

A conversation with Friends for International Tuberculosis Relief, May 8, 2019

Participants

- Luan Vo – CEO, Friends for International Tuberculosis Relief (FIT)
- Andrew Codlin – Monitoring and Evaluation Director, FIT
- Rachel Forse – Program Director, FIT
- Andrew Martin – Senior Research Analyst, GiveWell

Note: These notes were compiled by GiveWell and give an overview of the major points made by Mr. Vo, Mr. Codlin, and Ms. Forse.

Summary

GiveWell spoke with Mr. Vo, Mr. Codlin, and Ms. Forse of FIT as part of the second round of investigating applicants to the 2019 GiveWell grants for Global Health and Development in Southeast Asia and Bangladesh (<https://www.givewell.org/research/grants-southeast-asia-bangladesh-2019/application-details>). Conversation topics included FIT's island tuberculosis (TB) case finding campaign in January, its funding sources, and how it might use additional funding.

Background information on an island TB case finding campaign

In January 2019, FIT and the Vietnamese government collaborated on a TB case finding campaign on Cu Lao Cham, a small island off the coast of central Vietnam. The campaign targeted the island's entire population with mass screening for TB and latent TB infection (LTBI). (LTBI is defined as the presence of TB bacteria without any clinical signs of TB disease.)

FIT notes that it works on TB case finding campaigns on islands in Vietnam because of high TB prevalence among island populations and because of the possibility of achieving TB elimination among relatively isolated populations. With additional funding, FIT could expand its case finding work to additional islands.

Summary of FIT's and the government's main roles in the January 2019 campaign

FIT's primary role was planning and coordination. One of FIT's field site coordinators drafted the objectives, priorities, planned activities, and budget for the project to present to the National Tuberculosis Control Programme (NTP) and the provincial health department for review and approval.

Two FIT staff members in Hoi An, alongside some district health staff, were in charge of visiting the island, doing the baseline assessment, and determining where to host the screening and how to invite people. Once the plan was finalized, those two staff members also worked with the commune- and district-level health system

to implement the activities, under the supervision of the NTP and the provincial health department. (See "Timeline of the campaign" for more.)

FIT provided stipends of about \$20 a day to government health workers who participated in the program. (The government provided health workers' base salaries, lab capacity, etc.)

FIT worked on data collection, analysis, and reporting on the program to government stakeholders and donors.

Screenings, readings, and patient consultations were performed by staff from the commune-, district-, and provincial-level health systems. The public health system also used the campaign as an opportunity to provide other, non-TB health services to the island population, including screenings for diabetes, hypoglycemia, cervical cancer, and breast cancer.

Timeline of the campaign

Prior to the campaign, FIT reached out to the island's community healthcare station and government officials to compile a list of the 2,022 inhabitants of the island. FIT sorted the list into adults and children (with the intention of reaching children through schools).

FIT also hung banners in the villages beforehand with the date and time of the event, and an announcement was made over the commune's loudspeakers when FIT's program was happening.

The campaign lasted eight days.

Application of tuberculin skin tests (TSTs)

For the first two-and-a-half days, health workers visited each village and administered TSTs to adults from about 7am to 4pm, with a lunch break. FIT then checked its list for individuals who hadn't come to the event, and FIT staff members, the commune's primary healthcare head, and a couple of local health workers went to the houses of those people and asked to administer the TST. (The local health workers generally knew where people lived.)

TSTs were ultimately administered to 1,804 of the 2,022 residents on FIT's list (91% of the enumerated population). Some people on the list were away on deep sea fishing excursions (though FIT scheduled the campaign during a low season for fishermen), and some people who were registered no longer lived on the island.

The TST tests for tuberculosis infection and requires patients to return for a reading within 48 to 72 hours. Patients were given an appointment sheet telling them what day and time to return for a reading and an x-ray.

TST reading, x-rays, and additional screenings

FIT invited all of the people who had received TSTs on the first day back on day three. Attendees went to a registration table where they gave their name, age, place

of residence, etc., which FIT checked against its pre-entered record of the island's residents. If someone had not been pre-entered (e.g. people who lived on the island but weren't on the list FIT received), FIT entered their information at that time. FIT then administered a basic screening questionnaire for TB symptoms.

TST reading, blood draw, and liver test

Attendees went to a TST reading station, where health workers read the skin tests that had been administered at the previous session. If the skin test indicated infection with TB bacteria, the health worker took a blood draw and centrifuged the blood sample. The blood sample was also used to do a rapid screen for hepatitis B and C. If the hepatitis B screen came back positive, the worker also did a rapid screen for hepatitis E.

As part of the new regimen for LTBI treatment, the NTP also requested a liver function test for every eligible person who indicated for TB infection (or for active TB disease). This is arguably overcautious, but given that this is the first time this regimen has been used at scale, FIT thinks it is reasonable. Liver function testing added some costs.

X-ray screening and collecting sputum samples

FIT rented an x-ray truck from the mainland and brought it to the island. X-rays were performed by the company FIT rented the truck from, along with some government staff.

Because the provincial health department requested that everybody on the island receive an x-ray screening, all attendees, including people whose TSTs didn't indicate infection, were sent to the x-ray station.

About 1629 people (of the 1,804) received an x-ray screening. Those who weren't x-rayed included children too young to x-ray, pregnant women, and some people who preferred not to be x-rayed.

A technician read the x-rays on the spot. If they noticed anything abnormal, the technician printed the patient an image of their x-ray and directed them to the next station, where a provincial-level physician put the x-ray image in a lightbox and diagnosed the anomaly. If the image was read as abnormal with suspicion of TB, the physician indicated for the patient to go to a station where a lab professional collected a sputum sample.

In total, 75 people had abnormal x-rays with suspicion of TB, and 71 of those people provided sputum samples (people who were unable to provide sputum entered a separate diagnostic pathway).

Additional health screenings

People who had provided sputum samples were then re-merged with people not suspected of TB infection to undergo respiratory function measurement (via inhaling into a spirometer to check for asthma or COPD). The local health

department also administered screenings for a) cervical and breast cancer, b) hypertension, c) hypoglycemia and diabetes, and d) depression; these screenings were only administered to a sample of the population because the health department had a limited level of funding and specific objectives for its report.

At the final station, patients handed back the paper they received upon arrival, signed out, and received a stipend for their time and to cover transportation cost.

Testing sputum samples on the mainland

Each day at 2pm, the lab technician took the collected sputum samples to the mainland by boat to for rapid molecular SPR (surface plasmon resonance) testing. (Tests collected after 2pm were stored in a fridge on the island till the following day.) Results for the tested samples were reported back to FIT's coordinator by telephone. FIT then worked with local health workers on the island to follow up with those patients by phone or by visiting their homes to deliver their test results and counsel them about next steps for treatment.

Active TB disease

Of patients who provided sputum, 10 were diagnosed with active TB.

Individuals with TB disease have to be initiated into treatment on the mainland. The ferry ride to the mainland (which takes about 20 minutes and costs about \$10) is often a major hurdle for many people who might otherwise seek out TB diagnosis or treatment. FIT gave stipends to patients whose SPR tests came back positive for drug-susceptible TB to travel to the district TB unit on the mainland to be enrolled in treatment by the NTP. FIT also helped those patients with the required paperwork.

Three patients had SPR tests that indicated drug-resistant TB. Those patients had to travel to the provincial TB hospital 60 miles away, where another confirmatory SPR and culture were done. FIT helped organize that transportation and provided stipends.

One of the confirmatory SPR tests indicated rifampin-susceptible TB; the other two indicated multidrug-resistant TB (MDR-TB). Second-line testing was done for the drug-resistant patients to confirm the disease, during which time the patients returned home. Once the final test results came in, the patients returned to the provincial hospital and were hospitalized for MDR-TB treatment; FIT helped facilitate their transportation.

At present, FIT has all 10 active TB patients still enrolled and on treatment.

Latent tuberculosis infection (LTBI)

Individuals with LTBI were started on treatment on the island during the campaign. Patients on the island who are receiving LTBI treatment are generally able to walk to their community health station and access care for free if needed.

FIT provided the district TB officer with a list of people with LTBI whose liver function tests had indicated ALT levels of under 40 and AST of under 56 (i.e. normal liver function). The district TB officer returned to the island a couple of weeks later with medicine and enrolled people for ongoing LTBI treatment who were eligible and volunteered, in batches of 50 to 60 patients at a time.

Ultimately, 404 out of about 460 eligible people (88%) were enrolled in LTBI treatment.

Cost of the program

The January island elimination program cost \$20,000 in program-specific costs (i.e. all the incremental costs needed to make the program happen). This included the costs of:

- Transportation, ferry costs, lodging, and food for staff who went to the island
- Stipends and additional labor
- Rapid tests for hepatitis
- Liver function tests

It also included the cost of LTBI drugs, which accounted for close to \$7,000 of the \$20,000.

The \$20,000 figure does not include:

- Costs associated with the program's training and planning period
- Salaries or overhead for FIT staff or government workers
- FIT's site coordinator's time (who didn't take a salary)
- Medication for active TB disease
- SPR cartridges
- TB skin tests (which FIT already had at the ready)
- The costs of the non-TB screenings that the provincial health department contributed

FIT estimates that, with these additional costs included, the program's total cost was roughly \$35,000.

Costs to patients of TB treatment

Under Vietnam's current healthcare system, the government pays for TB diagnosis, care, and medicine for eligible participants, i.e. people with symptoms or who have had exposure. The central government currently pays for first line drugs out of its discretionary budget. Vietnam is in the process of shifting those costs to a new social health insurance policy it is rolling out, under which people would be expected to buy a social healthcare plan for their household, which would cover TB services. In some cases, that plan wouldn't cover the true cost of treatment, since there are often hidden costs (e.g. transportation). The government also has an agreement under which the Global Fund covers all costs related to drug-resistant TB.

Several indirect costs to patients, such as transportation and lost wages, are not covered by insurance. The majority of costs to TB patients before and during treatment are in the form of lost wages, either from missing work (government health centers are usually only open during the week and often have long wait times, which can cause patients to miss work) or because they get fired (TB affects many low-income people whose jobs don't have good job protection). People then need to access savings (which they often don't have), sell assets, or take on loans.

Some people have begun going to the private sector for care; in these cases, health insurance reimburses patients a certain amount for e.g. consultations and x-rays but may not cover the whole fee, in which case the patient pays the balance.

Impact and monitoring

Before FIT began working in Hoi An through the Zero TB Vietnam initiative, no active TB case-finding was occurring. In 2017, there were only two known active TB patients on the island. After implementing active case-finding, the Zero TB Initiative found seven new cases on the island in 2018. FIT decided the next step would be a more intense campaign, screening the whole population for TB and treating TB infection with the goal of eliminating the TB reservoir.

During the one week campaign in January 2019, identified 10 people with TB disease, including two drug-resistant cases, and over 500 people with TB infection. This represents a major scale-up of diagnosis and treatment.

A local FIT staff member is supporting government primary care workers to monitor patient treatment for both LTBI and TB disease.

Case for focusing on islands

FIT has chosen to focus on island screening (i.e. going to high-risk, high-burden islands and screening the entire population) both because a) given their level of isolation, there is a better chance of eliminating TB in those populations, and b) there is a higher TB burden in those populations (for instance, the 2018 notification rate on the island of FIT's January campaign was 3.5 to 4 times higher than the national average).

In urban areas, it's difficult to model how high levels of migration in and out of the city impact transmission dynamics.

Counterfactual if FIT had not run this program

If FIT had not run this program, FIT thinks it is possible the number of identified active TB cases on the island might have risen to three or four, but almost certainly not 10. FIT thinks the Vietnamese government likely would not choose to do island elimination campaigns on its own unless funding for them were included in the Global Fund envelope. Active case-finding of this kind is not included in the Global Fund's 2018-2020 envelope (though that might change next round due to new prevalence survey results, etc.).

Absent FIT's program, LTBI testing and treatment on the island would almost certainly not have happened. The Global Fund has now added a couple hundred thousand dollars to Vietnam's portfolio for scale-up of LTBI testing and treatment, but this is currently still concentrated on a couple of provinces and large cities; there is still not support to screen for and treat LTBI on a population basis.

The most significant bottleneck for the government running programs like this on its own is funding; these programs fall outside of the routine TB activities for which government funds are available. (The government is trying to establish legislation to request more TB funding, but that funding wouldn't necessarily go to activities like these.) Even with funding, FIT thinks the government would be somewhat limited by its human resources.

Monitoring active TB disease treatment

Treatment monitoring for TB disease is happening within the national routine system. Patients with drug-susceptible TB need to visit the city once a month, bring their medication back to the health station on the island, and do directly observed therapy on the island. FIT's impression is that the procedure is similar for patients with drug-resistant TB (though those patients need to visit the provincial health center).

The health program's resources don't allow for directly observed treatment for all patients. FIT believes infectious individuals who were taking treatment for TB disease likely did have some kind of directly observed therapy with a health worker, as well as weekly check-ins during the intensive phase of treatment.

Monitoring LTBI treatment

FIT is monitoring adherence and treatment completion rates for people taking treatment for LTBI. Because FIT is the first group to aim to address LBTI in Vietnam at any scale, there was no existing routine monitoring system for LTBI in place.

Patients receiving LTBI treatment had in-person check-ins weekly for the first month, then monthly check-ins after that. FIT has patients bring their medication blisters to check-ins to monitor whether they've been taking the treatment

Two health care facility staff members are also making weekly phone calls to patients on LTBI treatment to ask whether they've experienced any symptoms or adverse events. FIT has recorded about 20 adverse events in LTBI patients so far, none of which were serious (e.g. itchiness, headaches, nausea), but which have led some patients to discontinue of treatment. Other patients have discontinued treatment because a) they left the island (e.g. members of the military) or b) family members or other doctors counseled them that their treatment wasn't necessary.

FIT would ordinarily have done monthly check-ins for patients being treated for LTBI. However, because FIT was using a new LTBI regimen and a new drug (which is recommended by the WHO but had not been previously used in Vietnam), the NTP

asked FIT to do weekly follow-ups. FIT thinks it will likely scale back the frequency of follow-ups for LTBI in the future.

Comparing short-course and normal-length treatment regimens

The government gave FIT permission to implement a non-standard short-course regimen (three months) for LTBI treatment. Once a cohort of FIT's patients in Ho Chi Minh City have finished the standard nine-month LTBI regimen, FIT hopes to compare the short-course regimen to the standard regimen to see whether using a short-course regimen improved adherence in this population (though it has not done a controlled trial to look at adherence rates).

Longer-term monitoring and follow-up

FIT has several ideas for longer-term follow-up and for measuring the effectiveness of the program:

1. For people who a) were eligible for preventative treatment but didn't accept, or b) started preventative treatment but were lost to follow-up, FIT plans to do surveys to learn why. FIT plans to use these survey responses to help it tailor its messaging as it scales up preventative treatment in other areas.
2. FIT is monitoring official TB statistics in the region to see how notifications have changed following the 2019 intervention, compared to the baseline level of notifications in the period from 2016 to 2018. It expects to see a spike in notifications in areas where its program has worked (as more cases are diagnosed), followed by a decline as fewer new TB cases are reported.

FIT can carry out those activities with relatively limited funding, without additional support beyond its existing grants. With GiveWell funding, FIT might be interested in pursuing additional, more robust measurements of impact, including:

3. FIT has considered revisiting the island 9 to 12 months after the January intervention and running additional TB screenings to see whether an active search using the most sensitive diagnostic algorithms identifies people in the community who still have TB and who have not yet decided to seek care. In addition to determining the proportion of patients with abnormal x-rays, TB diagnoses, etc., FIT would also be interested in looking at the health status of people who started preventative treatment in January to see whether any have any relapsed, are experiencing symptoms, whether their chest x-rays indicate any change in TB status, etc.
4. FIT would be interested in looking at the impact of its programs on patient costs and spending, in addition to health outcomes. TB is a significant driver of poverty in Vietnam.

Impact of LTBI treatment and risk of reintroduction following TB elimination

While the evidence base for preventative treatment for TB is generally strong, there is a very limited evidence base for the impact of LTBI treatment in high-burden settings, and there have not been many long-term follow-ups. One 20-year follow-

up, led by G.W. Comstock, on LTBI treatment in the Inuit population in Alaska showed a reduction in TB rates from 300 in 100,000 down to rates more similar to most other parts of the US.

While there is some evidence on the long-term persistence of the effects of TB treatment in high-risk populations, there is very limited literature on the risk of reintroduction after TB elimination in a high-burden setting. TB transmission dynamics are not fully understood, and it is difficult to predict e.g. how likely someone who has been treated for TB infection is to be reinfected due to ongoing transmission in the community.

FIT believes there is some risk that, even if TB were eliminated, it could be reintroduced onto the island. FIT would like to monitor the community to see how long TB elimination persists and to generally get better evidence about the long-term effect of a one-time intervention in a high-burden setting.

Because FIT has administered preventative treatment to so many individuals with TB infection, the reservoir of infected individuals who could develop active TB is significantly smaller. If the disease were reintroduced, it would likely take a long time to reach its current scale again.

Current funding sources

Several different donors contribute to FIT's work. Most of FIT's funding comes from large grants; individual donors make up 5% or less of FIT's total receivables.

FIT operates almost exclusively in Vietnam and works mainly in urban areas. The majority of FIT's urban work is funded by a grant from the European Commission Horizon 2020 program for operational research for scaling up proven interventions. FIT also has some funding from the Zero TB Initiative in Vietnam. FIT has also received smaller grants, e.g. for bringing delamanid into Vietnam.

FIT also has a grant from the Stop TB Partnership, which is focused on mobile chest x-ray campaigns. In urban areas of Ho Chi Minh City, FIT is using those funds primarily to screen elderly people (who have the highest rates of TB, and the highest risk of being overlooked by government health services). In Hoi An and Haiphong, FIT has used those funds to do island screening.

Potential uses of additional funding

FIT believes there are many areas that could be productively targeted by its programs, including both islands and other areas (e.g. particularly high-burden urban areas), as FIT's approach matures and the evidence base for this type of intervention expands.

FIT did a scoping exercise to explore activities it might pursue if it received a GiveWell grant, looking into islands with populations of up to 200,000, additional grants it might apply for, etc.

If FIT receives the larger \$250,000 grant, it would likely plan to:

- Run a program on Cat Ba, an island in the north of the country with a population of about 16,000. FIT could cover the entire island.
- Revisit the island of the January campaign to get an understanding of the medium- to long-term impact of its program on TB prevalence.
- Synthesize its results and attempt to publish them in international journals.

If FIT receives the smaller \$25,000 grant, it might engage in a program on another island in the same province as its January campaign, which it has visited for some initial scoping. The population of that island is a bit larger than the island from the January campaign, so FIT might need to commit some co-financing from other grants it has on hand to run a program there. The head of the provincial health department for that island has expressed interest in having FIT come work there; having support at that level of government is very helpful.

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