# WORKSHOP REPORT: ZERO TB VIET NAM AND IMPACT TB – WORKSHOP FOR SHARING EXPERIENCES AND IMPROVING MANAGEMENT OF TB INFECTION

## Hanoi, 21-22 November 2017


The IMPACT TB project is funded by the European Union's Horizon 2020 research and innovation programme under grant agreement No 733174. Zero TB Viet Nam is co-funded by the Stop TB Partnership and Johnson & Johnson. This workshop is co-funded by FIT and Qiagen.

**Workshop report**
**Workshop for sharing experiences and improving management of TB infection**
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## Background

Tuberculosis has proven to be one of the most intractable challenges to public health in low and middle-income countries. In Viet Nam, 125,000 new patients developed TB including 5,200 MDR-TB cases, while 13,000 people died of the disease in 2016. As Viet Nam has made steady progress in reducing TB prevalence and mortality, the national government has decreed for TB to be eliminated by 2030. Considering that an estimated 25,000 cases including ~3,000 MDR-TB patients are missed by the National TB Control Program (NTP) each year, the NTP is seeking comprehensive solutions to end TB.

There is a growing momentum in the TB community behind the idea that a comprehensive set of activities is needed to achieve global end TB targets and bring the TB epidemic into the elimination phase. This set of activities needs to focus on actively *searching*, testing and detecting all forms and cases of TB, *treating* them timely and properly, and *preventing* infected people from developing active TB. These tenets of *Search-Treat-Prevent* are the foundation of the Zero TB Viet Nam (ZTV) initiative and the IMPACT TB project in Viet Nam. The *Prevent* component of ZTV and the IMPACT project specifically addresses TB infection through screening and testing contacts of patients and high-risk groups for latent TB using tuberculin skin test (TST) and interferon gamma release assays (IGRA), then referring for treatment in the case of infection.

It is estimated that each individual with active pulmonary TB can infect up to 15 individuals each year until the patient is started on treatment and rendered non-infectious. Studies have documented an infection rate of 30-50% amongst household contacts of infectious adults. The infection rate in children under 5 has been reported as high as 72%. (Davies P. D., 1961; Starke, Jacobs, & Jereb, 1992) Of those infected with TB, 10-20% develop the disease during their lifetime. The risk for immunocompromised individuals such as PLHIV is even higher. (Bloom & Murray, 1992; Vynnycky & Fine, 2000) The rate of development of the disease in household contacts under 5 years has been reported to be between 15 to 20%. (Devadatta, et al., 1970; Schaaf, et al., 2002) In Viet Nam, the estimated rate of subclinical infection of TB is 38% and according to the HCMC Health Department, the city's rate of TB infection is estimated to be 44%. (Nguyen, 2011) Studies have also shown that to meet WHO 2050 elimination targets, treatment for TB infection is needed given the large reservoir of TB infection, which continues to fuel TB cases. Both etiological routes of TB disease will have to be addressed – prevention of transmission via treatment of active disease and treatment of TB infection – to significantly reduce the burden and move towards the elimination targets. (Dye, Glaziou, Floyd, & Raviglione, 2013)

In light of this context, on November 21-22, 2017, in Hanoi, the National Tuberculosis Programme in partnership with Friends for International TB Relief (FIT) convened a workshop on the management of TB infection in Viet Nam in general and in the Zero TB Viet Nam and IMPACT project in particular. The workshop was sponsored by the EU through the IMPACT TB project and Qiagen, and brought together TB experts, public health practitioners, community representatives and technicians to discuss experience in managing TB infection worldwide and in Viet Nam; share information about new technologies in testing and treating

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TB infection; and discuss strategies in the scaling up of latent TB infection (LTBI) screening, testing and treatment in Viet Nam.

On the first day of the workshop, participants included leaders from the NTP, provincial departments of health and provincial lung hospitals in Ho Chi Minh City, Hai Phong and Quang Nam province (representing Hoi An), as well as important civil society stakeholders. Presentations on Viet Nam LTBI management strategies, the global and Viet Nam specific experience, and LTBI management under the scope of Zero TB Viet Nam and IMPACT TB. New technologies such as QuantiFERON (QFT) Gold Plus were introduced, and evidence on a new treatment regimen (3HP) was presented and discussed.

On the second day of the workshop, participants included implementers from the three provinces. Techniques to screen and test for LTBI were presented, including the Tuberculin Skin Test and QuantiFERON Gold Plus. Experiences in implementing programs related to LTBI were also shared among participants.

The objectives of the workshop were to:

1. Review current NTP guidelines and standard operating procedures for TB infection management;
2. Introduce QuantiFERON Gold Plus as a next generation diagnostic tool for TB infection; and
3. Train Zero TB Viet Nam and IMPACT TB implementation sites, partners and other stakeholders on diagnosis, treatment and management of TB infection.

**Pre-workshop survey**

At the beginning of the workshop, a brief survey (Annex III) was conducted of all participants (n=48) to gain an understanding of the biggest barriers and gaps to programmatic expansion of TB post-exposure prophylaxis (PEP) in Viet Nam as well as three key interventions on which the Zero TB Viet Nam and IMPACT TB projects should focus to address some of the barriers listed above.

Of the options listed as potential barriers, participants identified the top three as: 1) lack of patient awareness (50%); 2) lack of provider prioritization (35%); and 3) lack of acceptability (31%). Additional barriers identified by survey respondents included training for community volunteers, the coordinating and monitoring of distribution and use of isoniazid at the management level between TB and HIV, lack of management capacity from health workers on patients and contacts and consensus between family members for LTBI treatment. The top three interventions on which the ZTV and IMPACT TB projects should focus were identified as: 1) Patient and household contact counseling (81%); 2) Use of alternative, shortened regimen (44%); and 3) Capacity building for commune- and district-level TB officers (44%). Additional potential interventions identified included improvement of coordination between related projects and more technical support.

Based on these responses, it appears that the main barriers to uptake of TB PEP are at the community level and particularly on the health-seeking side, where priority interventions of IMPACT TB and Zero TB Viet Nam should focus on raising awareness and acceptability of TB PEP. Given the existing state of TB PEP in Viet Nam and in high TB burden countries around the world, both projects will offer ample opportunity to generate evidence of the feasibility and scale-up of TB PEP.

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## Day 1 – TB infection management workshop

**Prof. Le Van Hoi, NTP - Welcome speech and Scale up of LTBI screening, diagnosis and treatment: a country perspective**

Professor Le Van Hoi, NTP's Deputy Manager opened the two-day workshop at 8:30 AM on November 21, 2017 by reminding participants about the commitment and responsibilities to achieve the NTP's ambitious goal of bringing down TB incidence to 20/100,000 by 2030. Prof. Hoi reiterated the role of prevention in managing TB infection in Viet Nam and the roles of partners in the room and presented the structure of the two-day workshop. He then went on to present on the "Scale up of LTBI screening, diagnosis and treatment: a country perspective", where the successful implementation of BCG vaccinations was presented in juxtaposition with ambitious targets in TB control and LTBI management as part of the new national TB control strategy. The status of LTBI program implementation was discussed, whereby screening subjects (household or close contacts among children under 5-year-old; HIV infected children under 14-year-olds), the limited use of diagnostic tests for LTBI (TST and IGRA), treatment regimen (6 months INH for children; 9 months INH for adults) were mentioned and their associated challenges analyzed. Prof. Hoi then presented new areas for expansion of LTBI management, which included expanded criteria for screening persons at risk, applications of tests including TST and IGRA, as well as the 3HP treatment regimen. Prof. Hoi also stressed the importance of collaborating with the private sector in LTBI control.

**Dr. Nguyen Binh Hoa - NTP - Summary of LTBI interventions in Viet Nam**

Dr. Hoa gave an overview of TB epidemiology in Viet Nam, where he pointed out that in Viet Nam, >2.2% contacts of TB patients would contract TB disease in the first two years of exposures. He gave a brief introduction to the current policies regarding LTBI from the WHO. Currently, Dr. Hoa pointed out, subjects for testing and treatment for LTA included PLHIV, TB patients contacts (both adult and children), patients going through cancer treatment, and patients going through organ transplants**.** Dr. Hoa recommended that we should also consider testing and LTA in prison inmates, health workers, migrants from countries with high burden of TB, and homeless people. He introduced the two tests that were used in Viet Nam: QuantiFERON and Mantoux and the national LTBI control strategy.

**Dr. Tran Ngoc Buu - Woolcock Institute of Medical Research - Initial results of project "Enhancing the public health impact of latent TB infection diagnosis and treatment: a pragmatic cluster randomized trial in Quang Nam and Danang**

Dr. Buu gave a presentation on a research study by Woolcock that aimed to evaluate an intervention package that would improve number of contacts identified, screened, and completing medical evaluation and starting LTBI treatment. This was a pragmatic, cluster-randomized, stepped-wedge intervention carried out in Danang and Quang Nam provinces in the central region of Viet Nam from October 2016 to September 2017. The study had two phases: in phase I, the current standard of care package for LTBI was evaluated as a baseline and in phase II the new intervention was conducted. According to the baseline evaluation, health education about LTBI needed to be promoted, the supplies of tuberculin and other medicine following NTP's regimen needed monitoring, and LTBI management should be implemented at the district level. Initial results of the study showed positive effects, with 100% of contacts identified in comparison with estimated number, most of whom are children over 5 years old; 80% of contacts identified who agreed to get LTBI treatment; 80% of contacts complete LTBI screening in total number of contacts who start screening; 44% of contacts complete medical evaluation (vs. 4% before), and nearly 30% of contacts agreed LTBI treatment

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(vs. <1% before). These encouraging results suggest further evaluation and training for greater sustainability of the intervention.

**Dr. Tran Thi Huong Lien - PATH - Breath for Life "LTBI treatment in children under 5"**

Dr. Lien from PATH presented the project Breath for Life (B4L) or LTBI treatment in children under 5 in Nghe An province in 2016 and 2017. The partners were NTP, Path, J&J; Nghe An department of health, National Lung Hospital; and public and private clinics. The goal was to reduce childhood TB morbidity and mortality in one high TB burden province (Nghe An) of Viet Nam. The main objectives included: 1) increase case detection and early treatment for TB in children in both NTP and non-NTP health facilities; 2) strengthen screening, management and isoniazid preventive therapy (IPT) for children in close contact with TB cases; 3) improve recording and reporting system for TB in children; and 4) evaluate the pilot model to highlight results and lessons learned. The project employed WHO guidance for the symptom-based screening approach to child contact management, and guidance from the NTP for child TB contact investigation and screening and IPT. Results showed significantly increased number of eligible and enrolled children on IPT before and after B4L in the intervention districts. The systematic implementation of screening and management of children in close contact with TB patients was evaluated to be an effective approach to increase the proportion of children receiving IPT, and also to improve case detection.

**Dr. Liesl Page-Shipp - IRD - TB infection management: a core component of ZTV**

Dr. Page-Shipp from Interactive Research and Development presented on TB infection management as a core component of the ZTV project. Dr. Liesl gave examples of Alaska, New York, Tomsk where TB incidence plummeted with the comprehensive strategy of Search, Treat, and Prevent. She drew the attention to the Lancet series on *How to eliminate tuberculosis*, whereby evidence from international experts were presented. In this series, it was indicated that preventive therapy for TB was effective (non-HIV infected, and high-risk groups exhibited 60% effectiveness when put under IPT -- according to 11 studies of isoniazid vs. placebo; this number for HIV-positive, TST-positive was 62%) and newer, shorter regimens were effective. She also emphasized that preventive therapy must be a part of a comprehensive approach, since it would not be durable when background rate of disease was not addressed. According to Dr. Liesl, the people who would benefit the most from IPT would be:

- Close contacts of sick TB patients
- PLHIV
- Recent converters on TST or interferon y release assay
- Residents of congregate living facilities
- Smokers, homeless ppl, ppl with diabetes, silicosis
- Health care workers and people who visit health-care facilities in high TB burden areas.

**Dr. Masae Kawamura - Qiagen - QuantiFERON TB Gold Plus**

Dr. Kawamura from Qiagen gave a broad overview of latent and subclinical forms of TB infection. Pursuit of the targets set by the WHO's End TB Strategy in 2015 has led to an increase in interest in diagnosing and treating LTBI among high-risk groups, particularly children and people living with HIV. Dr. Kawamura

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emphasised the importance of LTBI detection and treatment, and that to have major impact on TB disease rates, diagnosing and treating active TB and LTBI must be addressed simultaneously.

Next, Dr. Kawamura reviewed the current types of diagnostic tests for TB infection. TB screening, which includes screening for symptoms and testing for TB, can in fact accomplish both early case detection and LTBI identification for TB prevention. The two current FDA-approved immunodiagnostics are Tuberculin Skin Tests (TST) and Interferon-Gamma Release Assays (IGRA). Both tests measure a person's immune reactivity to M. tuberculosis, and are standard tests for TB infection diagnosis in high-income settings. Both tests cannot distinguish between LTBI and active TB, but despite limitations, IGRA tests have better specificity than TST. Moreover, IGRAs are not affected by Bacille Calmette-Guerin (BCG) vaccines and are thus better at detecting LTBI in BCG-vaccinated individuals. This distinction, she noted, is particularly important in low-income countries where BCG vaccinations are routinely administered.

Nevertheless, Dr Kawamura acknowledged that the usefulness of IGRAs are limited in these high-burden settings due to high cost and the need for laboratory equipment. She presented several studies in which IGRAs, also known commercially as QuantiFERON, where used as a surveillance and public health tool. Despite the drawbacks, through these case studies, she concluded that IGRAs perform better and have higher specificity compared to TSTs.

Comments from Dr. Nguyen Binh Hoa:

- The QuantiFERON Gold Plus Test showed very high specificity. This had been used in the National Lung Hospital and the Pham Ngoc Thach Hospital in Ho Chi Minh City, but this new test seemed to be much improved.
- A disadvantage of TST: BCG vaccination was very high in children in Viet Nam

**Dr. Liesl Page-Shipp - IRD - TB infection management in Zero TB Karachi**

Dr. Page-Shipp gave a second presentation on TB infection management in Zero TB Karachi. The objectives of the project were to access household contacts, to initiate TB infection treatment and to implement a 12 dose INH-Rifapentine regimen for treatment of TB infection. The scope was to deliver infection treatment to individuals who lived with a DR-TB patient in Karachi and to individuals living with Susceptible TB patients in Korangi and Landhi towns of Karachi and to introduce the 3HP regimen for treatment of TB infection in Pakistan. Services included HHC tracing of TB patients, verbal screening by health care workers, clinical investigation by medical officer, counseling of all index patients and HHC, referral for active TB treatment, and PET for household contacts. Operational and technical challenges of the project were discussed focusing on the implementation of 3HP as the new preferred post-exposure prophylaxis (PEP) regimen.

**Sofia Imad - Sanofi - The Role of Rifapentine in LTBI: 3HP Regimen**

Ms. Imad from Sanofi presented on the role of rifapentine and the 3HP regimen in LTBI management. Reiterating previous presenters, Ms. Imad reiterated that treating LTBI has a significant impact at the programme level, for the community and the individuals. Ms. Imad emphasised the importance of LTBI as part of the WHO strategy for TB elimination; that eliminating TB by 2050 requires a simultaneous attack on two components: 1) cut TB transmission by treating active cases, and 2) neutralise the reservoir of latent infection by preventing activation in high-risk groups.

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Next, she discussed the new WHO-recommended 3HP regimen, which consisted of 12 doses of weekly RPT and INH. In their 2015 guideline on the management of latent TB infection, WHO reported that the 3HP regimen was as effective and well-tolerated as 9INH, and had advantages over other regimens. Given the shorter regimen, lower pill burden and direct observation, treatment adherence and completion rates were substantially higher for 3HP. It showed fewer incidents of hepatotoxicity and was better tolerated in patients with LTBI, particularly children and for people living with HIV. Other local studies in Asia also highlighted the higher completion rates and cost-effectiveness of 3HP. She pointed out that despite the benefits, there were also risks involved, including higher incidence of hypersensitivity reactions, although generally mild to moderate in effect.

The 3HP regimen was increasingly recognised as the best option for scaling up LTBI treatment. Ms. Imad highlighted a study conducted in Taiwan that concluded the cost-effectiveness of 3HP and higher completion rates of 3HP compared to 9INH (97% vs. 87%). Ms Imad noted that with the global recognition, WHO and other activists were calling for expedited access to rifapentine. Following pilot clinical trials using 3HP in Taiwan, other countries in the Asia region were also preparing for roll-out of 3HP, including India, Indonesia and Cambodia in 2018.

**Dr. Alyssa Finlay-Vickers - CDC - Existing Guidance and Evidence on the Use of 6-9H and 3HP for TBI management**

Following Ms. Imad's presentation on the role of Rifapentine in LTBI, Dr. Finlay-Vickers of the US Center for Disease Control and Prevention (CDC) reported on the existing guidance and evidence on the the use of 3HP for LTBI management. First, she described the CDC TB clinical trials consortium studies on 3HP treatment, the PREVENT TB Study, also known as Study 26. The study evaluated the effectiveness, efficacy and tolerability of 12-weekly 3HP doses compared to 9 months of isoniazid (9H), drawing the following conclusions: 1) effectiveness of 3HP is non-inferior to 9H; 2) completion rate of 3HP (82%) was significantly higher than 9H (69%); 3) rates of discontinuation due to adverse drug events were significantly higher in 3HP (4.7%) than 9INH (3.6%); 4) rates of death were low (<1%) and not different between the two evaluation groups; and 5) there was no difference in drug resistance among TB outcomes. In children and adolescents, 3HP was as well-tolerated and as effective as 9H, had a higher treatment adherence and completion rate, and was generally safer. Similarly, for people living with HIV who are not yet on ART, 3HP was just as well-tolerated and effective as 9H, showed higher treatment adherence and completion rates, and was effective in both HIV-positive and -negative individuals.

When considering implementing shorter LTBI treatment regimens in low-incidence settings, there were a few lessons learned from the 3HP Post-Marketing Surveillance Project. Dr. Finlay-Vickers summarised the initial programmatic experience of 3HP implementation in the US and how it closely mirrors the treatment trial experience. Generally, the 3HP regimen is being used successfully in the US, recording high completion rates, particularly in difficult and diverse population groups.

Lastly, Dr. Finlay-Vickers referenced current treatment choices for LTBI in the US, including 6H, 9H, 3-4RH, 3-4R and finally 3HP. Of these, she acknowledged that the CDC recommends 12 weekly DOT doses of 3HP. She mentioned some eMonitoring guidelines and reports, other additional published observational reports

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that cite high completion rates using 3HP, as well as consolidated WHO LTBI guidelines, the most recent of which was published in September 2017.

**Vo Nguyen Quang Luan - FIT - TB infection treatment on Zero TB Viet Nam and IMPACT TB**

Current global efforts showed a reduction of 1.65% in global TB incidence annually, which would yield TB elimination to occur in 2082. Mr. Luan, Chairman of FIT, voiced the case for urgency: that Viet Nam incidence reduction rate in 2015 is estimated at -2.6% annually means there is a wide gap between current reality and the desired targets as set out by the National Strategic Plan. Zero TB Viet Nam and its innovative, comprehensive active case finding could have a significant population-impact on the TB epidemiology in Viet Nam. Given the mounting evidence for LTBI management in TB elimination, Mr. Luan outlined the goals and objectives of TBI intervention under ZTV and IMPACT TB. These include: 1) Contribute to the optimization of standard operating procedures for programmatic screening, treatment and follow-up of TBI patients, and 2) Enroll 900 additional TB infected patients onto Post-Exposure Prophylaxis. The latter entails: developing SOPs for TB infection intervention integrated into the project's intensified diagnostic algorithm; systematically counselling and screening eligible contacts in the community; employing chest x-ray, clinical screening and smear to rule out active TB; sourcing and employing proven and novel sensitive tests for TB infection; and employing a standardized reporting system for all enrolled patients.

Mr. Luan then elaborated on the SOP for TB post-exposure prophylaxis, which seeks to provide guidelines for detection, linkage and follow-up for TB infected patients. In the model, community health workers will engage persons at risk of TB infection, refer them to the NTP and provide follow-up support during treatment, and the TB officers at the District TB Unit will implement TST and IGRA testing, enrol and manage TBI patients. He further explained key components of the standard operating procedures, including 1) determining persons at risk for TB infection, particularly patient contacts and vulnerable groups, i.e. children and people living with HIV; 2) screening households with CXR, sputum smear and/or Xpert to rule out active TB disease. All eligible contacts for whom active disease was ruled out will be invited for TB infection testing; 3) establishing TB infection using Mantoux tuberculin skin test or IGRA/QuantiFERON; and 4) treatment follow-up.

**Nguyen Phuong Lan - FIT - LTBI Recording and Reporting System**

Following Mr. Vo, Ms. Lan, Programme Manager for ZTV and IMPACT TB of FIT gave an overview of the current recording and reporting systems, as well as how LTBI will be reported in ZTV and IMPACT. NTP's reporting system is built around the TB screening and isoniazid tracking registration, referral, TB child contacts report and IPT forms. The TB screening and isoniazid tracking registration form (S1) records information such as HIV status, symptoms, TB screening results, from child contacts of TB patients. The referral form (M1-TE) includes information such as the source of infection, TB symptoms, and risk of TB infection. The TB child contacts and IPT form (M2-TE) provides quarterly reports of child TB contacts who have been screened and are eligible for prophylaxis and IPT.

Ms. Lan then continued describing the existing recording and reporting systems. A new and recent development of the project is the switch to a digital patient management system called Access to Care

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Information System (ACIS) developed in partnership with the Clinton Health Access Initiative (CHAI) that has been linked with VITIMES, the NTP's electronic recording and reporting system.

**Discussion**

Prof. Nguyen Viet Nhung, Manager of the NTP, mentioned that with the bedaquiline study, Viet Nam has demonstrated robust pharmacovigilance (PV) to the world and expressed hope that we could provide the same evidence for LTBI control. He expressed his opinions on LTBI test, that the world needed a test that can properly evaluate subclinical TB. In Viet Nam, he said, we had QuantiFERON, which was good, but the price was still quite high. Prof. Nhung pointed out that in a program setting, we would not be able to scale up IGRA nationwide. A new test from Russia, the Dia Skin Test, showed comparable specificity and sensitivity to QuantiFERON with the operational ease of implementation of Mantoux. He anticipates to implement this test in Viet Nam in the near future.

Questions from the audience:

- Dr. Thu Anh from Woolcock asked if using Xray first as screening to rule out TB then TST would create a burden on the healthcare system, since Xray for all contacts would cost a lot of money as a screening test. She added that the quality of X-Ray reading at the community level would also need close monitoring since we would not be certain that it would be of good standard. Dr. Thu Anh emphasized that these factors needed to be taken into consideration. She also expressed the hope to apply ACIS, the information system in ZTV and IMPACT TB into ACT4. In response Prof. Nhung indicated that Xray and Xpert is a revolution and that the Viet Nam NTP will use that as the testing algorithm.

- Dr. Thu Anh expressed concerns about the applicability of QuantiFERON, which probably would not be as good as TST, and urged that the NTP take into consideration the cost and operational issues, including quality control, not just about the tubes for blood. Lastly, she hoped that the NTP can issue LTBI treatment with 3HP.

- To this, Prof. Nhung answered that QuantiFERON can offer challenges in quality control. TST did not have good specificity, but quality was fairly consistent. The NTP did not intend to scale up QuantiFERON nationwide and understood that QuantiFERON was different in a research setting and in a programmatic setting. However, this was not to say that Viet Nam will not use any innovation. Even without WHO recommendation, a country could still use innovation. The new skin test from Russia, according to Prof. Nhung, showed potential.

- Prof. Hung (Head of NTP Laboratory and Chair of the Microbiology Department) also confirmed that QuantiFERON in a hospital setting was different than in a community setting. The time for transportation of the sample had also also a challenge and we would need lab quality control for the ELISA tests in order to perform QuantiFERON tests well. Prof. Hung also expressed the hope for 3HP, acknowledging the high prevalence of isoniazid monoresistance in Viet Nam at the moment. The importance of LTBI testing was re-emphasized and that it was important for parents to trust the system to test and treat their children.

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- Dr. Masae from Qiagen expressed that with IGRA, there was better quality control than for TST since it would be done at the lab. IGRA also had much higher specificity, which guaranteed that people wouldn't be treated unnecessarily, a huge issue with using TST. Prof. Nhung acknowledged this but also pointed out that giving blood test for children probably difficult.

- Dr. Le Truong Giang, Chairman of the Ho Chi Minh City Public Health Association expressed confidence in ending TB in Ho Chi Minh City since we now had a better regimen and better screening mechanism. However, he had concerns about the cost effectiveness of each intervention and that bespoke intervention models and investments may be needed for different areas and burdens of TB within Viet Nam and even within individual cities. To this, Prof. Nhung said we needed to standardize all techniques and that patients counted on the NTP to receive the same quality drugs for TB treatment and MDR-TB treatment everywhere. The techniques we apply depend on the capacity of staff. He stressed that ZTV and IMPACT TB were a pilot in three provinces whereby we would want to see what worked and how much money it would cost. However, Prof. Nhung also emphasized that we shouldn't count on money to do the job and that we needed to minimize the cost to keep the program running even after the project ended.

- Dr. Van Anh from CDC raised challenges with interventions for people living with HIV who were coinfected with TB. She pointed out that national data on this particular group were available yet not dependable, such as the percentage of PLHIV registered to receive IPT was 26%, but this number was questionable. Supply of isoniazid was also recognized as a big issue at various levels in the supply chain. Provincial AIDS Centers said that there was coordination, but drugs were not there. Decision 773 indicated that the TB program was assigned to manage isoniazid supply and would like to draw the leadership attention to this issue.

- Dr. Nhung responded that the NTP was not assigned but volunteered to manage isoniazid and that supplies of INH had been stable. The issue probably lay with the request from the AIDS program and the CDC should verify the issues and continue to coordinate with the NTP.

- Dr. Hiep, representing a local NGO, raised question on the cost of Xray since insurance would only Cover 170,000 VND per person at one commune. She also asked about the adverse drug reaction (ADR) of rifapentine, since one of the ADR in her project was that the child would lose appetite, leading to malnutrition and treatment discontinuation. Lastly, she raised the issue of the thousands of diabetic patients with and the screening procedure for diabetic patients.

- To this, Prof. Hoi answered:
  - Xray would be in free in the projects.
  - ADR: we had a PV system at the NTP. In this project, we didn't have a stand-alone PV system but would use the one created with the Hanoi Pharmacy University.
  - Diabetes: we will prioritize along with HHC including children, then the elderly and PLHIV.
  - Dr. Nhung added that the project should include diabetic patients in the high-risk group in the first phase as recommended by the WHO.

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- Dr. Hiep added that in her project, in a commune with 200,000 people, there were 7,000 with diabetes. It would be impossible to screen all these diabetic patients using Xray, so there should be a screening step of diabetes and other opportunistic infections. Prof. Nhung acknowledged the comment and stressed the importance of SOPs for ZTV and IMPACT, as all procedures and steps needed to be documented.

- Dr. Thai from Qiagen added that QuantiFERON was a test that was undoubtedly superior to all other equivalent tests, and not just for LTBI. The test would be particularly valuable for patients who were immuno-compromised and were at high risk of TB infection. Dr. Thai urged that Viet Nam should advocate for ethical and rational use of QuantiFERON.

- Luan Vo from FIT concluded the discussion by adding that resource was always limited, so we should choose the most efficient way to look at this issue. However, he indicated that focusing too much on sustainability is in direct contradiction with the goal of eradicating TB. He further posited that the most sustainable way to fight TB is to eliminate it as a public health threat. He further suggested that detailed costing should be performed before sustainability concerns are raised that stifle momentum and progress. Specifically, he suggested that screening all household contacts of bacteriologically-confirmed TB cases in Viet Nam, a previous point of contention among several workshop participants, between now and 2030 would cumulatively cost USD 11 million, which according to him was a small amount to pay for a robustly developing economy such as Viet Nam.

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## DAY 2 - Training for TB officers in the project implementation sites

**Prof. Le Van Hoi and Prof. Dinh Ngoc Sy, Welcome and Introduction**

Prof. Le Van Hoi, NTP's Deputy Manager opened Day 2 of the two-day workshop on November 22, 2017 by reiterating the importance of detecting, screening and treating TB infection. The ZTV and IMPACT projects had committed with donors to manage latent TB infection. The projects needed to recognise the importance of managing LTBI in eliminating TB, learn from previous project experience to efficiently manage and scale up LTBI management nationally. He outlined 5 implementation strategies: 1) Systematically screen for TB infection, 2) Apply new technologies for improved and more accurate diagnosis, 3) Develop private-public partnerships in health, 4) Prioritise vulnerable groups, 5) Set targets for LTBI management.

Prof. Le Van Hoi continued by describing the growing global interest in LTBI. The shift was marked in recent years to focus on prevention for total elimination of TB. There are still millions around the world who are exposed to Mycobacterium tuberculosis and are at risk of progressing to active disease. ZTV and IMPACT must set strategies to treat active patients and intervene to prevent and control disease progression in others. According to Dr. Le, health professionals play a large role in educating health staff and sharing experiences in managing TB. They, along with the project, are instrumental in introducing new methods, tools, technologies and resources for implementation in Viet Nam. He concluded his welcome message by emphasising the top-down approach and how the project relies on bringing knowledge and experience to the community and adapting them to fit the local context.

**Dr. Masae Kawamura - Qiagen - Latent TB Infection: Why prevent TB? Diagnosis and Treatment**

Following the opening remarks by Prof. Dinh Ngoc Sy and Prof. Le Van Hoi from the National Lung Hospital, Dr. Kawamura from Qiagen began Day 2 of the workshop with a broad overview of latent and subclinical forms of TB infection. Pursuit of the targets set by the WHO's End TB Strategy in 2015 has led to an increase in interest in diagnosing and treating LTBI among high-risk groups, particularly children and people living with HIV. Dr. Kawamura emphasised the importance of LTBI detection and treatment, and that to have major impact on TB disease rates, diagnosing and treating active TB and LTBI must be addressed simultaneously.

Next, Dr. Kawamura reviewed the current types of diagnostic tests for TB infection. TB screening, which includes screening for symptoms and testing for TB, can in fact accomplish both early case detection and LTBI identification for TB prevention. The two current FDA-approved immunodiagnostics are TST and IGRA. Both tests measure a person's immune reactivity to M. tuberculosis, and are standard tests for TB infection diagnosis in high-income settings. Both tests cannot distinguish between LTBI and active TB, but despite limitations, IGRA tests have better specificity than TST. Moreover, IGRAs are not affected by Bacille Calmette-Guerin (BCG) vaccines and are thus better at detecting LTBI in BCG-vaccinated individuals. This distinction, she noted, is particularly important in low-income countries where BCG vaccinations are routinely administered.

Nevertheless, Dr Kawamura acknowledged that the usefulness of IGRAs are limited in these high-burden settings due to high cost and the need for laboratory equipment. She presented several studies in which IGRAs, also known commercially as QuantiFERON, where used as a surveillance and public health tool.

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Despite the drawbacks, through these case studies, she concluded that IGRAs perform better and have higher specificity compared to TSTs.

**Dr. Arya Wibitomo - Sanofi - Rifapentine and 3HP**

Dr. Wibitomo began his presentation with a reaffirmation of the importance of LTBI in TB elimination; that eliminating TB by 2050 requires a simultaneous attack on two components: 1) cut TB transmission by treating active cases, and 2) neutralise the reservoir of latent infection by preventing activation in high-risk groups. Then he proceeded to cover current and new regimens for TB treatment, such as 6INH, 9INH, 3-4RH, 3-4R and finally 3HP. Rifamycins and its derivatives rifampin and rifapentine are antibiotics part of the first-line TB treatment regimen. Like the 4-month daily RIF regimen, 3HP is increasingly widely recommended as an appropriate alternative to 9H. Studies show that the new regimen, which consists of 12 doses of weekly 3HP is equivalent to 9 months of isoniazid in preventing disease progression. In 2015, a WHO report concludes that "3HP has advantage over the other regimens". Given the shorter regimen and direct observation, treatment adherence and completion rates were substantially higher for 3HP. It has less hepatotoxicity and is better tolerated in patients with LTBI, particularly children and for people living with HIV. Other local studies in Asia also highlighted the higher completion rates and cost-effectiveness of 3HP. Dr. Wibitomo brought up some key risks associated with rifapentine, but concluded that using Rifapentine could lead to better acceptance, implementation and results in clinical settings.

**Nduku Ndunda - Qiagen - QFT-based Screening for TB Infection**

If Dr. Kawamura gave a brief introduction on the use of IGRAs and QuantiFERON (QFT) as one of two standard diagnostic tests, Ms. Ndunda from Qiagen followed up with an in depth review of the evolution of QFT technology, its uses, processes, as well as an evaluation of QTF-Gold in Tube and QFT-Plus. Now in its 4th generation, QFT technology is a unique approach to disease detection and monitoring of cell-mediated functions of the immune system from whole blood samples, and offers many advantages including accuracy, scalability, and rapid turn around. QFT-Gold stimulates primarily CD4+ T cells. The latest technology, QFT-Plus utilises two antigen tubes to elicit an immune response from CD4+ and CD8+ T-cells in TB patient contacts. According to Ms. Ndunda, this new class of peptide antigens improves performance: increased sensitivity and application in particularly immunocompromised populations, e.g. HIV positive subjects. To allow a practical side to the presentation, she demonstrated with QFT blood collection tubes, clearly explaining the differences as indicated by the cap colour, and walking the audience through the blood collection process. Ms. Ndunda then evaluated the performance of QFT, and QFT-Plus in particular, through a series of case studies. The results indicate that QFT-Plus in contact screening has improved performance compared to QFT-Gold, and the WHO Global TB Report in 2016 points to the promise of being better able to identify people at greater risk of progression to active TB.

**Dr. Nguyen Thi Bich Phuong - Woolcock Institute for Medical Research - Implementation of QFT: lessons Learned from the Field**

To demonstrate how QFT is applied in the field, Dr. Phuong from the Woolcock Institute for Medical Research reported on rolling out QFT at the district and commune levels and mobile incubation and other techniques used to optimise diagnostic quality in these settings. The case study she highlighted was a 4-year

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project in Ca Mau Province in the South of Viet Nam, representative of a high-burden setting. When implementing community-wide screening for TB at the district and commune level, active case finding and performing door-to-door screening is more effective than requiring contacts to come to a health centre. According to Ms. Phuong, in low-resource, rural areas of Ca Mau, this requires adaptation of standardised techniques to fit the local context. Equipment, including centrifuge, timers, thermometers, and portable incubators, need to be readily packaged for fieldwork. In order to prepare for QFT, samples need to be collected in tubes, shaken 10 times, and then immediately either 1) incubated before being shipped to the lab, or 2) sent to the lab directly for incubation. The portable incubator was a prime example of how the issue of incubation was addressed in the field: QFT was stored inside Coleman box with Techni ice to ensure optimal temperature. Overall, the project had 1622 child participants (born in 2012), of which 935 blood samples were collected, and 31 participants had QFT positive (3.3%). Not only was this a project that illustrated successful implementation of new technologies in field settings, the project also had no indeterminate results. Dr. Phuong attributed this to thorough preparation, training and techniques in the field.

**Dr. Le Thi Nguyet - NTP - TST-based Screenings for TB Infection**

Much has been presented during the workshop on QFT and other new technologies in screening for LTBI. Dr. Nguyet gave an overview on the Tuberculin skin test (TST) that are still widely used as an important test for diagnosing TB infection. She presented on the history of tuberculin, its chemical properties, standard methods of tuberculin testing and their practical uses. Dr. Nguyet then demonstrated how tuberculin is administered and how results are interpreted. The results of this test must be interpreted carefully. The person's medical risk factors determine the size of induration for a positive result (5 mm, 10 mm, or 15 mm). Dr. Nguyet also pointed out that the test's interpretation may vary by factors such as age, immunological status, etc. that can influence the immune response and thus the test's interpretation. Lastly, she indicated that there is no correlation between the size of induration and the likelihood of current active TB disease.

**Dr. Pham Quang Tue - NTP - TB infection treatment and follow-up in children**

Part of the workshop is to understand LTBI implementation can be applied to one particular vulnerable group: children. Dr. Pham heading LTBI for the NTP reported on the management of children who are patient contacts and the monitoring of TB infection treatment as part of the NTP. First, he described the process: 1) Identify child contacts of TB patients; 2) Register into patient records; 3) Refer children with symptoms to District TB Unit for diagnosis; 4) Identify children who need to be put on Isoniazid Preventive Therapy (IPT); 5) Prevention and monitoring; 6) Evaluation of results; 7) Reporting. Next, he discussed the roles and responsibilities of all levels of implementation in the treatment and monitoring of LTBI. This includes healthcare workers, health professionals, and TB officers at the ward/commune, district, provincial and national levels. Finally, he noted several standard guidelines and other management tools, and reported on general indicators for 2016 and 3 quarters of 2017, including IPT administration in children.

**Nguyen Phuong Lan - FIT - TB Infection Treatment for Zero TB Viet Nam and IMPACT TB and LTBI Recording and Reporting System**

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Following Dr. Pham, Ms. Lan provided a summary of LTBI intervention in the projects and the standard operating procedures for the interventions. ZTV was launched in September 2017 promoting a comprehensive TB patient care model across 3 cities in Viet Nam. Now given the evidence and case for urgency, Ms. Lan reports, the project is scaling up to incorporate LTBI intervention on ZTV as well as IMPACT. She explained key components of the standard operating procedures, including 1) determining persons at risk for TB infection, particularly patient contacts and vulnerable groups, i.e. children and people living with HIV; 2) screening households with CXR, sputum smear and/or Xpert to rule out active TB disease. All eligible contacts for whom active disease was ruled out will be invited for TB infection testing; 3) establishing TB infection using Mantoux tuberculin skin test or IGRA/QuantiFERON; and 4) treatment follow-up. Subsequently, Ms. Lan gave an overview of NTP's current LTBI reporting system and the proposed recording and reporting systems for ZTV and IMPACT TB. She then elaborated the recent transition to a digital patient management system called Access to Care Information System (ACIS) in partnership with the Clinton Health Access Initiative (CHAI) that has been linked with VITIMES, the NTP's electronic recording and reporting system. Ms. Lan then described how LTBI in ZTV and IMPACT would now be reported in the new system: CHWs enter initial screening data, i.e. TB symptoms, diabetic and HIV status, into tablets with ACIS provided by the project. The information is then pushed back to VITIMES and reported to NTP, contributing to better TB case detection and referral rates.

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## Annex I: Workshop agenda

**Workshop for Zero TB Viet Nam and IMPACT TB implementation sites, partners and other stakeholders to build capacity and share best practices on management of TB infection in Viet Nam**

- Date: 21-22 November 2017
- Time: 8:00-16:30
- Place: La Thanh Hotel, 218 Doi Can, Ba Dinh, Hanoi, Viet Nam

## Day 1: TB infection workshop agenda

| | | |
|---|---|---|
| 07:30-08:00 | Registration & Breakfast | |
| 08:00-08:05 | Welcome & Introduction – Day 1 | A/Prof. Nguyen Viet Nhung,<br>Viet Nam NTP Manager |
| 08:05-08:20 | Viet Nam roadmap on programmatic management of TB infection | A/Prof. Le Van Hoi,<br>Viet Nam NTP Vice Manager |
| 08:20-08:40 | Experiences in programmatic management of TB infection in Viet Nam<br>• Programmatic roll-out of pediatric TBI treatment<br>• Adult TBI treatment pilot activities | Dr. Nguyen Binh Hoa,<br>Viet Nam NTP Secretary |
| 08:40-09:00 | TB infection research studies in Viet Nam<br>• Experiences and learnings in access to diagnosis and treatment of TBI<br>• Preliminary results from Da Nang & Quang Nam | Dr. Tran Ngoc Buu,<br>Woolcock IMR |
| 09:00-09:20 | PET among children under 5 years on Breath 4 Life<br>• Breath 4 Life TBI testing and treatment protocol<br>• Preliminary results | Tran Thi Huong Lien,<br>PATH |
| 09:20-09:40 | TB infection management – a core component of the Zero TB Initiatives | Dr. Liesl Page-Shipp,<br>TB/HIV Technical Director, IRD |
| 09:40-10:00 | TB infection management in Zero TB Karachi<br>• Initial results<br>• TB infection testing and treatment protocol<br>• Experiences in 3HP vs. 6H/9H | Dr. Liesl Page-Shipp,<br>TB/HIV Technical Director, IRD |
| 10:00-10:20 | *Tea and coffee* | |
| 10:20-10:40 | Presentation of QuantiFERON (QFT) Gold Plus<br>• New features and data of QFT Gold Plus<br>• Comparative data on QFT Gold Plus, GIT and TST | Dr. Masae Kawamura<br>Medical Officer, Qiagen |
| 10:40-11:00 | Presentation of 3HP for TB infection management<br>• Introduction of 3HP<br>• Efficacy and safety of 3HP<br>• Plans for 3HP globally and Viet Nam | Dr. Arya Wibitomo,<br>Medical Director, Sanofi |
| 11:00-12:30 | *Lunch* | |
| 12:30-13:00 | Existing guidance and comparative evidence on the use of 6H/9H and 3HP for TB infection management<br>• Efficacy and safety of alternative TBI regimen<br>• Alternative methods of treatment administration and follow-up to DOT | Dr. Alyssa Finlay,<br>Regional TB Director, CDC VN |

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|---|---|---|
| | • Review of current CDC's and WHO's 3HP recommendations<br>• Current development and research | |
| 13:00-13:15 | TB infection management on ZTV and IMPACT TB<br>• Project goals, objectives related to TB infection<br>• Key activities and SOPs<br>• Supply chain considerations | Luan Vo,<br>FIT/IRD |
| 13:15-13:30 | Systematic recording and reporting<br>• Existing national TB infection treatment registers<br>• Incremental data collection and reporting for ZTV and IMPACT TB | Lan Nguyen,<br>FIT/IRD |
| 13:30-14:40 | Discussion: Feasibility of the proposed TB infection management protocol – Screening and diagnosis<br>• Systematic, integrated screening for TB infection<br>• Subject and site selection for QFT, TST testing<br>• Implementation, supply chain and logistics<br>• Key roles and responsibilities | Facilitator: A/Prof. Le Van Hoi,<br>Luan Vo |
| 14:40-15:00 | *Tea and coffee* | |
| 15:00-16:15 | Discussion: Feasibility of the proposed TB infection management protocol – Treatment and follow-up<br>• Administration, follow-up and reporting<br>• 6H/9H vs. 3HP (FDC or H+P)<br>• Key roles and responsibilities | Facilitator: A/Prof. Le Van Hoi,<br>Luan Vo |
| 16:15-16:30 | Summary, policy outlook & closing | A/Prof. Nguyen Viet Nhung,<br>Viet Nam NTP Manager |

**Day 2: Implementation site training agenda**

| | | |
|---|---|---|
| 07:30-08:00 | Registration & Breakfast | |
| 08:00-08:05 | Welcome & Introduction – Day 2 | A/Prof. Le Van Hoi,<br>Viet Nam NTP Vice Manager |
| 08:05-08:15 | Goals and objectives of Day 2 training | Luan Vo |
| 08:15-08:30 | Overview of latent and insipient forms of TB infection – why we must treat TB infection | Dr. Masae Kawamura,<br>Medical Officer, Qiagen |
| 08:30-09:30 | Comparative review of current types of diagnostic tests for TB infection<br>• TST<br>• T-SPOT<br>• QFT GIT / Gold Plus | Dr. Masae Kawamura,<br>Medical Officer, Qiagen |
| 09:30-10:00 | Existing and new regimen for TB infection treatment: efficacy, tolerability and safety | Dr. Arya Wibitomo,<br>Medical Director, Sanofi |
| 10:00-10:20 | *Tea and coffee* | |
| 10:20-11:00 | QFT-based screening for TB infection:<br>• Sample collection<br>• Storage & transport<br>• Sample processing & testing<br>• Logistics and capacity (HP & HCMC) | Nduku Ndunda, Qiagen |
| 11:00-11:30 | Implementation of QFT – learnings from the field:<br>• Rolling out QFT at district and commune levels | Dr. Nguyen Thi Bich Phuong,<br>Woolcock IMR |

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| | | |
|---|---|---|
| | • Mobile incubation and other techniques to optimize diagnostic quality | |
| 11:30-13:00 | *Lunch* | |
| 13:00-13:40 | TST-based screening for TB infection<br>• Administration & reading of TST<br>• Roles & responsibilities | National Reference Lab |
| 13:40-14:20 | TB infection treatment & follow-up<br>• SOPs<br>• Roles & responsibilities | NTP, Pediatrics team |
| 14:20-14:40 | *Tea and coffee* | |
| 14:40-15:00 | Zero TB Viet Nam: a pilot in the NTP roadmap for TB infection treatment in Viet Nam | A/Prof. Le Van Hoi,<br>Viet Nam NTP Vice Manager |
| 15:00-15:20 | TB infection management on Zero TB Viet Nam<br>• Project goals, objectives related to TB infection<br>• Key activities and SOPs on Zero TB Viet Nam | Lan Nguyen,<br>FIT/IRD |
| 15:20-15:45 | Systematic recording and reporting<br>• Existing national TB infection treatment registers<br>• Incremental data collection and reporting for Zero TB Viet Nam | Lan Nguyen,<br>FIT/IRD |
| 15:45-16:15 | Discussion, questions & answers | |
| 16:15-16:30 | Summary and closing | A/Prof. Le Van Hoi,<br>Viet Nam NTP Vice Manager |

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## Annex II: List of Participants

## List of Participants

| # | Name | Organization |
|---|---|---|
| 1 | Nguyen Viet Nhung | Viet Nam NTP |
| 2 | Le Van Hoi | Viet Nam NTP |
| 3 | Nguyen Binh Hoa | Viet Nam NTP |
| 4 | Vu Quynh Hoa | Viet Nam NTP |
| 5 | Le Hai Minh | Viet Nam NTP |
| 6 | Vu Xuan Hung | Hai Phong Provincial Health Services |
| 7 | Mac Huy Tuan | Hai Phong Provincial TB Hospital |
| 8 | Dang Hung Cuong | Hai Phong Provincial TB Hospital |
| 9 | Nguyen Thi Thu Huong | Le Chan District TB Unit staff |
| 10 | Duong Thi Lien | Ngo Quyen District TB Unit staff |
| 11 | Le Thi Thanh Phuong | Hai An District TB Unit staff |
| 12 | Nguyen Ngoc Hao | Hong Bang District TB Unit staff |
| 13 | Nguyen Van Van | Quang Nam Provincial Health Services |
| 14 | Nguyen Ngoc Phap | Quang Nam Provincial TB Hospital |
| 15 | Tran Van Nam | Hoi An TB Unit staff |
| 16 | Nguyen Huu Lan | HCMC Provincial TB Hospital |
| 17 | Do Chau Giang | HCMC Provincial TB Hospital |
| 18 | Dang Thi Minh Ha | HCMC Provincial TB Hospital |
| 19 | Nguyen Van Hoi | D6 District TB Unit Staff |
| 20 | Ho Van Nho | D7 District TB Unit Staff |
| 21 | Nguyen Van Thom | D8 District TB Unit Staff |
| 22 | Ly Hong An | D12 District TB Unit Staff |
| 23 | Phan Thi Minh Tan | Hoc Mon District TB Unit Staff |
| 24 | Hoang Van Thang | Tan Binh District TB Unit Staff |
| 25 | Nduku Ndunga | Qiagen |
| 26 | Masae Kawamura | Qiagen |
| 27 | Dinh Ngoc Sy | VATLD |
| 28 | Le Truong Giang | HPHA |
| 29 | Vu Nguyen Thanh | HPHA |
| 30 | Mai Thanh Binh | Johnson & Johnson |
| 31 | Nguyen Thien Huong | KNCV |
| 32 | Alyssa Finlay | CDC |
| 33 | Yen Nguyen | FIND |
| 34 | Tran Thi Huong Lien | PATH |
| 35 | Nguyen Hoai Giang | Union |
| 36 | Phan Thi Thu Ha | University of San Francisco |
| 37 | Luu Ho Thanh Tuan | Clinton Health Access Initiative |
| 38 | Khuat Thi Hai Oanh | SCDI |

| | | |
|---|---|---|
| 39 | Nguyen Thu Anh | Woolcock IMR |
| 40 | Nguyễn Thị Bích Phượng | Woolcock IMR |
| 41 | Tran Ngoc Buu | Woolcock IMR |
| 42 | Nguyen Thien Huong | KNCV |
| 43 | Liesl Page-Shipp | IRD |
| 44 | Vo Nguyen Quang Luan | FIT/IRD VN |
| 45 | Rachel Forse | FIT |
| 46 | Nguyen Phuong Lan | FIT/IRD VN |
| 47 | Mo Thi Lan Huong | FIT/IRD VN |
| 48 | Nguyen Thi Hong Minh | FIT, Hoi An |
| 49 | Le Thi Thao Nguyen | FIT, HCMC |
| 50 | Bui Nadine | FIT, HCMC |

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## ANNEX III: PRE-WORKSHOP SURVEY RESULT

**Survey question 1: What are the biggest barriers and gaps to programmatic expansion of the eligibility criteria and scale-up of TB infection interventions and TB post-exposure prophylaxis (PEP) in Vietnam?**

Please rank the following items in order of importance from 1 = most important (first priority) to 10 least important (last priority). Circle the appropriate number in the box.

Total surveys answered: N=48

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Lack of patient awareness | **1** | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Lack of health-seeking | 1 | 2 | 3 | 4 | 5 | 6 | **7** | 8 | 9 | 10 |
| Lack of acceptability of treatment | 1 | **2** | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Currently used regimen (6H/9H) | 1 | 2 | 3 | 4 | **5** | 6 | 7 | 8 | 9 | 10 |
| Lack of provider prioritization | 1 | 2 | **3** | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Lack of provider capacity | 1 | 2 | 3 | 4 | 5 | 6 | 7 | **8** | 9 | 10 |
| Availability of diagnostics | 1 | 2 | 3 | 4 | 5 | **6** | 7 | 8 | 9 | 10 |
| Cost of diagnostics (to patient or health system) | 1 | 2 | 3 | **4** | 5 | 6 | 7 | 8 | 9 | 10 |
| Current eligibility criteria (WHO/Nat'l guidelines) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | **10** |
| Availability of medicine | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | **9** | 10 |

Missing issues that were suggested:

- Training for CHWs
- The coordinating and monitoring of distribution and use of INH at management level between NTP and HIV
- Lack of management capacity from health workers on patients and contacts
- Consensus between family members for LTBI treatment

**Survey question 2: What are three key interventions on which Zero TB Vietnam and IMPACT TB should focus to address some of the barriers listed above?**

2.1. Please circle three interventions:

Patient and household contact counseling
Use of alternative, shortened regimen
Alternative means of patient follow-up (e.g., VDOT, mHealth)
Capacity building for commune- and district-level TB officers
Improvement of (electronic) recording and reporting for TB infection management
Provision of diagnostic tools for TB infection
Stipend for TB screening and infection testing for patient contacts

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Patient advocacy material and handouts on TB infection

N = 48

| # | Items | n | % |
|---|---|---|---|
| 1 | Patient and household contact counseling | 39 | 81% |
| 2 | Use of alternative, shortened regimen | 21 | 44% |
| 3 | Capacity building for commune- and district-level TB officers | 21 | 44% |
| 4 | Provision of diagnostic tools for TB infection | 17 | 35% |
| 5 | Improvement of (electronic) recording and reporting for TB infection management | 12 | 25% |
| 6 | Stipend for TB screening and infection testing for patient contacts | 13 | 27% |
| 7 | Patient advocacy material and handouts on TB infection | 6 | 13% |
| 8 | Alternative means of patient follow-up (e.g., VDOT, mHealth) | 4 | 8% |

<u>The THREE interventions that should be focused more on are:</u>

- Patient and household contact counselling
- Use of alternative, shortened regimen
- Capacity building for commune- and district-level TB officers

2.2. Other suggested interventions:

- Enhancement of coordination among stakeholders
- Technical supports for SCs, CHWs and TB officers at all levels.

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