion and exchange, we found individual interviews to be appropriate to provide participants with a protected space to express their views and elaborate on sensitive issues where they arose. As such, the interviews enabled us to gain in-depth insights into people’s individual experiences. Data were triangulated by gathering information from multiple sites. Incorporating observations from the ACF implementation into the data collection may have offered further triangulation (229).

Sample characteristics and biases

Studies II and III included a large number and diverse range of experts who collectively had many years of experience in the field of ACF, which increased the studies’ trustworthiness, including their confirmability and transferability (230). Yet, the transferability of the findings of Studies II and III may still be limited as the sample underrepresented participants from low- and middle-income countries and women. The gender bias reflects the lack of gender parity in leadership positions in the field of global health (231). The bias in country representation may have been partly due to the Guideline Development Group involved in the 2013 WHO guidelines which informed our sampling base; 70% of the group were from high-income countries (1). Acknowledging this lack of balance in recruitment, we paid careful attention to patterns in the findings, in terms of country income level and gender and highlighted participants’ affiliations when quoting them. We did not find systematic differences in perceptions according to country classification or gender. Where differences were noted, we included these in the results.

Studies V and VI gave voice to key stakeholders with in-depth knowledge about ACF activities, as well as valuable insights for future implementation and scale-up. Moreover, both studies involved experienced data collectors who were familiar with the country contexts, the health systems, TB and ACF. Their experience helped generate high-quality data for the studies. In addition, the iterative approach in collecting the data, which included frequent reflections on design and implementation as well as extensive discussions among members of the research teams, were considered important to ensure the dependability, accuracy, breadth and depth of the data collected. The co-authors in Studies V and VI provided both “outsider” and “insider” perspectives on the IMPACT TB ACF model; some had been involved in the planning and/or implementation, while co-author Kerri Viney and I had not had any role in planning or

implementing IMPACT TB. Both perspectives strengthened the study, but the insider perspective of some co-authors may have also introduced bias.

Key considerations for both Studies V and VI are the potential for selection bias and social desirability bias. The fact that project staff selected participants might have caused participants to not convey the full extent of their experiences or thoughts, and triangulation between participants' perspectives was done to ensure high quality. The data collectors tried to mitigate social desirability bias by building rapport with the participants and by following up statements that were made by the participants with clarifying and probing questions during the interviews rather than strictly adhering to the interview guides. In Study V, we did not conduct interviews with District Program Officers, laboratory personnel, health workers in TB treatment facilities or leaders of District TB and Leprosy Units. Their perspectives could have added important information to this study. Finally, the participants' rationale for implementing/participating in ACF was not always clear, which may affect the reliability of the data.

Information power

Information power was used to guide the sample size in all qualitative studies (Studies II, III, V and VI) (150). Studies II and III were originally planned as one study, but the 39 interviews yielded so much information that we decided to present the contents in two separate papers. Each paper held adequate information power based on the respective research questions. We had initially deemed the large number of participants necessary to capture opinions from the diverse range of experts, all of whom had significant experience related to different aspects of ACF policy development and implementation. Had the resources been constrained to writing only one paper, the number of interviews should have been limited to avoid generating excess information that may have been overabundant for the scope of one study only.

We assessed that the final samples of 17 interviews in Nepal (Study V) and 39 interviews in Vietnam (Study VI) were sufficient, based on the research questions and expected variation in the data set. The difference in the two studies, and thus in the sample sizes used, was that Study VI included interviews with a variety of local leaders in addition to the interviews with implementers of ACF and people with TB identified through ACF. Moreover, Study VI included stakeholders from six instead of four districts. Given that the samples provided a lot of pertinent information and themes we judged topics to repeat near the end of the interviews, we found the samples to hold high information power.

6.5.3 Mixed methods

The use of mixed methods allowed us to better understand the NTP managers' attitudes related to ACF policy development, implementation and scale-up in the 30 high TB burden countries (Study IV). We were able to quantify and compare findings across the high TB burden countries, while also understanding the NTP managers' reasoning behind some of their survey answers.

For Study IV, we developed a new mixed methods questionnaire. Though innovative, the questionnaire had not been validated and included Likert scales with limited reliability based on Cronbach's Alpha (232). Moreover, the survey was conducted in English, which is at least partly the working language for most NTP managers, especially given that they participate in many international meetings and collaborations. Nevertheless, English was not the native language for all, which may have decreased the quality of the responses. We aimed to increase the reliability of the NTP managers' answers by implementing the survey as structured interviews. I was able to conduct some interviews in person; those were generally longer and the quality of the responses may be better compared to those interviews conducted via telephone/Skype. We shared the completed survey transcripts with the participants for validation, which helped us to further ensure data quality. Backing up the survey findings with information from the NSPs allowed us to add another dimension to the study and to illuminate some similarities and differences between perceptions, policies and implementation.

Survey questionnaires are prone to various types of biases (233). On the one hand, item social desirability may have been prevalent, i.e., in terms of the questions being written in such a way as to reflect more socially desirable attitudes (234). We attempted to minimise this type of bias by involving two independent researchers from the Evaluation Unit at Karolinska Institutet to critically assess our survey questionnaire before implementing it. On the other hand, mood state bias (234) may have occurred, i.e., the inclination of the NTP managers to view the topic in certain terms, e.g., generally positive. Mood state bias may have been further influenced by the timing of the survey interview, e.g., the NTP managers who participated in the survey while at a WHO meeting might have been in a certain state of mind and away from their day-to-day work. Moreover, it is possible that questions about the use of evidence may have been biased, as the NTP managers who participated in the survey while at a WHO meeting may have been exposed to the WHO guidelines more recently and thus valued them more in their responses. We tried to mitigate this type of bias by giving the NTP managers opportunities to reflect, take breaks and elaborate on their responses.

6.5.4 Reflexivity

In the following, I reflect on how I, as a researcher, may have influenced the studies that form part of this thesis and their findings. First and foremost, my training in global health and work experience with the Evidence-informed Policy Network Europe at the WHO Regional Office for Europe greatly informed the project's development. During the years prior to starting my PhD, I had developed a keen interest in evidence-informed policymaking. This interest influenced the health policy and systems perspective my thesis took. For example, I explored many questions on the use of evidence in ACF policy development. Importantly, the work on this thesis ingrained in me the desire not only to build bridges between evidence and policy, but between policy and implementation.

My interest in evidence-informed policymaking also sparked my motivation to actively engage in knowledge translation and dissemination activities related to my studies. As such, I have

published web articles, social media posts and video summaries, many of which are collected on Karolinska Institutet's website (<https://staff.ki.se/people/olivbi>).

In addition to sharing the research results with study participants, I observed meetings by the WHO Guideline Development Group, which convened in 2020 to examine the evidence and update the 2013 WHO guidelines on systematic screening for active TB. I have also been in regular direct contact with the WHO Global TB Department. The WHO has consequently cited Studies III and IV in the new operational handbook for systematic screening for active TB (38).

I have had a steep learning curve throughout the work on my thesis as the topics of TB and ACF were new to me and I had never been to Nepal and Vietnam before. Especially in the beginning of my PhD, I needed time to become acquainted with the topics to understand the main issues and knowledge gaps. My supervisors guided me and facilitated my learning, enabling me to select appropriate study participants and ask relevant questions. To learn more about the local contexts, I first visited BNMT in Nepal and FIT in Vietnam in February 2018. These visits were important to build relationships and trust, setting the scene for the collaboration that was to follow. I was subsequently based in Nepal and Vietnam for the data collection for Studies V and VI in 2019, as described in section 4.5. As a half-Korean German my appearance is Asian; in both countries, my local colleagues often pointed out that I was able to “blend in” and people would not recognise me as a foreigner at first sight. This may have had some positive influence in terms of not “sticking out” and distracting, e.g., when I observed the interviews in Nepal.

The work in Nepal (Study V) and Vietnam (Study VI) taught me valuable lessons about how to prepare and implement a research project in different settings, e.g., I learned how crucial it was to take time to familiarise myself with the context to be able to better analyse and interpret the data. It was also crucial for me to recognise that as a person coming from another country (especially a high-income country), there would always be limitations as to how much I could possibly understand the context. Being humble and collaborating closely with the local teams of BNMT and FIT were fundamental. This collaboration between local “insiders” and me as an “outsider” opened up different perspectives on the context and enriched the interpretations of the data.

7 CONCLUSIONS

The evidence base for ACF has been growing, especially since 2010. Yet, evidence remains scarce, particularly concerning the factors influencing ACF policy development. The WHO's emphasis on ACF has been described as a critical antecedent of the increasing interest in ACF in high TB burden countries (Study I).

Yet, experts have opposing views on ACF. They highlight the importance of stakeholder engagement and the use of different types of evidence to mitigate “power plays” that might otherwise mislead ACF policy development and implementation (Study II).

According to experts, the perceived benefits of ACF for people with TB and for communities are often linked to its inherent aim of finding and treating people with TB early, while perceived harms are often associated with inappropriate design and implementation. The potential benefits and harms must be considered throughout the screening and diagnostic pathway to avoid the possible negative effects of ACF (Study III).

Importantly, the NTP managers unanimously agree on the need for scaling up ACF in high-burden countries, which is also reflected in the national TB strategic plans. Yet, 90% of the NTP managers also state that human and financial resources are insufficient, and funds for ACF might have to be sought from alternative domestic and external sources. The managers in districts or regions are considered key stakeholders for ACF policy development, implementation and scale-up in high-burden countries (Study IV).

The participants in Nepal and Vietnam described a range of facilitators, barriers and “how-to” strategies for ACF implementation. Most factors were similar across contexts, but there were also nuances, e.g., based on the predominant social determinants of TB (Studies V and VI).

Projects such as IMPACT TB can provide a conducive social and organisational context for ACF implementation. Yet, implementation still depends on individuals; implementers determine the success of ACF implementation, as they have to be able to capitalise on their own strengths which they bring to the screening process, while also addressing patient-level barriers (Studies V and VI).

Ultimately, if done well, ACF can be an important, complementary tool to contribute towards ending TB, while more resources and evidence are needed to improve ACF policy development and implementation.

8 RECOMMENDATIONS FOR RESEARCH, POLICY AND PRACTICE

The following recommendations for research, policy and practice may inform decision-makers, practitioners, researchers and donors with the ultimate goal of improving ACF policy development and implementation.

Consider and communicate the potential benefits and harms of ACF throughout the screening and diagnostic pathway to ensure maximal benefits and mitigation or avoidance of harms.

- Contextual considerations are vital to ensure that ACF is well designed and implemented and that both the potential benefits and harm are considered throughout the screening and diagnostic pathway.*
- High quality evidence, including trials, are required not only on the potential but the actual benefits and harms of ACF for people with TB and communities.
- Research could help quantify the benefits and harms of ACF through standardised measurements, which could complement existing frameworks for balancing the benefits, harms, costs, values and preferences to support decision-makers.
- The perspectives of implementers and people with TB should be further explored to assess whether or not, and how, ACF contributes to raising awareness about TB and decreasing TB-related stigma.
- Further research, debate and analysis regarding the benefits and harms of ACF are needed to inform the contextual optimisation of the design and implementation of ACF.
- A utilitarian perspective on ACF can help decision-makers, i.e., ACF should only be considered if the design and implementation minimise harms and maximise benefits.

Strengthen stakeholder engagement and the use of diverse evidence for ACF policy development.

- Different types of evidence are needed for different levels of ACF policymaking, e.g., global, national or local decisions.
- Operational research that builds on available local data (e.g., TB notifications) may help further build the local evidence base to inform local policymaking on ACF, in line with the WHO guidance on the monitoring and evaluation for ACF.
- Research capacity building and strengthening of research infrastructure are needed in high TB burden countries to strengthen the generation of local evidence for local decisions.

- Key stakeholders should be involved in ACF policy development, including district or regional managers, who are often familiar with specific implementation challenges as well as policy processes.*
- Stakeholder engagement in ACF policy development is especially critical in contexts with weak evidence on ACF where policy development may heavily rely on stakeholders' experience, values and preferences.

Identify and address facilitators and barriers for ACF implementation at all levels.

- Research should provide a more in-depth understanding of how to capitalise on facilitators and overcome barriers for ACF implementation, especially at the “social context level”, such as community support and awareness about TB, or lack thereof.
- Implementation research and health economic evaluations of human and financial resource strategies for ACF may be useful to explore the “how-to” questions, which this thesis started to assess.
- Perspectives of people with TB should be further studied and acted upon, e.g., on how trust in the implementers and the health system is built and maintained.
- NTPs may not have allocated funding for ACF implementation and funds might have to be sought from alternative domestic and external sources.*
- Strategies for increasing financial resources include: generation of evidence to show impact, the advocacy for domestic funding, the diversification of funding sources, and the development and exploration of new funding mechanisms.
- Available systems, processes and experiences within a given health system, e.g., from other screening programmes, should be considered to facilitate ACF implementation. Meanwhile, research should help to further contextualise and integrate ACF.
- Implementers should be considered at the heart of ACF implementation, alongside people with TB, due to their key role in ACF and given that they are often vulnerable populations themselves. Adequate training and remuneration are paramount. Moreover, additional indicators for measuring the impact of ACF could include increased capacity, knowledge and empowerment of the implementers.
- For ACF implementation to be successful, action is needed to address underlying barriers, such as the social determinants of TB, e.g., by providing people with TB with socioeconomic support.
- Many facilitators, barriers and “how-to” strategies for ACF are consistent across contexts; lessons learned should therefore be shared within and between countries to inform the planning and implementation of ACF.

*These findings from Studies III and IV have been cited in the “WHO operational handbook on tuberculosis. Module 2: Screening. Systematic screening for tuberculosis disease” published on 22 March 2021 (33).

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APPENDIX 1: POPULAR SCIENCE SUMMARY IN DIFFERENT LANGUAGES

Arabic

من السياسة العالمية إلى التنفيذ المحلي: تجارب من البلدان التي تعاني من عبء مرض السل حول عملية الكشف النشط للحالات

ملخص العلوم الشعبي

داء السل (TB) هو جائحة موجودة منذ آلاف السنين ولا يزال القاتل الرائد بين الأمراض المعدية حول العالم، وأنه يؤثر بشكل خاص على الفقراء في البلدان المنخفضة والمتوسطة الدخل. وتقدر منظمة الصحة العالمية أن 10 ملايين شخص يصابون بمرض السل سنوياً، منهم حوالي 3 ملايين شخص لا يتم تشخيصهم، مما يساهم في زيادة المعاناة وانتقال المرض. يعد فحص الكشف عن السل من إحدى الطرق لتشخيص ومعالجة السل مبكراً من أجل الحصول على نتائج صحية أفضل ووقف نقل المرض للآخرين. ومع ذلك، فإن فحص الكشف عن مرض السل ليس بالمهمة المباشرة؛ فهناك العديد من الطرق للقيام به، وتختلف الآراء حول فوائده ومخاطره، وهناك عدد قليل نسبياً من الدراسات العلمية لدعمه.

ثلاثة مجالات متعلقة بفحص السل يجب فهمها بشكل أفضل لتحسين عملية اتخاذ القرار. أولاً، من المهم فهم القوى التي تؤثر على استراتيجيات فحص السل، مثلاً نتائج الدراسات العلمية وتأثير المال والسياسة وتفضيلات متخذي القرار. ثانياً، من الضروري معرفة العوامل المساعدة والعقبات التي تحول دون إجراء فحوصات الكشف عن السل، كتوافر الموارد ودرجة الوعي عن مرض السل بين الأشخاص الذين يتم فحصهم. ثالثاً، من المهم تحديد الدروس المستفادة حول كيفية استخدام هذه العناصر التمكينية والتغلب على العقبات. تتناول الدراسات في هذه الأطروحة هذه المجالات الثلاثة من خلال تقييم ما توصلت له الدراسات العلمية حول هذه الموضوعات، ومن خلال إبراز آراء الخبراء الدوليين، ومديري البرامج الوطنية لمكافحة السل في البلدان التي تعاني من عبء مرتفع من هذا الوباء، والقادة المحليين، والمنفذين لبرامج تتعلق بالسل وبالإضافة إلى المصابين بالسل.

تقدم النتائج المقدمة في هذه الأطروحة نظرة مُعمّقة لتجارب فحص السل، وتتراوح بين الاستراتيجيات العالمية إلى الممارسات المحلية. لفهم الممارسات المحلية، اتُخذت دولتي النيبال والفيتنام كدول نموذجية. على الصعيد العالمي، لوحظ نشر المزيد من الدراسات العلمية حول فحص السل في السنوات الأخيرة، ولكن لا تزال هناك نقص في المعرفة فيما يتعلق بالعوامل التمكينية والعقبات لإجراء فحص الكشف عن السل، وخاصة فيما يتعلق بالقوى التي تؤثر على استراتيجيات فحص السل. بناءً على ما وصفه الخبراء الدوليون، فإن لفحص السل جوانب إيجابية وسلبية، اعتماداً على كيفية تصميمه وتطبيقه. وحذر الخبراء من أن استراتيجيات الكشف عن مرض السل يمكن أن تتأثر من خلال "لعبة القوى" المُضَلَّلة، على سبيل المثال بين الحكومات والجهات المانحة والمنظمات غير الحكومية. على عكس بعض الخبراء الدوليين، دعم مديرو البرنامج الوطنية لمكافحة السل فحص مرض السل، لكن أجمعوا على مشكلة نقص المال والموظفين للقيام به. وذكروا أن مديري الرعاية الصحية المحليين يُعتبرون أشخاصاً مهمين للغاية لتطوير استراتيجيات فحص السل ووضع هذه الاستراتيجيات حيز التنفيذ. في النيبال والفيتنام، وصف القادة المحليون والمنفذون للبرامج والأشخاص المصابون بالسل الدور الأساسي للأفراد في ممارسات فحص

السلّ، ووصفوا أيضًا كيف يمكن للمشاريع المتعلقة بالفحص أن تساعد في جعل فحص السل حقيقة، على سبيل المثال من خلال توفير التمويل والموظفين والمعدات والتدريب اللازمين.

بناءً على هذه النتائج، يمكن تحسين استراتيجيات وممارسات فحص السل من خلال الإجراءات التالية: إشراك الأشخاص الرئيسيين كمديري الرعاية الصحية المحليين المعمّقين بمعرفة الاستراتيجيات والممارسات المطلوبة، واستخدام أنواع مختلفة من الدراسات العلمية كبوصلة الإرشاد والتوجيه. علاوة على ذلك، يجب وضع الجوانب الإيجابية والسلبية لفحص السل في عين الاعتبار من البداية إلى النهاية لتقليل الآثار السلبية أو تجنبها بين الأشخاص الذين يتم فحصهم وكذلك في المجتمعات والأنظمة الصحية. علاوة على ذلك، يجب زيادة التمويل وتأمين العدد الكافي من الموظفين في البلدان التي تعاني من ارتفاع عبء السل للاستفادة الفعلية من الفحص. أخيرًا، يجب فهم العوامل التي تُمكن أو تُعيق فحص السل، بالإضافة إلى الاستراتيجيات "التطبيقية" لمساعدة صانعي القرار والممارسين والباحثين والمانحين على اتخاذ قرارات أفضل - ليس بشأن ما إذا كان يجب القيام بالفحوصات أم لا، ولكن حول "متى وكيف" يجب تطبيق فحص مرض السل خارج المرافق الصحية.

إذا تم إجراء فحص السل بشكل جيّد، يمكن أن يكون فحص السل خارج المرافق الصحية أداة مهمة للكشف عن المزيد من المصابين بالسل مبكرًا والمساهمة في إنهاء هذا المرض. ولكن بالوقت نفسه، هناك حاجة إلى مزيد من التمويل والموظفين والدراسات العلمية لتحسين عملية اتخاذ القرارات والممارسات المتعلقة بفحص السل.

全球政策到地方实施：来自结核病高负担国家主动筛查的经验

科普综述

结核病作为一种古老的传染病危害人类已有几千年的历史，目前仍然是世界上最主要的致死传染病之一，尤其是中低收入国家的贫困人口。据世界卫生组织估计，每年约有1000万人感染结核病，其中约300万人从未确诊，这导致了受病人群的增加和疾病的传播。在医疗机构外进行结核病筛查，也被称为结核病主动病例筛查，是帮助人们尽早获得结核病治疗的一种方法，以便获得更好的临床预后，并防止将疾病传染给他人。然而，结核病筛查并不是一项直截了当的任务；有多种方法可以做到这一点，人们对其实用性和风险有不同的看法，而且支持它的科学研究相对较少，例如揭示结核病筛查的优势的研究。

为改进结核病筛查决策和实践，我们必须更好地了解以下三个方面的内容。第一，关键是要了解影响结核病筛查策略的因素，例如科学研究的结果、资金、政治因素和决策者的偏好。第二，重点了解结核病筛查的促成因素和障碍，例如资源的可获得性和筛查人群对结核病的认知或认识盲区。第三，深刻学习和应用克服以上障碍的经验教训也十分重要。该博士论文通过分析相关主题的科学研究以及揭示国际结核病专家、结核病高负担国家结核病规划管理者、地方领导人、筛查实施者和结核病患者所提出的观点，来深入探讨这三方面内容。

该博士论文提供了从全球战略到地方实践相关的结核病筛查经验及见解。该论文以尼泊尔和越南作为研究对象，深入研究了地方结核病筛查实践。近年来在全球范围内有越来越多关于结核病筛查的文献报道，但在结核病筛查的促成因素和障碍方面，尤其在如何形成结核病筛查策略方面，仍然存在重要的知识空白。根据国际专家的描述，结核病筛查既有积极的一面，也有消极的一面，取决于筛查方案的设计和实施方式。专家们警告说，结核病筛查策略可由误导性的“权力游戏”促成，如政府、捐助者和非政府组织之间的权力游戏。与一些国际专家不同的是，当地国家结核病项目管理人员支持结核病筛查，但均表示缺乏相关资金和人力资源。他们指出，地方卫生保健管理人员在制定结核病筛查策略和实施策略方面至关重要。在尼泊尔和越南，当地领导人、实施者和结核病患者描述了个人积极参与是促成结核病筛查的关键，同时他们也描述了例如如何通过提供资金、人员、设备和培训何促成结核病筛查成为现实。

基于以上研究结果，以下方案可改进结核病筛查策略和实施方法。包括让关键人员及了解策略和实施方法的当地卫生保健管理人员参与，并以多种科学研究为指导。此外，关注结核病筛查的积极面和消极面，以降低或避免对被筛查人员以及社区和卫生系统的负面影响。此外，在结核病负担沉重的国家应增加资金和人力资源，以便做到真正有意义的筛查。最后，了解哪些因素促进或阻碍结核病筛查，以及制订“如何做”的策略，以帮助决策者、从业者、研究人员和捐赠者做出更好的决策——其决策关键不在与是否进行结核病筛查，而是何时以及如何可在医疗机构外进行结核病筛查。

有效的结核病院外筛查可促成结核病患者的早期发现并成为终结结核病的关键措施。同时，改进结核病筛查决策和实践需要注入更多的资金、人员及科研。

Politique globale à la mise en œuvre locale: Expériences du dépistage actif de la tuberculose dans des pays où la tuberculose est endémique

Resume vulgarisé des résultats

La tuberculose est responsable d'une pandémie qui sévit depuis des millénaires et reste la plus grande responsable de mortalité infectieuse, tout spécialement dans les pays à revenu faible ou intermédiaire. L'Organisation Mondiale de la Santé estime que dix millions de personnes tombent malades de la tuberculose chaque année, dont environ trois millions ne seront jamais diagnostiquées contribuant ainsi à la souffrance et à sa transmission. Le dépistage de la tuberculose en dehors des établissements de soins, aussi connu sous le nom de dépistage actif, est une des manières d'aider les populations à accéder plus tôt à un traitement afin d'améliorer le résultat clinique des patients mais aussi d'arrêter la transmission de la maladie. Cependant, le dépistage de la tuberculose n'est pas une tâche évidente: en plus des différentes façons de l'effectuer, il y a différentes opinions concernant son utilité ainsi que sur les risques associés. De plus, le nombre d'études scientifiques sur lesquelles s'appuyer est relativement faible, notamment en ce qui concerne les bénéfices du dépistage.

Trois sujets doivent être mieux compris afin d'améliorer le processus de décision et la pratique du dépistage de la tuberculose. Premièrement, il est important de comprendre les forces déterminant les stratégies de dépistage, tel que les études scientifiques, les moyens financiers, les politiques ainsi que les préférences des preneurs de décisions. Deuxièmement, il est crucial de comprendre quels sont les catalyseurs et les obstacles au dépistage comme par exemple la disponibilité des ressources, et la sensibilisation à la tuberculose parmi les populations dépistées. Troisièmement, il est fondamental d'identifier les enseignements tirés sur la façon d'utiliser ces catalyseurs, mais aussi de surmonter ces obstacles. Les études incluses dans cette thèse adressent ces trois sujets en évaluant ce que concluent les études scientifiques sur ces sujets, et en apportant les points de vue d'experts internationaux, de responsables de programmes nationaux contre la tuberculose dans des pays à forte prévalence, ainsi que ceux de dirigeants locaux, d'exécutants en charge du dépistage, et de personnes vivant avec la tuberculose.

Les résultats présentés dans cette thèse fournissent des indications sur les expériences relatives au dépistage de la tuberculose, des stratégies internationales aux pratiques locales. Pour comprendre les pratiques locales, le Népal et le Viêtnam furent utilisés comme pays exemples. À l'échelle mondiale, nous avons trouvé que de plus en plus d'études scientifiques sur le dépistage ont été publiées ces dernières années mais qu'il existe encore des lacunes en termes de connaissances des catalyseurs et des obstacles liés à l'exécution d'un dépistage à la tuberculose, et en particulier en ce qui concerne les forces déterminant les stratégies de dépistage. Fondé sur la description d'experts internationaux, le dépistage possède à la fois des côtés positifs et négatifs en fonction de comment il est conçu et mis en œuvre. Les experts sont

inquiets que les stratégies de dépistage puissent être induites en erreur par des « enjeux de pouvoir » entre les gouvernements, les donateurs et les organisations non-gouvernementales. Au contraire, les responsables de programmes nationaux contre la tuberculose furent favorables au dépistage, même si presque tous évoquèrent aussi le manque de moyens et de personnels afin de le mettre en œuvre. Ils mentionnèrent que les responsables de la santé locaux sont particulièrement importants dans le développement mais aussi dans la mise en œuvre des stratégies de dépistage. Au Népal et au Viêt Nam, les dirigeants locaux, exécutants et personnes vivant avec la tuberculose décrivirent comment les individus pouvaient « faire ou briser » les pratiques de dépistage, mais ils décrivirent aussi comment les projets de dépistage pourraient faire du dépistage une réalité, par exemple grâce à un apport en argent, en main d'œuvre, en équipement ou en formation.

Grace à ces résultats, les stratégies et pratiques de dépistage de la tuberculose peuvent être améliorées en prenant les mesures suivantes: inclure les personnes clés notamment les responsables de santé locaux qui comprennent les stratégies et les pratiques, mais aussi utiliser différents types d'études scientifiques en tant que guide. De plus, il faudrait considérer les aspects positifs et négatifs du dépistage, du début à la fin, ou du moins éviter les effets négatifs pour les populations dépistées, ainsi que pour les communautés et les systèmes de santé. En outre, il faudrait augmenter les moyens en effectifs et financiers dans les pays avec une charge élevée due à la tuberculose pour que des dépistages pertinents puissent être vraiment mis en place. Enfin, il faudrait comprendre quels sont les catalyseurs, les obstacles ainsi que les stratégies de « comment faire », afin d'aider les preneurs de décisions, les cliniciens, les chercheurs, et les donateurs afin de prendre de meilleures décisions; pas seulement concernant la décision de faire un dépistage ou non, mais plutôt de décider quand et comment effectuer un dépistage en dehors des établissements de soins.

Si effectué correctement, le dépistage de la tuberculose en dehors des établissements de soins peut être un outil important afin de détecter tôt plus de personnes avec la tuberculose et ainsi contribuer à la fin de cette maladie. Dans le même temps, plus d'argent, de personnel, et d'études scientifiques sont nécessaires pour améliorer le processus de décision et la pratique du dépistage.

Von globaler Politik zur lokalen Umsetzung: Erfahrungen mit Tuberkulose-Screening außerhalb von Gesundheitseinrichtungen in Ländern mit hoher Tuberkulose-Belastung

Populärwissenschaftliche Zusammenfassung

Tuberkulose (TB) ist eine seit Jahrtausenden bestehende Pandemie. Sie ist die Infektionskrankheit, die weltweit die meisten Menschen tötet. Betroffen sind vor allem arme Menschen in Ländern mit niedrigem und mittlerem Einkommen. Die Weltgesundheitsorganisation schätzt, dass jedes Jahr circa 10 Millionen Menschen an Tuberkulose erkranken. Davon werden etwa 3 Millionen nie diagnostiziert. TB-Screening, das außerhalb von Gesundheitseinrichtungen durchgeführt wird, kann Menschen dabei unterstützen, eine frühzeitige Diagnose zu bekommen und geheilt zu werden. Dadurch kann die Übertragung der Krankheit auf andere Menschen vermieden werden. TB-Screening ist jedoch kompliziert; es gibt viele verschiedene Arten und Weisen des TB-Screenings, Meinungen scheiden sich über Kosten und Nutzen, und es gibt relativ wenige wissenschaftliche Studien, die die Vorteile von TB-Screening belegen.

Drei Bereiche müssen verstanden werden, um die Entscheidungsfindung und Durchführung von TB-Screening zu verbessern. Erstens: Was beeinflusst die Strategieentwicklung für TB-Screening (z.B. Ergebnisse wissenschaftlicher Studien, Geld, Politik und Präferenzen der Entscheidungsträger)? Zweitens: Welche Faktoren ermöglichen oder erschweren das TB-Screening (z.B. Verfügbarkeit von Ressourcen und Wissen über die Krankheit)? Drittens: Welche Lehren können aus erfolgreicher Umsetzung von TB-Screening gezogen werden? Die in der Doktorarbeit enthaltenen Studien befassen sich mit diesen drei Bereichen. Sie bewerten die Literatur zum Thema, sowie die Ansichten internationaler Expert*innen, Manager*innen nationaler TB-Programme in Ländern mit hoher TB-Inzidenz, sowie lokaler Führungskräfte, Gesundheitspersonal und TB-Patient*innen.

Die Ergebnisse dieser Arbeit bieten Einblicke in Erfahrungen mit TB-Screening, von globaler Politik zur lokalen Umsetzung. Für Letzteres dienten Nepal und Vietnam als Beispiele. In den letzten Jahren wurde vermehrt wissenschaftliche Literatur zum Thema veröffentlicht. Dennoch gibt es immer noch bedeutende Wissenslücken in Bezug auf Faktoren, die das TB-Screening beeinflussen, insbesondere die damit zusammenhängende Strategieentwicklung. Expert*innen beschrieben sowohl positive als auch negative Aspekte des TB-Screenings, je nach Konzipierung und Umsetzung. Expert*innen warnten, dass TB-Screening-Strategien durch irreführende „Machtspiele“ geprägt sein könnten, beispielsweise zwischen Regierungen, Gebern und Nichtregierungsorganisationen. Im Gegensatz zu einigen internationalen Expert*innen unterstützten die Manager*innen nationaler TB-Programme das TB-Screening. Jedoch sagten fast alle Manager*innen auch, dass Geld und Personal dafür fehlten und betonten

die Bedeutung lokaler Gesundheitsmanager*innen, sowohl für die Entwicklung als auch die Umsetzung von TB-Screening-Strategien. In Nepal und Vietnam beschrieben TB-Patient*innen, Gesundheitspersonal und lokale Führungskräfte, dass die Durchführung von TB-Screening mit Einzelpersonen steht oder fällt. Sie beschrieben auch, wie Screening-Projekte dazu beitragen können, dass TB-Screening in die Realität umgesetzt wird, z.B. durch die Bereitstellung von Geld, Personal, Ausrüstung und Fortbildungen.

Basierend auf diesen Ergebnissen kann die Strategieentwicklung und Durchführung von TB-Screening durch folgende Maßnahmen verbessert werden: 1) Einbeziehung von Schlüsselpersonen (z.B. lokale Gesundheitsmanager*innen) und Anwendung verschiedener Arten wissenschaftlicher Studien. 2) Berücksichtigung positiver und negativer Aspekte des TB-Screenings während des gesamten Screening-Prozesses, um negative Auswirkungen zu vermeiden. 3) Erhöhung von Geld und Personal in Ländern mit hoher TB-Inzidenz, damit sinnvolles Screening tatsächlich stattfinden kann. 4) Verständnis der Einflussfaktoren, sowie Umsetzungsstrategien für TB-Screening, um Entscheidungsträgern, Gesundheitspersonal, Forscher*innen und Gebern zu helfen, bessere Entscheidungen zu treffen – nicht darüber, ob, sondern wann und wie TB-Screening außerhalb von Gesundheitseinrichtungen durchgeführt werden sollte.

Bei optimaler Durchführung kann das TB-Screening außerhalb von Gesundheitseinrichtungen eine wichtige Maßnahme sein, um mehr Menschen mit TB frühzeitig zu erkennen und zur Beendigung der Krankheit beizutragen. In der Zwischenzeit werden mehr Geld, Personal und wissenschaftliche Studien benötigt, um die Entscheidungsfindung und Umsetzung von TB-Screening zu verbessern.

विश्वव्यापी नीतिदेखि स्थानीय कार्यान्वयन: क्षयरोगको उच्च भार भएका देशहरूमा सक्रिय खोजपङ्तालको अनुभव

सारांश

क्षयरोग संसारमा हजारौं वर्षदेखि रहिरहेको एक महामारी हो । यस सङ्क्रमणजन्य रोग खासगरी न्यून तथा मध्यम आय भएका गरिब मुलुकका मानिसहरूको मृत्युको मुख्य कारकहरूमध्ये अग्रस्थानमा रहेको छ । विश्व स्वास्थ्य सङ्गठनका अनुसार क्षयरोगबाट प्रतिवर्ष एक करोड मानिस सङ्क्रमित हुने अनुमान गरिएको छ । यीमध्ये करिब तीस लाख मानिसहरू निदान नपाई उपचार सेवाबाट वञ्चित हुन्छन् जसका कारण सङ्क्रमण अभै फैंलिन पुग्छ । स्वास्थ्य संस्था बाहिर समेत सक्रिय खालका खोजी कार्यक्रम भएमा चाँडै क्षयरोगका बिरामीको पहिचान भई उचित स्वास्थ्य लाभ गराउन तथा अरूमा रोग सार्नबाट जोगाउन मद्दत पुग्दछ । यद्यपि विविध उपायहरूको उपलब्धता, जनमानसमा यसको उपयोगिता र जोखिमबारे आ-आफ्नै अवधारणा तथा तुलनात्मक रूपमा यसको सङ्क्रमण रोक्न सघाउने वैज्ञानिक अध्ययनको कमीका कारण सक्रिय रूपमा बिरामी पत्ता लगाउने काम सजिलो भने छैन ।

क्षयरोगका बिरामीको खोजी तथा पहिचानका लागि नीति निर्माण र कार्यान्वयनमा सुधार ल्याउन हामीले निम्नानुसारका तीनवटा पक्षहरू बारे बुझ्न जरुरी हुन्छ । सर्वप्रथम, क्षयरोगको स्क्रिनीङका रणनीतिलाई प्रभाव पार्ने वैज्ञानिक अध्ययनका नतिजा, आर्थिक र राजनैतिक पक्ष र नीति निर्माताको प्राथमिकताबारे बुझ्नु अत्यन्तै जरुरी हुन्छ । दोस्रो, क्षयरोगको स्क्रिनीङका सहजकर्ता र अवरोधकहरू, जस्तै स्रोतको उपलब्धता, परीक्षण गरिएकाहरूमा क्षयरोगका बारेमा हुने जनचेतना वा त्यसैको अभावबारे बुझ्नु महत्त्वपूर्ण छ । तेस्रो, यी सहजकर्ताबाट कसरी फाइदा लिने र अवरोधहरू कसरी सामना गर्ने भन्ने विषयका अनुभवहरू पहिचान गरी तिनको कार्यान्वयन गर्नु आवश्यक हुन्छ । प्रस्तुत शोधपत्रमा समावेश अध्ययनहरूमार्फत् यी तीनवटै पक्षमा वैज्ञानिक अध्ययनको ठम्याइ, अन्तर्राष्ट्रिय विज्ञहरूको धारणा, क्षयरोगको बोझ धेरै भएका देशका राष्ट्रिय क्षयरोग कार्यक्रमका प्रबन्धकहरू, स्थानीय अगुवाहरू, कार्यक्रम कार्यान्वयनमा खटिएका व्यक्तिहरू र क्षयरोगका बिरामीहरूको धारणा समेटिएको छ ।

प्रस्तुत शोधपत्रमा समावेश नतिजाहरूले क्षयरोगको स्क्रिनीङमा संसारभर अपनाइएका रणनीतिहरू देखि स्थानीय स्तरमा अवलम्बन भएका अभ्यासहरूमाथी प्रकाश पारेको छन् । स्थानीय अभ्यासहरूबारे बुझ्नका लागि नमुना मुलुकका रूपमा नेपाल र भियतनाममा अध्ययन गरिएको थियो । विश्वव्यापी रूपमा क्षयरोग स्क्रिनीङका बारे थुप्रै अध्ययनहरू प्रकाशित भए तापनि पहिचानका लागि रणनीतिक आधारहरूलाई निर्धारण गर्ने सहजकर्ता र अवरोधकहरूका बारेमा अभै पनि अध्ययन अपुग भएको देखिन्छ । अन्तर्राष्ट्रिय विज्ञहरूको भनाइलाई आधार मान्ने हो भने कसरी योजना बनाइयो र कसरी कार्यान्वयन गरियो भन्ने आधारमा क्षयरोगको स्क्रिनीङका सकारात्मक र नकारात्मक दुवै पक्ष रहेका छन् । सरकार, दाताहरू र गैर सरकारी संस्थाहरू बिच हुन सक्ने “शक्ति सङ्घर्ष”का अभ्यासहरूले क्षयरोगको स्क्रिनीङ सम्बन्धी रणनीतिलाई प्रभाव पार्नसक्ने हुँदा सावधानी अपनाउन विज्ञहरूले सुझाव दिएका छन् । यद्यपि केही अन्तर्राष्ट्रिय विज्ञहरूका विपरीत राष्ट्रिय क्षयरोग कार्यक्रममा संलग्न प्रबन्धकहरूले क्षयरोगको स्क्रिनीङलाई प्राथमिकतामा राखेर कार्यान्वयनमा ल्याउन सहयोग गरेका छन् । तर अधिकांशको भनाइमा उक्त कार्यका लागि आवश्यक जनशक्ति र आर्थिक स्रोतको अभाव रहेको छ । उनीहरूका अनुसार क्षयरोगको स्क्रिनीङका लागि रणनीति तर्जुमा र तिनको कार्यान्वयनमा स्थानीय स्वास्थ्य प्रबन्धकहरूको भूमिका असाध्यै महत्त्वपूर्ण रहेको छ । नेपाल र भियतनामका स्थानीय अगुवा, नीति कार्यान्वयनमा खटिएका व्यक्ति र क्षयरोगीका बिरामीहरूले खोजीकार्य र परीक्षण सम्बन्धी अभ्यासलाई केही व्यक्तिले कसरी “राम्रो बनाउन” वा “बिगार्न” सक्छन्

भन्नेबारे चर्चा गर्नुभयो । साथै आवश्यक बजेट, मानव स्रोत, उपकरण र तालिमको व्यवस्थाबाट क्षयरोग स्क्रिनीङका परियोजनाले कसरी यस कार्यलाई वास्तविकतामा परिणत गर्न मद्दत गर्छन् भन्नेबारे उहाँहरूले आफ्ना विचारहरू व्यक्त गर्नुभयो ।

अध्ययनबाट प्राप्त नतिजाका आधारमा क्षयरोगको स्क्रिनीङ सम्बन्धी रणनीति र व्यवहारहरूमा निम्न कार्यद्वारा सुधार ल्याउन सकिन्छ - प्रमुख, महत्त्वपूर्ण व्यक्तिहरूलाई समावेश गराउने, रणनीति र व्यवहारसम्बन्धी ज्ञान भएका स्थानीय स्वास्थ्यकर्मीलाई संलग्न गराउने र विभिन्न वैज्ञानिक अध्ययनहरूलाई मार्गदर्शकका रूपमा अवलम्बन गर्ने । यसका अतिरिक्त, हालसम्म अनुभूत गरिएका सकारात्मक र नकारात्मक पक्षलाई ध्यानमा राख्दै र क्षयरोगका बिरामीको खोजीबाट व्यक्ति, समाज र स्वास्थ्य प्रणालीमा देखा परेका नकारात्मक पक्षलाई कम गर्ने वा हल गर्ने । यसका अतिरिक्त क्षयरोगको बोझ धेरै भएका देशहरूमा यस रोगको वास्तविक र प्रभावकारी खोजीकार्य गर्नका लागि आवश्यक पर्ने बजेट र कर्मचारीको वृद्धि गर्ने । अन्त्यमा यस कार्यमा सहयोग पुऱ्याउने सहजकर्ता र अवरोधकहरू चिन्ने र स्वास्थ्य संस्था बाहिर सक्रिय खोजी कार्यबाट पनि बिरामी पत्ता लगाउने काम गर्ने वा नगर्ने भन्दा पनि कहिले र कसरी गर्ने भन्नेबारे नीति निर्माता, कार्यान्वयनकर्ता, अनुसन्धानकर्ता र दातासमेतलाई निर्णयमा सहयोग हुने गरी रणनीति बनाउने ।

राम्ररी कार्यान्वयन भएमा यसले स्वास्थ्य संस्था बाहिर क्षयरोगका बिरामीको खोजी गर्ने र बिरामीको पहिचान गर्ने महत्त्वपूर्ण विधि सावित भई चाँडै थप क्षयरोगका बिरामीको पहिचान गर्न र यस रोगको अन्त्य गर्न सकिन्छ । साथै क्षयरोगको खोजीसम्बन्धी नीतिनिर्माण र कार्यान्वयनमा सुधार ल्याउनका लागि थप बजेट, कर्मचारी र वैज्ञानिक अध्ययनको आवश्यकता पर्दछ ।

Глобальная политика к реализации на местах: опыт активного выявления случаев туберкулеза в странах с высоким бременем туберкулеза

Научно-популярное резюме

Туберкулез (ТБ) — это пандемия, которая существует на протяжении тысячелетий и остается ведущим инфекционным убийцей в мире, особенно поражая бедное население в странах с низким и средним уровнем дохода. По оценкам Всемирной организации здравоохранения, ежегодно туберкулезом заболевают 10 миллионов человек, из которых около 3 миллионов никогда не диагностируются, что способствует страданиям и передаче инфекции. Скрининг на туберкулез вне медицинских учреждений, также известный как активное выявление случаев, является одним из способов помочь людям получить доступ к лечению туберкулеза на раннем этапе, чтобы улучшить состояние здоровья и остановить распространение инфекции. Тем не менее, скрининг на туберкулез не такой простой процесс, каким кажется на первый взгляд, существует много разных подходов к скринингу, мнения расходятся о его полезности и риске, также недостаточно научных исследований, подтверждающих преимущества скрининга на ТБ.

Чтобы принять верное решение и улучшить практику скрининга на ТБ необходимо лучше понять три области. Во-первых, ключевым является понимание направления усилий, которые формируют стратегии скрининга на ТБ, например: результаты научных исследований, финансовые затраты, политика и предпочтения лиц, принимающих решения. Во-вторых, очень важно знать о факторах, способствующих и препятствующих проведению скрининга на ТБ, например: наличие ресурсов и осведомленность о туберкулезе среди людей, прошедших скрининг, или их отсутствие. В-третьих, важно определить извлеченные уроки о том, как использовать эти инструменты и преодолевать препятствия. Исследования, включенные в эту диссертацию, затрагивают эти три области путем оценки научных исследований, мнений международных экспертов, руководителей национальных программ по борьбе с туберкулезом из стран с высоким бременем туберкулеза, а также местных лидеров и исполнителей и людей, живущих с туберкулезом.

Результаты, представленные в этой диссертации, дают представление об опыте проведения скрининга на ТБ, от глобальных стратегий до местных практик. Непал и Вьетнам послужили примерами стран в данной работе. В глобальном масштабе мы обнаружили, что в последние годы публикуется все больше научных исследований по скринингу на ТБ, но все еще существуют важные пробелы в знаниях, касающихся факторов, способствующих и препятствующих проведению скрининга на ТБ, и относительно направления усилий, которые формируют стратегии скрининга на ТБ.

Согласно описаниям международных экспертов, скрининг на туберкулез имеет как положительные, так и отрицательные стороны, в зависимости от того, как он разработан и применяется на практике. Эксперты предостерегают, что стратегии скрининга на ТБ могут формироваться путем введения в заблуждение «силовых игр», например, между правительствами, донорами и неправительственными организациями.

В отличие от международных экспертов, менеджеры Национальной программы по борьбе с туберкулезом поддерживали скрининг на туберкулез, но почти все они также говорили, что для этого не хватает финансовых и кадровых ресурсов. Они заявили, что местные менеджеры здравоохранения являются важными людьми как для разработки стратегий скрининга на ТБ, так и для реализации этих стратегий на практике. В Непале и Вьетнаме местные лидеры, исполнители и люди, живущие с туберкулезом, рассказали, как индивидуумы способны „укрепить либо сломать“ практику скрининга на туберкулез, но они также описали, как проекты скрининга могут помочь сделать скрининг на туберкулез реальностью, например за счет обеспечения финансирования, персонала, оборудования и обучения.

Основываясь на этих результатах, стратегии и методы скрининга на ТБ могут быть улучшены следующими действиями: привлечением людей на ключевых должностях, включая местных менеджеров здравоохранения, которые понимают как стратегию, так и практику скрининга, и использование различных типов научных исследований в качестве ориентира. Кроме того, рассматривать положительные и отрицательные аспекты скрининга на ТБ от начала до конца, чтобы снизить или избежать отрицательных последствий для людей, прошедших скрининг, а также для сообществ и систем здравоохранения. Более того, увеличить денежные средства и персонал в странах с высоким бременем туберкулеза, для проведения продуктивного скрининга.

Наконец, понять, что позволяет или мешает проведению скрининга на ТБ, а также практические стратегии, чтобы помочь лицам, принимающим решения, практикующим врачам, исследователям и донорам принимать более правильные решения - не столько о том, стоит ли, а когда и как проводить скрининг на туберкулез вне медицинских учреждений.

При правильном проведении скрининга на туберкулез вне медицинских учреждений может стать важным инструментом для раннего выявления большего числа людей с туберкулезом и способствовать прекращению болезни. Между тем, необходимы дополнительные денежные средства, персонал и научные исследования для улучшения принятия решений и практики скрининга на ТБ.

De política global a implementación local: Experiencias de monitoreo de tuberculosis en países endémicos

Resumen de divulgación científica

La tuberculosis (TB) es una pandemia que existe desde hace milenios y continúa como la principal causa de muerte por un agente infeccioso. La TB afecta especialmente a las personas de bajos recursos en países de ingreso mediano bajo. La Organización Mundial de la Salud estima que 10 millones de personas se contagian de tuberculosis cada año, de las cuales cerca de 3 millones nunca son diagnosticadas, lo que contribuye al sufrimiento de las personas y a la transmisión de la enfermedad. El monitoreo de TB fuera de los establecimientos de salud, también conocido como búsqueda activa de casos, es una forma de ayudar a las personas a acceder a tratamiento de manera temprana para tener mejores resultados de salud y dejar de transmitir la enfermedad a otras personas. Sin embargo, este proceso no es una tarea sencilla; Hay muchas formas diferentes de llevarlo a cabo y se tienen diferentes opiniones sobre su utilidad y riesgos, aunado a esto, existen relativamente pocos estudios científicos que lo respalden y que hayan mostrado beneficios de esta práctica.

Debe profundizarse el entendimiento de principalmente tres áreas para mejorar la toma de decisiones y la práctica del monitoreo de TB. Primero, es clave comprender las fuerzas políticas y sociales, que afectan a las estrategias para el proceso, como lo son: resultados de estudios científicos, factores económicos y/o políticos, así como preferencias de los gobernantes. En segundo lugar, es fundamental conocer los facilitadores y barreras para realizar el monitoreo, por ejemplo: disponibilidad de recursos y concientización sobre la enfermedad entre las personas sometidas a pruebas de detección. En tercer lugar, es importante identificar las lecciones aprendidas sobre cómo utilizar los facilitadores y superar las barreras. Los estudios incluidos en esta tesis abordan estas tres áreas de mejora, evaluando lo que dicen hallazgos científicos sobre cada uno de estos aspectos y resaltando opiniones de expertos internacionales, dirigentes de Programas Nacionales de TB de países con una alta incidencia de TB, así como líderes locales, y personas con tuberculosis.

Los resultados presentados en esta tesis brindan información sobre experiencias en el monitoreo de TB, desde estrategias globales hasta prácticas locales. Para comprender las prácticas locales, Nepal y Vietnam sirvieron como países ejemplo. A nivel mundial, descubrimos que en los últimos años se han publicado más y más estudios científicos sobre el monitoreo de TB, sin embargo, existen aún importantes lagunas de conocimiento sobre los facilitadores y obstáculos para realizarla, especialmente sobre las fuerzas políticas y sociales que dan forma a las estrategias de detección de TB. Según lo que describen expertos internacionales, el monitoreo de TB tiene aspectos positivos y negativos, según cómo se

diseño y se ponga en práctica. Los expertos advierten que las estrategias de detección podrían ser moldeadas por "juegos de poder" entre por ejemplo gobiernos, donadores y organizaciones no gubernamentales. A diferencia de algunos expertos internacionales, los dirigentes del Programa Nacional de tuberculosis apoyaron el monitoreo de TB, sin embargo, casi todos ellos también mencionan la falta de recursos humanos y económicos para llevarlo a cabo. Afirman que los administradores locales de atención médica son clave en el proceso. En Nepal y Vietnam, los líderes locales, trabajadores comunitarios y pacientes con TB describen cómo las personas pueden "determinar o arruinar" el monitoreo. También describen cómo los proyectos de monitoreo pueden ayudar a que la detección activa de la tuberculosis sea una realidad, mediante la provisión de dinero, personal, equipo y capacitación entre otros.

Con base en estos resultados, las estrategias y prácticas del monitoreo de TB pueden mejorar mediante las siguientes acciones: Involucrar a personas como los administradores de atención médica locales, quienes comprenden tanto la estrategia, como la práctica y utilizan diferentes tipos de estudios científicos como guías. Además, consideran los aspectos positivos y negativos de la detección de TB, a fin de mitigar los posibles efectos adversos para las personas examinadas, así como para las comunidades y los sistemas de salud. De igual manera mediante el aumento de apoyo económico y recursos humanos en los países con alta incidencia de tuberculosis, de modo que realmente se pueda llevar a cabo un monitoreo epidemiológico significativo. Por último, comprender qué facilita o dificulta el monitoreo de TB tuberculosis, así como las estrategias sobre cómo ayudar a los responsables de la toma de decisiones, profesionales de salud, investigadores y donadores a tomar mejores decisiones sobre cuándo y cómo llevar a cabo la detección activa de TB fuera de los establecimientos de salud.

Si es bien implementada, el monitoreo de TB fuera de los establecimientos de salud puede ser una herramienta importante para detectar a más personas con TB de forma temprana y contribuir a poner fin a la enfermedad. Mientras tanto, se necesitan más apoyo económico, mayor personal y estudios científicos para mejorar la toma de decisiones y la práctica de este método.

Global policy till lokalt genomförande: Erfarenheter från uppsökande tuberkulos-screening i länder med hög tuberkulos-börda

Populärvetenskaplig sammanfattning

Tuberkulos (TB) är en pandemi som har funnits i årtusenden och förblir världens ledande dödsorsak bland infektionssjukdomar. Tuberkulos drabbar främst fattiga människor i låg- och medelinkomstländer. Världshälsoorganisationen uppskattar att 10 miljoner människor insjuknar i tuberkulos varje år, varav cirka 3 miljoner aldrig diagnostiseras, vilket både bidrar till lidande och fortsatt smittspridning. Uppsökande TB-screening utanför sjukvården, även känd som "active case finding", är ett sätt att hjälpa människor att tidigt få tillgång till TB-behandling för att snabbt bli friska och sluta sprida sjukdomen vidare. Men TB-screening är komplicerat; det finns många olika sätt att genomföra det, folk har olika åsikter om dess nytta och risker, och det finns relativt få vetenskapliga studier som visar fördelarna med TB-screening.

Det behövs mer kunskap kring tre områden för att förbättra beslutsfattande och genomförande av TB-screening. För det första är det viktigt att få en bättre förståelse för de krafter som påverkar utformningen av strategier för TB-screening, till exempel resultat av vetenskapliga studier, pengar, politik och beslutsfattares preferenser. För det andra är det viktigt att veta mer om faktorer som underlättar och hindrar genomförandet av TB-screening, till exempel tillgång eller brist på resurser och kunskap om tuberkulos bland personer som screenas. För det tredje är det viktigt att identifiera vilka lärdomar som finns för hur man kan underlätta genomförandet och övervinna eventuella hinder. Studierna som ingår i denna avhandling analyserar dessa tre områden, dels genom en systematisk genomgång av tidigare publicerad vetenskap, dels genom intervjuer och enkäter som syftar till att bättre förstå vilka synpunkter och erfarenheter som finns bland internationella experter, chefer för nationella TB-program från länder med hög TB-börda, liksom lokala ledare, hälsoarbetare som genomför screeningen och personer med TB.

Avhandlingen bidrar med nya insikter om erfarenheter av TB-screening, från globala strategier till lokala metoder. För att förstå lokala metoder använde vi Nepal och Vietnam som exempel. Globalt fann vi att allt fler vetenskapliga studier om TB-screening har publicerats de senaste åren men att det fortfarande finns betydande kunskapsluckor gällande faktorer som underlättar och hindrar TB-screening, och i synnerhet kring de krafter som påverkar utformningen av TB-screeningsstrategier. Internationella experter beskrev att TB-screening både har positiva och negativa sidor, beroende på hur den är utformad och omsatt i praktiken. Experterna varnade för att strategier för TB-screening kan påverkas av vilseledande "maktspel", till exempel mellan regeringar, biståndsgivare och icke-statliga organisationer. Till skillnad från vissa internationella experter stödde alla nationella TB-programchefer TB-screening, men uttryckte att pengar och personal saknas för att screening ska kunna genomföras. De uppgav att lokala

vårdchefer hade en nyckelroll i att både utveckla TB-screeningstrategier och att omsätta dessa i praktiken. I Nepal och Vietnam beskrev lokala ledare, hälsoarbetare som genomför screeningen och personer med tuberkulos hur enstaka individer kunde vara avgörande för om TB-screening lyckas eller inte. De beskrev också hur lokala projekt kan hjälpa till att katalysera TB-screening, till exempel genom tillhandahållande av pengar, personal, utrustning och utbildning.

Baserat på dessa resultat identifierar avhandlingen följande åtgärder för att förbättra utvecklingsprocessen och genomförandet av lämpliga screeningstrategier: När vetenskap och beprövade erfarenheter från andra länder ska tolkas, ligga till grund för strategi och översättas i praktik är det viktigt att involvera nyckelpersoner, inklusive lokala vårdchefer som förstår både strategi och förutsättningar för genomförande. Vidare behöver man genom hela processen överväga både positiva och negativa aspekter av TB-screening för att undvika negativa effekter för personer som screenas, såväl som för samhället och hälsosystemet. Dessutom är det nödvändigt att från början vara medveten om behovet att utöka både budget och personalresurser som är dedikerade till TB-screening, så att meningsfull screening faktiskt kan äga rum. Slutligen behövs fortgående analyser av faktorer som underlättar eller hindrar TB-screening, för att hjälpa alla berörda aktörer att fatta beslut om strategier och implementeringssätt. Fokus bör inte vara på huruvida man ska screena eller inte, utan på när och hur TB-screening ska göras utanför vården.

Med rätt strategi och genomförande kan uppsökande TB-screening utanför vården vara ett viktigt verktyg för att upptäcka fler personer med TB under ett tidigt stadium och bidra till att minska smittspridning. För att möjliggöra detta behövs mer pengar, personal och vetenskapliga studier.

Vietnamese

Đưa chính sách toàn cầu vào công tác triển khai tại địa phương: Kinh nghiệm chủ động tìm kiếm ca bệnh lao tại các quốc gia chịu gánh nặng lớn do bệnh lao gây ra

Tóm tắt khoa học phổ thông

Bệnh lao (TB) là một đại dịch đã tồn tại hàng thiên niên kỷ và vẫn đang là nguyên nhân gây tử vong do lây nhiễm hàng đầu thế giới, đặc biệt ảnh hưởng đến người nghèo tại các quốc gia có thu nhập thấp và trung bình. Tổ chức Y tế Thế giới ước tính mỗi năm có 10 triệu người mắc bệnh lao, trong đó có khoảng 3 triệu người không được chẩn đoán, gây đau đớn cho người bệnh và khiến dịch bệnh lan truyền rộng hơn. Việc sàng lọc bệnh lao bên ngoài các cơ sở y tế, hay còn được gọi là tầm soát chủ động, là một cách giúp mọi người tiếp cận điều trị lao sớm để hồi phục sớm hơn cũng như ngăn chặn sự lây lan. Tuy nhiên, sàng lọc bệnh lao không phải là việc đơn thuần. Có nhiều cách để thực hiện việc này và có nhiều ý kiến khác nhau về tác dụng cũng như rủi ro của việc sàng lọc. Đồng thời, có tương đối ít các nghiên cứu khoa học để làm cơ sở tiến hành sàng lọc, chẳng hạn như các nghiên cứu về lợi ích của việc sàng lọc bệnh lao.

Có ba khía cạnh cần nghiên cứu rõ hơn để cải thiện quá trình hoạch định chiến lược và thực hiện sàng lọc bệnh lao. Đầu tiên, cần hiểu rõ những yếu tố quyết định chiến lược sàng lọc bệnh lao, ví dụ như kết quả nghiên cứu khoa học, khả năng tài chính, các yếu tố chính trị và mức độ ưu tiên của vấn đề. Thứ hai, cần biết những yếu tố thuận lợi và khó khăn đối với việc sàng lọc bệnh lao, ví dụ như tài nguyên đã có sẵn hay chưa và người được sàng lọc đã nhận thức được về bệnh lao hay chưa. Thứ ba, cần rút ra bài học kinh nghiệm về cách tận dụng những yếu tố thuận lợi và khắc phục khó khăn. Những nghiên cứu được đúc kết trong luận án này giải quyết ba vấn đề trên thông qua đánh giá nội dung nghiên cứu khoa học xoay quanh chủ đề này, đồng thời trình bày quan điểm của các chuyên gia quốc tế, lãnh đạo Chương trình Chống lao Quốc gia ở những nước có tỉ lệ mắc lao cao, cũng như cấp lãnh đạo ở địa phương, đội ngũ triển khai và người mắc lao.

Kết quả được trình bày trong luận án này cung cấp thông tin chi tiết về kinh nghiệm trong sàng lọc bệnh lao, từ các chiến lược toàn cầu cho tới phương thức thực hiện của từng quốc gia. Để hiểu về các phương thức thực hiện của từng quốc gia, Nepal và Việt nam được đưa ra làm ví dụ. Ở phạm vi toàn cầu, chúng tôi nhận thấy rằng ngày càng có nhiều nghiên cứu khoa học về sàng lọc bệnh lao được công bố trong những năm gần đây. Tuy nhiên, vẫn còn nhiều hạn chế về kiến thức liên quan đến những yếu tố thuận lợi và khó khăn đối với sàng lọc bệnh lao, đặc biệt liên quan đến những yếu tố quyết định chiến lược sàng lọc bệnh lao. Theo quan điểm của các chuyên gia quốc tế, sàng lọc bệnh lao có cả những mặt tích cực và tiêu cực, tùy thuộc vào cách thiết kế và triển khai trên thực tế. Các chuyên gia cảnh báo rằng chiến lược sàng lọc bệnh lao có thể mang tính lệch lạc do bị chi phối bởi “trò chơi quyền lực”, ví dụ như giữa các chính phủ, nhà hảo tâm và tổ chức phi chính phủ. Khác với các chuyên gia quốc tế, các cấp lãnh đạo của Chương trình Chống lao Quốc gia ủng hộ việc sàng lọc bệnh lao, nhưng hầu hết cho biết chương trình không có đủ tài chính và nhân lực để thực hiện việc này. Họ cho rằng các cấp

lãnh đạo và nhân viên ở y tế địa phương rất quan trọng đối với việc xây dựng chiến lược sàng lọc bệnh lao và triển khai những chiến lược này trên thực tế. Tại Nepal và Việt Nam, các cấp lãnh đạo địa phương, nhân viên triển khai và người mắc bệnh lao đã cho thấy cách mà cá nhân có thể “thành công vang dội hoặc thất bại thảm hại” trong thực hành sàng lọc bệnh lao, nhưng họ cũng mô tả về cách mà các dự án có thể giúp triển khai sàng lọc bệnh lao, ví dụ như thông qua cung ứng tài chính, nhân lực, thiết bị và đào tạo.

Dựa trên những kết quả này, các chiến lược và phương thức sàng lọc bệnh lao có thể được cải thiện bằng những biện pháp sau đây: Có sự tham gia của nhân lực chủ chốt, bao gồm các cấp lãnh đạo và nhân viên ở y tế địa phương – là những người hiểu biết về cả chiến lược lẫn phương thức thực hiện, đồng thời sử dụng nhiều kết quả nghiên cứu khoa học làm định hướng. Ngoài ra, cần nhắc hết mọi khía cạnh tích cực và tiêu cực của việc sàng lọc bệnh lao để giảm thiểu hoặc tránh ảnh hưởng tiêu cực đối với người được sàng lọc cũng như cộng đồng và hệ thống y tế. Bên cạnh đó, tăng cường ngân sách và nhân lực tại các quốc gia có số lượng người nhiễm bệnh lao cao để có thể thực hiện sàng lọc một cách hiệu quả. Cuối cùng, tăng cường hiểu biết về những yếu tố thuận lợi hoặc khó khăn cho việc sàng lọc bệnh lao cũng như các chiến lược thực hiện để giúp những nhà hoạch định chiến lược, bác sĩ, nhà nghiên cứu và các nhà hảo tâm đưa ra những quyết định đúng đắn hơn – không phải về việc có thực hiện hay không mà về thời điểm và cách thức thực hiện sàng lọc bệnh lao bên ngoài các cơ sở y tế.

Nếu được thực hiện tốt, việc sàng lọc bệnh lao bên ngoài các cơ sở y tế có thể là công cụ quan trọng giúp sớm phát hiện thêm người mắc bệnh lao và góp phần xóa sổ căn bệnh này. Trong thời gian đó, cần đầu tư thêm tiền bạc, nhân lực và tiến hành thêm nhiều nghiên cứu khoa học để cải thiện quá trình hoạch định chiến lược và thực hành sàng lọc bệnh lao.

APPENDIX 2: SEARCH STRATEGY FOR MEDLINE (STUDY I)

We implemented the search strategy on 24 January 2018. The search yielded 4640 results.

1 exp Tuberculosis/ or exp Mycobacterium tuberculosis/

2 (tuberculosis or tb or pulmonary consumption or consumption, pulmonary or pulmonary phthisis or tuberculoses).ti,ab.

3 1 or 2

4 exp Mass screening/ or exp Mass chest x-ray/ or exp Contact tracing/ or exp Health surveys/ or exp Cross-sectional studies/ or exp Epidemiologic studies/ or exp Systematic review/

5 (Mass chest x ray\$ or screen\$ or mass screening\$ or population screening\$ or survey\$ or screening survey\$ or household survey or health survey\$ or cross-sectional or detect\$ or active case or case detect\$ or case finding or tuberculosis case finding or active case finding or contact tracing or contact examination or contact screening or contact investigation or employment testing or intensified case finding or prevalence stud\$ or prevalen* or inciden* or algorithm or undiagnosed or checking or pre-entry or passive or TB suspect\$ or notification or notified).ti,ab.

6 4 or 5

7 (view\$ or barrier\$ or block\$ or obstacle\$ or hinder\$ or constrain\$ or facilitat\$ or enabl\$ or benefit\$ or opportun\$ or attitude\$ or opinion\$ or belief\$ or perceiv\$ or perception\$ or aware\$ or personal view\$ or motivat\$ or reason\$ or incentiv\$ or cost\$ or cost-effective\$ or cost analys\$ or cost comparison or cost-minimization or cost measure\$ or affordab\$ or resource\$ or resource allocation or resource\$ or efficiency).ti,ab.

8 exp Attitude/ or exp Motivation/ or exp Cost/ or exp Cost analysis/ or exp Resource allocation/

9 7 or 8

10 exp Policy Making/ or exp Health Plan Implementation/ or exp Health Priorities/

11 (policy mak\$ or policy develop\$ or policy analys\$ or health polic\$ or policy implement\$ or health plan implement\$ or priorit\$ or health priorit\$).ti,ab.

12 10 or 11

13 9 or 12

14 (((((((((((((((hard\$ adj2 reach) or hard\$) adj2 locate) or hard\$) adj2 find) or hard\$) adj2 treat) or difficult) adj2 locate) or Difficult) adj2 engage) or social\$ exclu\$ or social inequalit\$ or difficult\$) adj2 reach) or difficult\$) adj2 find) or difficult\$) adj2 treat).ti,ab.

15 ((geograph\$ or transport\$ or physical) and barrier\$).ti,ab.

16 ((low\$ or poor\$ or negative) and (quality adj2 life)).ti,ab.

17 ((vulnerable or disadvantaged or at risk or high risk or low socioeconomic status or neglect\$ or marginal\$ or forgotten or non-associative or unengaged or hidden or excluded or transient or inaccessible or underserved or stigma\$ or inequitable) and (people or population\$

or community\$ or neighbourhood\$1 or neighborhood\$1 or group\$ or area\$1 or demograph\$ or patient\$ or social\$)).ti,ab.

18 vulnerable populations/

19 17 or 18

20 poverty area/

21 (refuser\$1 or non-user\$1 or discriminat\$ or shame or prejud\$ or racism or racial discriminat\$).ti,ab.

22 social support/ or *social conditions/ or stigma/ or Social Isolation/ or *quality of life/ or Prejudice/ or Socioeconomic Factors/

23 (immobile or (disabled and (house bound or home bound)) or ((house or home) and bound)).ti,ab.

24 Homebound Persons/

25 23 or 24

26 ((hous\$ and (quality or damp\$ or standard\$ or afford\$ or condition\$ or dilapidat\$)) or ((emergency or temporary or inadequate or poor\$ or overcrowd\$ or over-crowd\$ or over-subscribed) and (hous\$ or accommodation or shelter\$ or hostel\$ or dwelling\$))).ti,ab.

27 housing/st

28 26 or 27

29 (rough sleep\$ or runaway\$1 or ((homeless\$ or street or Destitut\$) and (population or person\$1 or people or group\$ or individual\$1 or shelter\$ or hostel\$ or accommodation\$1))).ti,ab.

30 exp homeless persons/

31 29 or 30

32 ((drug\$ or substance) and (illegal or misus\$ or abuse or intravenous or IV or problem use\$ or illicit use\$ or addict\$ or dependen\$ or dependant or delinquency)).ti,ab.

33 *Substance-Related Disorders/ or Drug users/

34 32 or 33

35 ((alcohol\$ and (misus\$ or abuse or problem\$ use\$ or problem drink\$ or illicit use\$ or addict\$ or dependen\$ or dependant or delinquency)) or alcoholic\$1).ti,ab.

36 *Alcohol- Related Disorders/ or Alcoholics/

37 35 or 36

38 (prostitution or sex work\$ or transactional sex\$ or prostitute\$1).ti,ab.

39 rostitution/

40 38 or 39

41 (poverty or deprivation or financial hardship\$).ti,ab.

42 ((low-income or low income or low pay or low paid or poor or deprived or debt\$ or arrear\$) and (people or person\$1 or population\$1 or communit\$ or group\$ or social group\$ or neighbourhood\$1 or neighborhood\$1 or famil\$)).ti,ab.

43 poverty/

44 (low\$ and social class\$).ti,ab.

45 (traveller\$1 or gypsies or gypsy or Romany or roma).ti,ab.

46 gypsies/

47 45 or 46

48 (mental\$ and (health or ill or illness)).ti,ab.

49 *mental health/ or Mentally Ill Persons/

50 48 or 49

51 (((health care worker\$1 or health care) adj2 service provi\$) or health-care) adj2 provi\$).ti,ab.

52 (outreach adj2 worker\$1).ti,ab.

53 Community health aides/

54 52 or 53

55 (support adj2 worker\$1).ti,ab.

56 (case adj2 worker\$1).ti,ab.

57 (social adj2 worker\$1).ti,ab.

58 social care professional\$1.ti,ab.

59 ((social care adj2 service provi\$) or (social-care adj2 provi\$)).ti,ab.

60 (((language\$ or communicat\$) and (barrier\$ or understand\$ or strateg\$ or proficien\$)) or translat\$ or interpret\$ or (cultur\$ and competen\$)).ti,ab.

61 Communication Barriers/ or *Language/

62 60 or 61

63 (((immigrant\$ or migrant\$ or asylum or refugee\$ or undocumented or foreign born or born) adj overseas) or (displaced and (people or person\$1))).ti,ab.

64 (((Emigration.mp. and Immigration/) or refugees/ or Transients.mp.) and migrants/) or Emigrants.mp.) and immigrants/ [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

65 63 or 64

66 exp Diabetes Mellitus/

67 diabet\$.tw,ot.

68 (IDDM or NIDDM or MODY or T1DM or T2DM or T1D or T2D).tw,ot.

69 (non insulin\$ depend\$ or noninsulin\$ depend\$ or non insulin?depend\$ or noninsulin?depend\$).tw,ot.

70 (insulin\$ depend\$ or insulin?depend\$).tw,ot.

71 or/66-70

72 14 or 15 or 16 or 19 or 20 or 21 or 22 or 25 or 28 or 31 or 34 or 37 or 40 or 41 or 42 or 43 or 44 or 47 or 50 or 51 or 54 or 55 or 56 or 57 or 58 or 59 or 62 or 65 or 71

73 3 and 6 and 13 and 72

74 limit 73 to yr="1968 -Current"

75 animals/ not humans/

76 74 not 75

APPENDIX 3: INTERVIEW GUIDE (STUDIES II + III)

Basic information and active case-finding (ACF) policy and implementation work in your organization

1. What is your role in ACF policy development and/or implementation?
 - Since when have you been working in this role?
2. Could you briefly describe (current) ACF policy development and implementation supported by your organization?
 - What is the status of implementation and scale-up?
 - What do monitoring and evaluation efforts look like?
 - i. Which indicators are being used?
 - ii. Is there any data available/published?
 - What are the future plans for ACF in this context?

Personal view/values and preferences

3. What are the benefits of ACF in your view?
 - ... at the level of the individual?
 - ... at the community level?
 - ... at the level of the health system?
 - ... compared to other interventions for early case detection?
 - Have you/has your organization deprioritised other activities in order to prioritise resources for ACF?
 - i. If so, why do you/does your organization prioritise ACF?
 - What other activities for early case detection are you/is your organization engaging in? (e.g., improve lab/diagnostic services, train health workers in identifying people with possible tuberculosis (TB), reduce financial/access barriers, address social protection)
 - Do you think the scale-up of ACF is essential for reaching the goals outlined in the End TB Strategy?
 - i. If so, what's the most important action to achieve this scale-up?
 - ii. Should anything else instead be prioritised less?
4. What are the risks of ACF in your opinion? (e.g., harm for individual, stigma and discrimination, cost, operational risks)
 - ... at the level of the individual?
 - ... at the community level?
 - ... at the level of the health system?
 - ... compared to other interventions for early case detection?
5. What do you think about the World Health Organization (WHO) guidelines related to ACF? (e.g., on improving early TB detection, screening guideline, screening operational guide, contact investigation)
 - Have you used any of the WHO guidelines?
 - Do you think others are using them?
 - Does anything need to be improved in these guidelines?

Engagement in ACF project, policy or scale up in specific country(ies)

6. Are you engaged in an ACF project in a particular country?
 - How are you engaged?
 - In which country are you engaged?
 - Could you describe an example(s)? (e.g., setting, risk group, activities, timeline)

7. Has this ACF project developed into/influenced policy?
 - If yes, what kind of policy? (e.g., become part of National Strategic Plan, sectoral policy or law)
 - If not, why?
8. Could you describe the/a ACF policy? (e.g., setting, risk group, activities, timeline)
9. Who was/is responsible for the different parts of the ACF policy cycle (agenda setting, policy formulation, implementation and evaluation)?
 - ... in terms of human resources?
 - ... in terms of collaboration?
 - ... when it comes to technical input?
 - ... when it comes to management?
10. Who was/is funding which part of the ACF policy cycle?
11. Which factors influence(d) the ACF policy development? / Which factors influence(d) the ACF policy implementation?
 - ... thinking about the overall country context?
 - i. How did it influence the ACF policy cycle?
 - ... in terms of the health system and policy context?
 - i. How did it influence the ACF policy cycle?
 - ... when it comes to financing?
 - i. How did it influence the ACF policy cycle?
 - Which factor is most powerful in influencing these processes?
12. Which other organizations/partners influence/influenced the ACF policy development? / Which other organizations/partners influence/influenced the ACF policy implementation?
 - ... Donors (e.g., Global Fund, bilateral donors, researchers, etc.)
 - i. How did they influence the ACF policy cycle?
 - ... Funding mechanisms, specific funds, existing resources
 - i. How did they influence the ACF policy cycle?
 - ... International technical agencies (WHO, Stop TB Partnership, etc.)
 - i. How did they influence the ACF policy cycle?
 - ... Other organizations (civil society organization, non-governmental organizations, etc.)
 - i. How did they influence the ACF policy cycle?
 - Which organization/partner is most powerful in influencing these processes?
13. When it comes to the use of evidence in the ACF policy development process... / When it comes to the use of evidence in the ACF policy implementation process...
 - ... Which type of evidence was/is being used? (e.g., global, local, scientific, tacit)?
 - ... What type of outcomes did/does the evidence focus on? (e.g., case detection, reduce delays, treatment outcomes, cost-effectiveness)
 - ... In which part of the policy cycle was/is evidence used (e.g., priority-setting, policy formulation, policy implementation, policy evaluation)?
 - ... What are the opportunities in using evidence for improving ACF policy cycle?
 - ... What are the challenges in using evidence for improving the ACF policy cycle?
14. What is your most important lesson learned related to ACF?
15. What would you like to say about future ACF policy?
16. Do you have any additional comments?

APPENDIX 4: SURVEY QUESTIONNAIRE (STUDY IV)

1 Personal background

1.1 Sex

Female	Male
--------	------

1.2 Age group (years)

20-29	30-39	40-49	50-59	60-69	>70
-------	-------	-------	-------	-------	-----

1.3 Country

--

1.4 Organization

--

1.5 Job title

--

1.6 Role

Policy-maker	Researcher	Other
--------------	------------	-------

1.6.1 If you identified yourself as a policy-maker or other stakeholder, please indicate if you have training and/or extensive experience as a researcher.

Yes	No
-----	----

1.6.2 If you identified yourself as a researcher, please indicate if you have training and/or extensive experience as a policy-maker.

Yes	No
-----	----

1.7 What year did you start working in this job?

--

1.8 What year did you start working in the area of TB?

--

2 ACF policies – general view

“Systematic screening for active TB is defined as the systematic identification of people with suspected active TB, in a predetermined target group, using tests, examinations or other procedures that can be applied rapidly.”

– World Health Organization

2.1 Specify if you agree with the following statements on the benefits of ACF:

2.1.1 ACF leads to early detection, diagnosis and treatment.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.1.2 ACF leads to reduced transmission and incidence of TB.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.1.3 ACF leads to improved treatment outcomes.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.1.4 ACF leads to reduced future health system cost.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.1.5 ACF has positive social and economic consequences for the TB patient.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.2 Are there other benefits of ACF you would like to mention? Please elaborate.

--

2.3 Why did you agree/disagree with the benefits of ACF? Please elaborate.

--

2.4 How would you rank the importance of ACF among other TB interventions for early case detection? Please rank from 1-7 (1 = most important)

- ☐ Implementing ACF
- ☐ Improving knowledge about TB among patients and the community
- ☐ Reducing access barriers to health care
- ☐ Reducing stigma
- ☐ Implementing proven diagnostic tools
- ☐ Training health workers
- ☐ Other (please specify) _____

2.4.1 Please elaborate on why you ranked the TB interventions for early case detection as you did.

--

2.4.2 ACF contributes to the goals of you National Strategic Plan.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

Please elaborate:

--

2.5 Specify if you agree with the following statements about the risks of ACF:

2.5.1 ACF leads to an increased risk of false-positive diagnoses of TB.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.5.2 ACF leads to increased risk of stigma and discrimination.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.5.3 ACF leads to increased worry about health among households screened.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.5.4 ACF leads to increased patient cost.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.5.5 ACF leads to increased health system costs in the short term.

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.5.6 ACF leads to increased health system costs in the long term (over 10 years).

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
----------------	-------	----------------------------	----------	-------------------

2.6 Are there other risks of ACF you would like to mention? Please elaborate.

--

2.7 Why did you agree/disagree with the risks of ACF? Please elaborate.

--

3 ACF policy in your country

3.1 Does a written ACF policy exist in your country (either stand-alone or as part of a national strategic plan)?

Yes	No
-----	----

- If no, continue at question 4.
- If yes, continue with the next question (3.2).

3.2 Explain the ACF policy in your country by briefly answering the following questions:

3.2.1 What year was the ACF policy published?

--

3.2.2 Which risk/priority group(s) are targeted for ACF according to the policy?

--

3.2.3 What screening algorithms are used?

--

3.2.4 Has the ACF policy been evaluated/formally assessed?

Yes	No
-----	----

- If no, continue with question 4.
- If yes, continue with the next question (3.1.5).

3.2.5 Describe the impact of the ACF policy in your country.

--

4 Use of evidence

4.1 Specify how often and when in the ACF policy process different types of evidence were used to inform the ACF policy:

4.1.1 How often have **WHO guidelines** been used in the ACF policy process?

Never	Rarely	Sometimes	Often	Always
-------	--------	-----------	-------	--------

4.1.2 When in the ACF policy process have **WHO guidelines** been used? Please tick all that apply.

- ☐ Agenda-setting
- ☐ Policy formulation
- ☐ Policy implementation
- ☐ Policy evaluation

Please elaborate:

--

4.1.3 How often has **international scientific evidence** (e.g., publications in international journals) been used in the ACF policy process?

Never	Rarely	Sometimes	Often	Always
-------	--------	-----------	-------	--------

4.1.4 When in the ACF policy process has **international scientific evidence** been used? Please tick all that apply.

- ☐ Agenda-setting
- ☐ Policy formulation
- ☐ Policy implementation
- ☐ Policy evaluation

Please elaborate:

--

4.1.5 How often has **national scientific evidence** (e.g., publications in national journals) been used in the ACF policy process?

Never	Rarely	Sometimes	Often	Always
-------	--------	-----------	-------	--------

4.1.6 When in the ACF policy process has **national scientific evidence** been used? Please tick all that apply.

- ☐ Agenda-setting
- ☐ Policy formulation
- ☐ Policy implementation
- ☐ Policy evaluation

Please elaborate:

--

4.1.7 How often has **expert knowledge** been used in the ACF policy process?

Never	Rarely	Sometimes	Often	Always
-------	--------	-----------	-------	--------

4.1.8 When in the ACF policy process has **expert knowledge** been used? Please tick all that apply.

- ☐ Agenda-setting
- ☐ Policy formulation
- ☐ Policy implementation
- ☐ Policy evaluation

Please elaborate:

4.1.9 How often has **personal experience** been used in the ACF policy process?

Never	Rarely	Sometimes	Often	Always
-------	--------	-----------	-------	--------

4.1.10 When in the ACF policy process has **personal experience** been used? Please tick all that apply.

- ☐ Agenda-setting
- ☐ Policy formulation
- ☐ Policy implementation
- ☐ Policy evaluation

Please elaborate:

4.2 Are there other types of evidence that were used to inform the ACF policy? Please elaborate.

5 Policy development

5.1 Which type of stakeholders were involved in the ACF policy development process? Please tick all that apply.

- ☐ Policy-makers in national government
- ☐ Policy-makers in sub-national government
- ☐ Managers in a district/region
- ☐ Managers in a healthcare institution (e.g., hospital)
- ☐ Managers in a non-governmental organization
- ☐ International researchers
- ☐ National researchers
- ☐ Civil society groups
- ☐ Professional associations

- ☐ International organizations
- ☐ Donor agencies
- ☐ Pharmaceutical or biotechnology companies
- ☐ Citizens
- ☐ Patients
- ☐ Others (please elaborate)

**5.2 Who do you consider the most powerful stakeholder in developing the ACF policy?
Please elaborate.**

5.3 Specify how much different contextual factors influenced the development of the ACF policy:

*5.3.1 Factors at the level of the **country context** (e.g., culture or political system) influenced the development of the ACF policy.*

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

*5.3.2 Factors at the level of the **health system context** influenced the development of the ACF policy.*

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

*5.3.3 Factors at the level of **organizations or the community** influenced the development of the ACF policy.*

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

5.3.4 Factors at the level of **funders' priorities** influenced the development of the ACF policy.

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

--

5.3.5 Factors at the level of the **individual** influenced the development of the ACF policy.

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

--

5.3.6 Other factors that influenced the development of the ACF policy:

--

5.4 What do you consider the most powerful **influence** in developing the ACF policy?

--

6 Policy implementation

6.1 Our country's ACF policy is being implemented.

Yes	Partly	No
-----	--------	----

Please elaborate:

--

6.1.1 Describe implementation strategy/strategies:

--

6.2 Which type of stakeholders are involved in the ACF policy **implementation** process?
Please tick all that apply.

- ☐ Policy-makers in national government
- ☐ Policy-makers in sub-national government
- ☐ Managers in a district/region
- ☐ Managers in a healthcare institution (e.g., hospital)
- ☐ Managers in a non-governmental organization
- ☐ International researchers

- ☐ National researchers
- ☐ Civil society groups
- ☐ Professional associations
- ☐ International organizations
- ☐ Donor agencies
- ☐ Pharmaceutical or biotechnology companies
- ☐ Citizens
- ☐ Patients
- ☐ Others (please elaborate)

6.3 Who do you consider the most powerful stakeholder in implementing the ACF policy?

6.4 Specify how much different contextual factors influenced the implementation of the ACF policy:

*6.4.1 Factors at the level of the **country context** (e.g., culture or political system) influenced the implementation of the ACF policy.*

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

*6.4.2 Factors at the level of the **health system context** influenced the implementation of the ACF policy.*

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

*6.4.3 Factors at the level of **organizations or the community** influenced the implementation of the ACF policy.*

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

6.4.4 Factors at the level of **fund**ers' priorities influenced the implementation of the ACF policy.

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

--

6.4.5 Factors at the level of the **individual** influenced the implementation of the ACF policy.

Very high degree	High degree	Moderate degree	Small degree	Not at all
------------------	-------------	-----------------	--------------	------------

Please elaborate:

--

6.4.6 Other factors that influenced the implementation of the ACF policy:

--

6.5 What do you consider the most powerful influence in implementing the ACF policy?

--

7 Scale-up

7.1 In your opinion, should ACF be scaled up in your country?

Yes	No
-----	----

7.1.1 If no, describe why:

--

7.1.2 If yes, describe the needs for improved implementation and scale-up at the following levels:

7.1.2.1 At the level of the **country context** (e.g., culture or political system)

--

7.1.2.2 At the level of the **health system** context

--

7.1.2.3 At the level of **organizations or the community**

--

7.1.2.4 At the level of **funders' priorities**

--

7.1.2.5 At the level of the **individual**

--

7.1.2.6 Other factors:

--

8. Resources

8.1 Do sufficient financial resources for ACF exist in our country?

Yes	No
-----	----

8.1.1 If no, could you describe any strategies for generating financial resources?

--

8.1.2 Describe the following resources:

8.1.2.1 Total budget of the National TB Programme (in USD)

--

8.1.2.2 List sources of the National TB Program's budget (incl. the approximate proportion of the total budget)

	Funding source	Proportion of total budget (in %)
1		
2		
3		
4		
5		

8.1.2.3 Estimated proportion of the National TB Program's budget spent on ACF

--

8.1.2.4 Estimated proportion of international donor funding received spent on ACF

--

8.1.3 Does your country receive Global Fund support for TB?

Yes	No
-----	----

8.1.3.1 If yes, what estimated proportion of the Global Fund budget is for ACF?

--

8.2. Do sufficient human resources for ACF exist in your country?

Yes	No
-----	----

8.2.1 If no, could you describe any strategies for fighting human resource constraints?

--

8.2.2 Describe the existing human resources:

--

9. Monitoring and evaluation

9.1 Does a system for monitoring and evaluation of ACF exist in our country?

Yes	No
-----	----

9.1.1 If no, could you describe any plans for monitoring and evaluation?

--

9.1.2 If yes, describe the most important indicators used.

--

10. Concluding questions**10.1 How important is ACF for TB prevention and care in your country?**

Very important	Important	So-so	Slightly important	Not at all important
----------------	-----------	-------	--------------------	----------------------

10.2 Describe the most important components of successful ACF:

--

10.3 Describe how to make ACF sustainable:

--

10.4 Describe your most important lesson learned related to ACF:

--

10.5 Do you have any additional comments?

--

Thank you very much for participating in this survey.

APPENDIX 5: INTERVIEW GUIDE (STUDY V)

Interview guide for key-informant interviews (with implementers and people with TB)

1. What should be done for early diagnosis of TB?
2. Could you please describe your experience in implementing ACF/when the volunteer came to your house to test you for TB?
3. From your perspective, what are the benefits of ACF?
4. And what would you consider risks of ACF?
5. Which would you consider the single most important facilitator in implementing/participating in ACF?
 - Thinking about the overall health system, including resources, incentives, management structures, turnover/access, etc.
 - Thinking about the/your community, including your neighbors, etc.
 - Thinking about yourself and any barriers in putting ACF into practice/participating in ACF yourself
 - Were there any other major facilitators?
6. Were you able to strengthen/take advantage of facilitator x (*note: Ask about the facilitator that the interviewee considered most important.*)?
 - If yes, how?
 - If no, why not?
7. What should be done to strengthen/take advantage of facilitator x in the future (*note: Ask about the facilitator that the interviewee considered most important.*)?
 - **How** can this strategy be put in practice?
8. Which would you consider the single most important barrier in implementing/participating in ACF?
 - Thinking about the overall health system, including resources, incentives, management structures, turnover, etc.
 - Thinking about the/your community, including your neighbors, etc.
 - Thinking about yourself and any barriers in putting ACF into practice/participating in ACF yourself
 - Were there any other major barriers?
9. Were you able to overcome barrier x (*note: Ask about the barrier that the interviewee considered most important.*)?
 - If yes, how?
 - If no, why not?
10. What should be done to overcome barrier x in the future (*note: Ask about the facilitator that the interviewee considered most important.*)?
 - **How** can this strategy be put in practice?
11. What would be an important action that *others* (e.g., healthworkers, colleagues) could do better to implement ACF?/ What would be an important action that *others* (e.g., your neighbors, friends and family) could do to support you in participating in ACF?
12. What would be an important action that *you* personally can do better to implement/participate in ACF?
13. (For FCHVs: How do you prioritize ACF amongst other tasks you have?)

Do you have any additional comments?

APPENDIX 6: INTERVIEW GUIDE (STUDY VI)

Stakeholder group 1: Implementers

1. Could you please describe your experience in implementing IMPACT TB's ACF?
Thinking about IMPACT TB's ACF and the way that it was put into practice:
2. What are three things you liked most about the implementation?
 - Why?
3. What were the three biggest challenges you faced in the implementation?
 - Were you able to overcome these challenges?
 - How?
 - Have any patients ever refused to be screened when you approached them?
What were the reasons for refusal?
4. From your perspective, how could ACF be done better in the future?
5. What could *others* (e.g., other employees/volunteers) do to better implement ACF?
6. If you could do it again, what would *you* do to better implement ACF?
 - Do have experience with implementing other ACF projects?
 - If yes, what was the difference to IMPACT TB's ACF implementation?
7. Do you have any additional comments?

Stakeholder group 2: Patients

1. Could you please describe your experience of when you met the volunteer/employee who screened you for TB?
Thinking about this TB screening activity and the way it was done:
2. What are three things you liked most about the screening?
 - Could you please elaborate on why you liked these?
3. What were your three biggest challenges in participating in the screening?
 - How did you overcome these challenges?
 - Do you know of other TB patients like yourself that are supported/advised by the volunteers/employees? Do they face any challenges?
4. Have you ever heard of any patients that refused to be screened when the volunteer/employee approached them? What were the reasons for refusal?
5. How do you think the screening could be done better for other TB patients in the future?
6. Do you have any additional comments?

Stakeholder group 3: Leaders from district, national or international institutions and organizations in Vietnam

Part 1

1. Could you please describe your experience with ACF implementation?
Thinking about ACF implementation:
2. Which do you consider the three most important facilitators for ACF implementation?
 - Why?
3. Which are the three most important barriers for ACF implementation?
 - Why?

4. From your perspective, how could ACF be done better in the future?
5. What could *others* (e.g., other employees/volunteers) do to better implement ACF?
6. What could *you* do to support better implementation of ACF?

Part 2 (Only use if person has experience with ACF data.)

7. Please describe your experience in working with ACF data.
8. From your experience, which are the three most important factors influencing the quality of ACF data in Vietnam?
 - At which stage do these factors influence the data quality, i.e., data collection, data entry, data analysis or any other?
9. How could the quality of ACF data in Vietnam be improved in the future?
10. Looking at the notifications in the IMPACT TB implementation and control districts (*Show the interviewee two graphs based on FIT's trend analyses*)...
 - How do you see ACF implementation barriers and facilitators reflected in those data/trends?
11. What lessons do the data from IMPACT TB teach us about ACF implementation?
12. How could the data from IMPACT TB be useful for informing ACF policy and practice in Vietnam?
 - What other evidence on ACF implementation (e.g., from operational studies) could/does inform policy and practice about ACF in Vietnam?
13. Do you have any additional comments?

APPENDIX 7: OVERVIEW FIGURE OF THE IMPACT TB PROJECT



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