Laboratories and migration: a case study from Nepal

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Introduction

Drawing from ongoing research into the role of laboratories in TB control, this paper focuses on a laboratory established by the International Organisation of Migration (IOM) - an intergovernmental organization - in Eastern Nepal. Supported by the CDC, its primary purpose is for the screening of refugees. From the 1990s, following a process of ethnic cleansing in Bhutan, over 100,000 Bhutanese of Nepalese origin migrated to Nepal and were housed in refugee camps. In 2007 the U.S. announced that they would offer settlement to most of those remaining in the camps in Nepal. The state-of-the-art lab was installed near the camps to screen (and then treat) infectious diseases, in particular tuberculosis, in the refugees prior to resettlement. However, these services are far superior technically and medically than those provided to the surrounding population through the Government of Nepal Primary Health Care setup and it National Tuberculosis Programme, and were dependent on policies and practices developed by the CDC. Aware of this medical, ethical and political dilemma, the IOM started to draw up protocols for greater "harmonization" with local services, and to support local laboratories through the provision of GeneXpert machines, a new technology, recently sanctioned by the WHO, used for speeding up the diagnosis of TB. In this paper we explore the geo-political, ethical, social and technical issues that followed in the wake of this complex assemblage, to pose questions to current thinking around the emergence of ideas to what makes up "global health".

This paper thus explores the question: What are the conditions of possibility under which a new diagnostic technology for tuberculosis (GeneXpert) comes to be in Nepal? What global and local historical and political conditions have both made this possible, and pattern its reception? What does its presence and use tell us of the political economy of laboratory provision in Nepal? What impact does the introduction of this piece of technology have on laboratory and health systems performance?

Scenario one:

The town and municipality of Rajbiraj, with a population of a little over 30,000 is in in the flatlands (Tarai) between the hills and the border with India, and acts as the centre for zonal government administrative offices, and hospitals for Saptari district. We have travelled for several hours to get here, through the fields and plains along the East-West Highway from Biratnagar. The government public health laboratory sits within the hospital compound, and acts, we were informed as the laboratory for diagnosing Malaria, TB and Kala Azar. To access it one walks through the compound, past a dilapidated building next door which acts as a dump filled with old beds and furniture. The lab itself is upstairs, and is situated on a terrace and consists of two red brick rooms. Beyond the open balcony is the space where the sputum is collected, and fixed (a metal bucket sits on the edge, and is stained a deep red from the Zeil-Neilson stains for the microscopy). From this balcony, one can gaze across the compound, and directly towards the hospital spaces and wards, and administrative buildings for the district and zone.

The laboratory space itself is divided into two by the corridor leading to the balcony. The first is where the samples are prepared. There is no safety cabinet for the preparation of samples, and biosafety seems to consist primarily of the wearing of surgical masks (no WHO recommended N90 masks here), and the capacity to open the windows. (While we had been told in Kathmandu that biosafety protocols had been made and distributed, they were not on evidence here, and they were not utilised an any of the labs we visited). Pots for the collection of sputum, and cartridges for the Xpert machine are sitting on the desk (a used syringe and needle sit on the desk, undisposed). There is a sink in the corner for staining. The second room, where the geneXpert is housed, is cramped and very dusty, and consists of a table, where the microscopy is also performed, and a cabinet for files, and a desk against the wall. The shiny new Xpert machine, and its associated desktop computer and generator backup for when the electricity inevitably fails, sits incongruously against the wall, seemingly out of place in this dusty and resource starved space. There are slides in a slide stand and lab register on the table. We are here to talk to staff and supervisors about this new technology and sit in the cramped room. As we wait the laboratory worker turns on the machine, and places the first cartridge in the Xpert. He explained how a consultant from Germany, working with the International Organisation of Migration (IOM) who had provided the machine, and undertake the technical support, had installed it and calibrated it ready for use, and trained them in its use.

The GeneXpert (Xpert MTB/RIF) was introduced as a supplement to the use of microscopy for the diagnosis of tuberculosis, and has been here since 2012. It is “an automated, cartridge-based nucleic amplification assay for the simultaneous detection of TB and rifampicin resistance directly from sputum in under two hours”[i]. GeneXpert is a classic “inscription device” in the Latourian sense (Latour 1978). Within the laboratory, this is “any item of apparatus or particular configuration of such items which can transform a material substance into a figure or diagram which is directly usable by one of the members of the office space” (p51). It takes a centrifuged sample of sputum or other tissue, and provides a reading on a screen after two hours that states whether genetic material from the tubercle bacillus is a) present or not and b) if it is present, whether it is resistant to the drug rifampicin. Staff at the laboratory prepare the cartridges in the other room – they use the second sputum sample for this from the national protocol of taking three sputums from everyone suspected of tuberculosis (that is if they have a cough for more than three weeks) and place these into machine, then wait for two hours till the result flashes up on the computer screen. They have been managing around 100 or so test per month. In the opinion of the laboratory technician this technology has been very beneficial; It detects hidden cases; It also does the work of culture, that is

identifying drug resistance in hours rather than months. It has been easier for treatment of patients he says.

Scenario two:

Visiting the International Organisation of Migration (IOM) laboratory and clinic in Damak (IOM-Migration Health Department (MHD)), East Nepal is a dislocating experience. We have travelled here after visiting Rajbiraj. It lies in the flatlands of the Tarai 2 hours east of Biratnagar, and sits opposite the guesthouse housing the international workers and visitors, both enclosed by barbed wire topped walls and they are heavily guarded. A sliding metal gate opens to allow buses carrying refugees from the nearby camps into the facility. Its primary purpose is the screening of Bhutanese refugees before they are sent to the US, who have agreed with Nepal to resettle the majority of these refugees. We are here to talk about GeneXpert.

We were walked through the facility, and were shown the waiting room, examination spaces, through to the areas where the refugees awaiting the travel to the US are x-rayed, bled, and sputum is collected and then in refined form moved to laboratory spaces where diagnoses are elicited. As we were told, they were not going to allow a single TB bacillus into the US. We were shown a white board hanging on the wall in the corridor. It had different sections drawn up on it - new cases, PDMS [pre-departure medical screening], pre-embarkation, follow up, TB follow up, TST reading, psychiatry and vaccination in the rows and there were multiple columns with the names of different refugee camps. Every day, this board is updated with numbers in the field given. It was explained that the pre-embarkation follow up is done 72 hours before the refugees leave for their host countries. We were shown where the digital x-rays are taken, and explained that these are simultaneously read here, and if a technician is not available, in the Philippines to where it only takes two minutes to send the images. They have the on-call facility of up to six doctors at any one time.

The laboratory itself is a bio-level safety 3 facility, based on the CDC ranking, because it primarily deals with *mycobacterium tuberculosis* (there are four levels in total, the highest – which deals with Ebola, for example – being level 4). We were not allowed in, but the negative pressure light, and the alarm system should this fail was pointed out. Standard Operating Procedures pointed to the exact procedures for gowning up, and the shift into this tightly controlled space. Through the glass gowned figures prepared samples within bio-safety cabinets. We were told, and then shown, the fluorescent microscope for reading the sputum samples, and had explained to us the liquid and solid culture for every sample, and that they do 9 culture in total for every person. We were shown the BACTEC machine for liquid culture[ii]. The laboratory technician in charge, from Thailand, explained that there are different types of TB strains and some grow in solid media and some grow in liquid media and therefore they do culture in both media for diagnosis of all kind of TB. None-the-less he explained that maintenance of system was a 'headache' for them. They have to maintain regular power back up, an issue these days throughout Nepal; that it costs USD 3 for every tube for liquid culture and stable power is required to run the machines. He also said that staff from IOM Thailand have to come over here for maintenance as there are no local providers. He also said that they use disposable gowns and masks and the costs for these are very high. We were shown the two Xpert machines, amongst all the other high technology equipment, and told that there were rarely used. Later, in the comfortable surrounds of the Director's office, drinking tea, we were informed that the laboratory follows CDC protocols. According to the director the GenXpert machine has not been approved by the CDC for use, so they rarely use it. He also reflected on the limits of its use, because it detects dead genetic material and thus cannot be used for previously treated or follow-up

patients. In short, its impact in this state of the art laboratory for diagnosis of tuberculosis is extremely limited.

Throughout the tour we couldn't shake the images of the government run laboratories we had just come from visiting, with their broken windows, frequently unused and broken equipment and all but non-existent bio-safety procedures. The difference between the standards of these IOM facilities, and those available elsewhere in the area was deeply distressing, reflecting massive resource disparities. As we had been told in Kathmandu prior to travelling down, we would be impressed with these facilities as the laboratory was one of the best in South Asia.

How then, did this laboratory come to be here? What were the political conditions that led to the existence of the refugee population it is here to screen?

Bhutanese refugees in Nepal, and IOM's role

Bhutan, is a landlocked and mountainous nation-state nestled in the Eastern Himalayas, sandwiched between India and China (Tibet). The Indian states of Sikkim and a thin strip of West Bengal sit between it and the eastern part of Nepal. With a population (depending on the source used) between 600,000 and 1,000,000 it is ethnically diverse, and subject to considerable orientalist imaginings here in the UK (two of the latest being its dependence on measures of "gross national happiness", an idea said to be liked by the British Prime Minister, David Cameron, and as the idealised home of the endangered Black-necked Crane, nestled amongst chanting Buddhist monks).

There is not enough space here to go into the complex history of how the refugee crisis came about (I refer the reader to Hutt 2003 for a detailed history of this, and relations to its ethnic politics). In short, the *Lhotshampa*, (the term used generically to refer to the ethnic Nepalese population – that is Nepali speaking, although they are diverse across caste lines and ethnic lines - in the southern part of Bhutan, but is the Bhutanese term for "Southern Bhutanese") started to move in increasing numbers from the 1990s from their homes in Southern Bhutan into the Terai in Eastern Nepal in the 1990s. This resulted from a series of Acts, and ethnic and cultural policies in Bhutan that made their acquisition of citizenship all but impossible, and with their re-classification as non-nationals. While Hutt is reticent to suggest that this migration resulted from "ethnic conflict" (p13) it did result from a series of shifts that increasingly came to recognise one particular ethnic identity as distinctively Bhutanese, and the *Lhotshampa* as a threat to this way of national being.

The first refugees from Bhutan entered Nepal in 1990. The Government of Nepal requested the UNHCR for help to coordinate emergency relief in September 1991, and a particular assemblage of organisations, particularly INGOs and NGOs started to work with the organising of the emergent camps (Lutheran Word Service, CARITAS Nepal, SCF UK, World Food Programme, Nepal Red Cross, OXFAM, CVICT). According to Hutt, the new arrivals in the camps had peaked by mid 1992, and down to only one or two per day during 1995. By 1994 there were Bhutanese refugee camps at five different sites: Timai, Goldhap, Beldangi, Khudunabari (in Jhapa district) and Sanishchare (in Morang). As of January 2000 there were nearly 100,000 people registered in seven camps.

Established in 1951, the International Organisation of Migration (IOM) is the leading intergovernmental organisation in the field of migration. An MOU was signed between the Nepalese government and IOM in 2007, the year after Nepal itself became one of the 151 member states of the organisation in 2006. In the overview section of Nepal on the IOM website, the challenges of

transition have created the situation where Nepal faces considerable problems with regards to managing migration. According to this narrative "push factors" for migration in the Nepal context include rising unemployment, the insurgency and poverty, and with high levels of illiteracy and many being unskilled this makes them particularly prone to being trafficked, a problem worsened because of the "porous" border with India.

Within the focus on refugees and the displaced is the resettlement programme for the Bhutanese refugees (http://nepal.iom.int/jupgrade/index.php/en/aboutus/18-topic-details/52-about-us-2). By December 2014 (since the start in February 2008), 94,651 Bhutanese refugees had been resettled under IOM's auspices, and collaborating with UNHCR, the Nepalese government and the (eight) governments where they are being resettled. This involves the medical screening process, based on the protocols of the receiving countries; and "cultural orientation" in preparation for travel to the country that will receive them, facilitating the various permits for leaving and entry, and the arranging of the travel itself[iii]. It is estimated that the IOM resettlement programme will run through till the end of 2016.

There are two IOM clinics and laboratories in Nepal. One in Damak, and the other in Kathmandu, with the former dealing with all the resettlement cases from the Bhutanese camps. The Damak laboratory also acts as the reference laboratory for the clinic that IOM run in Kathmandu. A contract with the private Yeti airlines Yeti allows the samples to be flown and transported to Damak in East Nepal (the same airline from which flights are chartered to fly the refugees to Kathmandu where they are held until their onward trip). The two IOM clinics are the only ones certified by the Government of the UK for pre-travel tuberculosis testing[iv].

Even as early as 1995 – prior to the arrival of IOM - it was reported that in terms of resources, "the refugee camp appears as an island of privilege", including clinics and medical health services (Voutira and Harrell Bond 1995, quoted in Hutt 2003: 258). Dealing with the fact of the difference between the availability and quality of services provided by IOM and those in the surrounding area has been an issue for IOM. The question of "harmonisation" involves attempts to align the management protocols of those with TB in the "resettlement pipeline", acknowledged as superior, to those available from the NTP[v]. This focuses on those individuals in camps who are not being resettled and involves making (some of) those technologies and procedures at the clinic in Damak more widely available: chest X rays, smear and cultures, contact tracing, drug susceptibility testing, and the isolation of those diagnosed with drug resistance in the especially built isolation unit (The Magic Mountain Isolation Centre), the latter built in partnership with the NGO AMDA[vi]. This includes training of some of the AMDA staff. Harmonisation here, then, extends the services available to those registered as refugees, but not to strengthening the existing services for NTP. For this IOM turned to the provision of geneXpert.

The question of why, we turn to next.

Why GeneXpert and what does it do?

GeneXpert was introduced into the world of global tuberculosis control – with considerable fanfare - after being sanctioned by the WHO in 2010 as a suitable adjunct to the use of microscopy for diagnosis. The Directly Observed Therapy, Short-course (DOTS) programme introduced since the mid 1990s had sputum smear microscopy as the main diagnostic cornerstone for the tuberculosis control

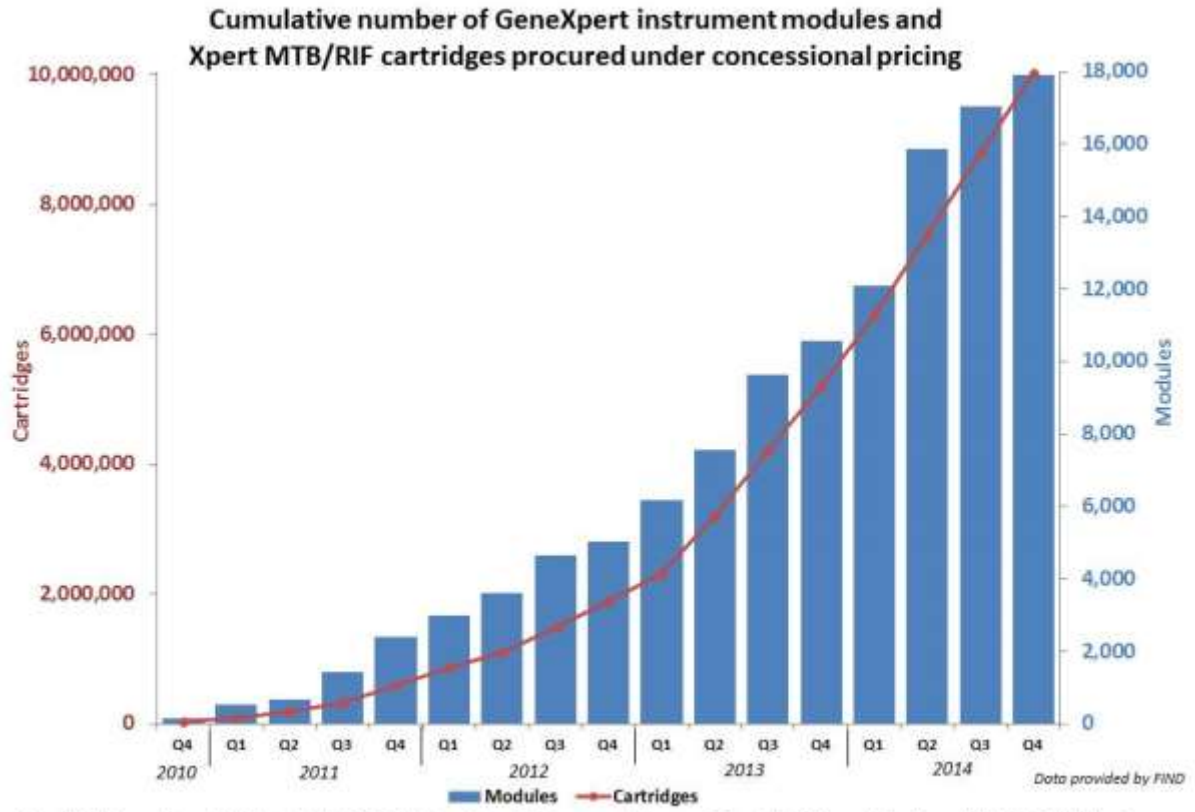
programmes. The clarion cry was that not since Koch and the staining and visualisation of bacilli with the microscope – a technology over 100 years old - had there been a new diagnostic tool used in TB control work. A paucity of the availability of diagnostic tools in TB control is said to add to the already large delays in diagnosis and recognition of those who have the disease[vii].

However, over the last decade there has been a shift in thinking behind so called case finding in tuberculosis control, and this has fed into the push to diagnose more TB. Passive case finding involves the principle "that affected individuals are aware of their symptoms, have access to health facilities, and are evaluated by health workers or volunteers who recognize the symptoms of TB and who have access to a reliable laboratory"[viii]. Active case finding is the active going out into communities and spaces of known transmission and finding those with the disease who may be transmitting it to others. The initial reluctance to become involved in active case finding was linked to the belief that those who self-presented to a diagnostic facility were more likely to finish the long duration of TB treatment than those actively sought out for diagnosis. The fear was that active case finding would generate a rise in drug resistance as the number of those with the disease not finishing treatment would increase. The demonstrated efficient treatment and follow-up of TB patients in many part of the world post DOTS and with the STOP TB Programme facilitated this shift in thinking.

A second discursive shift was the rise in ideas around point-of-care tests and diagnostics (POCT)[ix]. GeneXpert markets itself as just this, and is one of a range of new rapid diagnostic tests being developed and introduced into the market (Street et al 2014). The idea behind POCT is to make available diagnostic tests as close to the patient as possible that can then effect the subsequent treatment. GeneXpert's great value has been that it can act as a proxy for the diagnosis of Multidrug resistant tuberculosis, thus cutting this diagnosis from months with available culture tests, to just hours. Research around the world focused on this capacity to act as a proxy indicator for MDR.

Immediately GeneXpert was sanctioned by the WHO as the go to diagnostic tool for tuberculosis, there was a flurry of purchasing activity around the world. South Africa quickly became the first country to commit to country wide rollout for the technology. At IUATLD international and regional conferences, presentations began to be dominated by demonstrations championing its impact, and questioning the claims of its effectiveness. Sessions could be attended on how to plan, centrally, for the rollout of the technology and meetings were held on lessons learnt.

Currently, the WHO monitors the rollout. A graph (see below) shows the cumulative increase in the use of Xpert, and that over 3,700 machines and over 10 million cartridges by December 2014 had been procured world wide[x]. In addition data is available on an interactive website that allows us to see which countries (within the WHO regions – which are specific to the WHO; Nepal, for example, is in SE Asia) have availed themselves to the technology. Further filtering by technology is also possible, indicating how many Xpert machines, modules – each machine has either 2 or 4, and cartridges have been procured). Also available, a link to the FIND website shows a list of countries that can avail themselves to price concessions, and access to various implementers' meeting minutes. The initial 2011 workshop for "early implementers" has by 2014 become the "global forum" for Xpert implementers. This is a fast moving terrain, and at the same time the data and papers being produced are on the increase. WHO publications focused on increasing the diagnosis of tuberculosis in vulnerable groups, for example "Intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings" (2011); Publications assess the usefulness of targeted strategies addressing increased case-finding in certain at risk groups such as migrants, homeless people, illicit drug users, alcoholics and prisoners (see, for example, Zenner D, Southern J, van Hest R, DeVries G, Stagg HR, Antoine D, Abubakar I, 2013).



As of 31 December 2014, a total of 3,763 GeneXpert instruments (comprising 17,883 modules) and 10,013,600 Xpert MTB/RIF cartridges had been procured in the public sector in 116 of the 145 countries eligible for concessional pricing.

Publications of the results of using Xpert have also proliferated and feed the ongoing debate as to its value and use. A pubmed search for Xpert MTB / Rif reveals 372 articles published (two on Nepal) (Accessed 30 July 2015). Over the last four years significant numbers of papers and poster presentations at the global and regional International Union Against Tuberculosis and Lung Disease (IUATLD) organised conferences have focused on Xpert and its impact. By January 2013 the first review of published data of its accuracy as a diagnostic tool was published in the Cochrane Library[xi]. An editorial linked to this asks, given the paucity of existing diagnostic tools for TB (smear microscopy) what next?[xii]

Nepal, then, is one of the countries availing itself to this new, rapidly expanding technology. Prior to this focus had been on a network of laboratories across the country reliant on microscopy.

The National TB microscopy network

Across the country and in labs similar to that described at the beginning of this paper, protocol points to the need to collect three sputum samples, one of which has to be in the early morning, staining the smeared sputum on slides with the Ziehl–Neelsen technique (also known as the acid-fast stain – which preferentially stains the genus mycobacteria), examining this under a microscope and thus making a diagnosis. This is touted as the cheapest and most efficient means of eliciting a

diagnosis. One of the five pillars of the DOTS programme, this became the diagnostic cornerstone of the programme, and consequently this informs every other aspect of programmatic processing from treatment categories, treatment regimes, and recording and reporting. In Nepal this diagnostic function was carried out through a series of laboratories developed through the existing public health laboratories, with quality control support from a number of existing NGOs. The official website for the Nepal NTP suggests that there are 315 laboratories operating across the country.[xiii]

Sputum microscopy is a relatively time consuming operation and the laboratory staff have to spend at least ten minutes on each slide to ensure a negative diagnosis. Quality control in operation checks for false positive and negatives, and human error. All the positive slides and 10% of the negative are cross checked. This function has been devolved to the five regions, (Nepal is administratively carved into five regions and seventy five districts) and has been developed with NGO support. In East Nepal, this function has been undertaken since its inception by the INGO, the Britain Nepal Medical Trust, where we were informed the service consists of the following: Sputum Smear cross checking (Feedback provision); Reagent preparation and supply; Supervision and monitoring; and Training. The main issue faced is the relatively high turnover of government staff, and that inexperienced staff take on the role and are more likely to make mistakes.

Centrally there is a laboratory at the National Tuberculosis Centre, whose role is to act as the national reference laboratory. Under-resourced there has been a long standing relationship between the NTP and the work of the NGO GENETUP – a German funded INGO - which for all intents and purposes has been acting as the national reference laboratory for years. While it has been the intention of the NTC to become the national reference laboratory, linked to a supra national reference laboratory network they have to date been unable to perform this function. GENETUP performs the culture and Drug Sensitivity Testing (DST), and is linked to the only chest hospital in the country. They also perform much of the laboratory related research for tuberculosis, a point of some tension in the country. In Nepal, then, as Briggs and Mantini Briggs describe, in the context of Venezuela, a hierarchy of laboratories form a network from the local to national facilities, and beyond to the international reference laboratories (2004). Epidemiology lab departments are linked up and connected in crucial ways, and have a scientific monopoly on both the control and flow of epidemiological statistics (p257). The production of epidemiological statistics is what grants national and international institutions their legitimacy, and why it is almost impossible for other discourses, and counter claims to get a look in (p258). Official statistics strengthen the power of the nation and state. As Leach and Dry also point out, these narratives are also always about power (2010).

The network of laboratories that IOM is involved with for their refugee resettlement work has no links with the Nepal NTP. The presence of the IOM laboratory, with its links to the CDC, the Phillipines, and Thailand, have a network that not so much declares the Nepalese generation of knowledge as true or false, but just supplants the generation of national statistics completely. It has no faith or trust in their capacities at all for the migrant Bhutanese population.

Into this laboratory context, GeneXpert in Nepal was first introduced by the IOM.

TB REACH and GeneXpert in Nepal

TB Reach was established in early 2010 with the aim of providing “short-term and fast-track grants to projects that aim to achieve early and increased TB case detection using innovative approaches in

populations that are poor and vulnerable and have limited access to care"[xiv]. The office is housed in the STOP TB Partnership in Geneva, and it is funded by Canadian bilateral aid money (CIDA)[xv]. The Programme Steering Group has members from several national TB programmes, and a particular constellation of organisations (many of which appear regularly in other global TB initiatives as well)[xvi]. The funding is disbursed in waves (or rounds), and by the end of wave three of funding a total of 109 projects in 44 countries had been funded. At the time of writing (July 2015) wave four funding had been agreed.

In Nepal the following organisations were funded: Wave 1: Family Health International (FHI); Wave 2: The Britain-Nepal Medical Trust (BNMT); the International Organisation of Migration (IOM); Wave 3: Health Research and Social Development Forum (HERD) (Wave 4 includes three new projects, including another one by IOM – initiated after the main fieldwork for this project had been completed).

Thus the IOM project is one of a number of initiatives started in Nepal seeking to increase case finding of tuberculosis, and was linked directly to the procurement and use of GeneXpert machines. This they started in October 2011, becoming fully operational by January 2012, with the aim of increasing the early case detection of Tuberculosis through its use in the Eastern Region of Nepal. The website categorises these "point of care instruments", seven for the region and one each for the National Tuberculosis Centre, and one in Parsa district[xvii]. Thus with a target population of the entire Eastern Region and two other it aims were to reach "in particular impoverished, vulnerable and hard to reach populations, including, but not limited to, residents of hilly and mountain districts, labor migrants and people living with HIV".

While introducing the GenXpert, the IOM initiated a communications campaign through popular and widely available media – radio, health education materials and through community health. Glossy pamphlets and flyers were made (in English and Nepali) for both those visiting health sites and for health workers to raise awareness of the technology being introduced:

GeneXpert MTB/RIF Assay

An Introduction

What is GeneXpert MTB/RIF?

The Xpert MTB/Rif test is a cartridge-based fully automated NAAT (nucleic acid amplification test) for the simultaneous detection of *Mycobacterium Tuberculosis* (MTB) and Rifampicin (RIF) resistance directly from sputum. It purifies, concentrates, amplifies (by rapid, real-time PCR) and identifies targeted nucleic acid sequences in the TB genome, and provides results in 2 hours, with minimal hands-on technical time. **This test is available in Nepal now.**

Benefits of the test:

- Gives accurate results in 120 minutes
- Simultaneously detects TB and Rifampicin drug resistance (a reliable indicator for MDR-TB).
- Has high sensitivity and specificity to detect MTB. Using this test, case detection rate can be increased more than twice.
- Requires minimal bio-safety requirements and training thus can be installed in any laboratories.
- Allows physicians to treat TB rapidly and effectively

Who should be referred for test?

- New smear-negative patients with high suspicion of TB as judged by clinical symptoms and abnormal Chest X-ray consistent with TB.
- Re-treatment cases regardless of results of sputum smears.
- HIV positive patients with high suspicion of TB.

Three easy steps of test:

1. Mix "Sample Reagent" with the sample. Incubate for 15 minutes in room temperature.

2. Transfer diluted sample into cartridge

3. Insert cartridge and start the test

Where is the service available?

1. National TB Centre, Thimi, Bhaktapur
2. Narayani Sub-Regional Hospital, Birgunj, Parsa
3. District Hospital, Ilam Bajar, Ilam
4. NATA DOTS Plus Clinic, Biratnagar, Morang
5. NATA DOTS Clinic, Bhadrapur, Jhapa
6. BP Koirala Institute of Health Sciences, Dharan, Sunsari
7. Sagarmatha Zonal Hospital, Rajbiraj, Saptari
8. Mirchaiya Primary Health Care Centre, Siraha
9. District Hospital, Ghaighat, Udayapur

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IOM OIM

Stop TB Partnership TB REACH

Introducing the new technology was complicated by the fact that nearly immediately medical practitioners in the area started to demand that their patients were availed to the new technology. Patients too, on hearing of the new technology, and doubting the diagnostic abilities of the lab staff demanded the "computer test" for themselves. The IOM, however, had limited resources and a very specific remit in relation to their TB Reach grant. In order to rationalise the use of the Xpert IOM introduced an algorithm, one that became the template for the Tuberculosis programme.

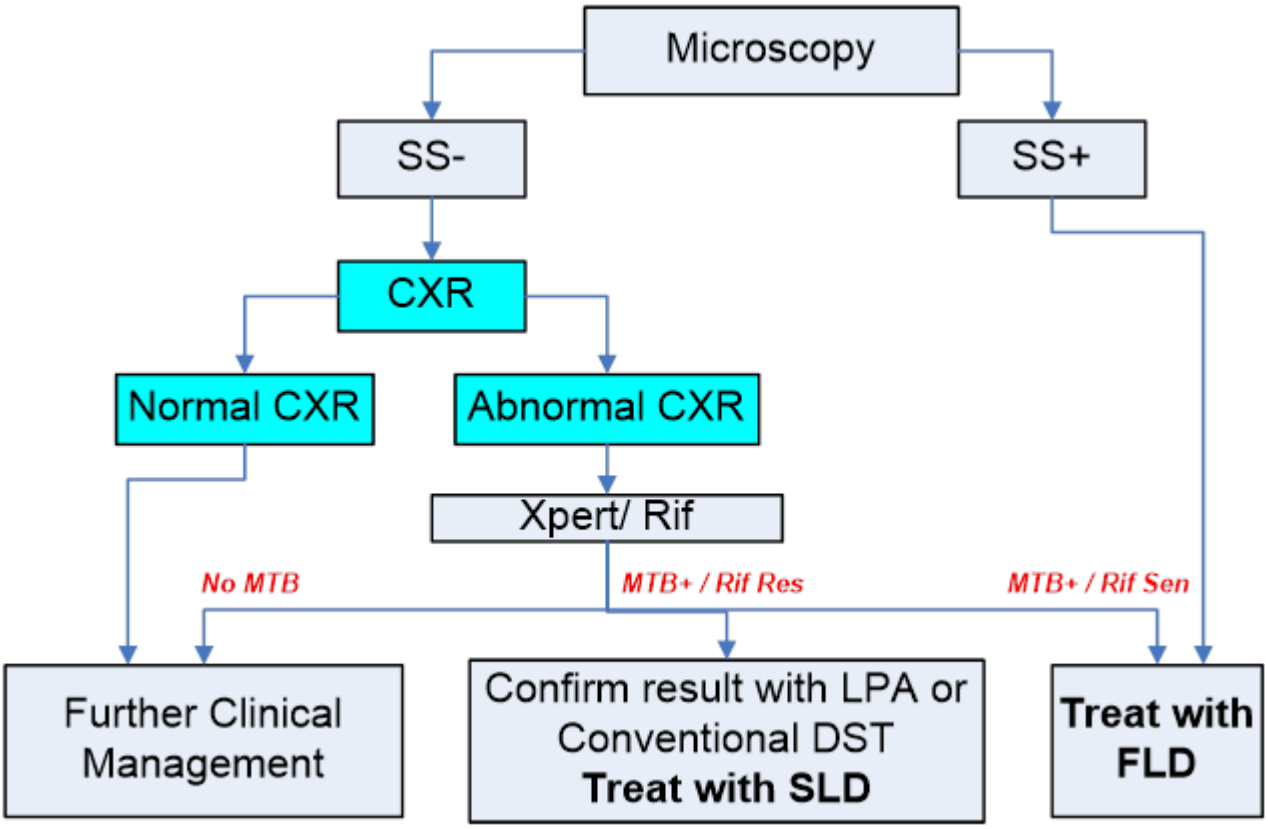

Figure 2: IOM logarithm for the introduction of Xpert.

As can be seen it was to be used – initially - as a supplement to existing tests, only on sputum smear negative patients with an abnormal X-ray. Issues with the use of this algorithm arose quickly. In many areas X-ray is not available, or too difficult to procure. Where do these patients fit? Immediately exceptions had to be incorporated and managed. Just as with the categories of treatment as part of the national programmes (Harper 2007), many just did not seem to fit. As STS scholars have asked, what is done when one test, or aspect of the clinic gives a different result to another? (Mol 2002). What happens when there is a potential lack of fit between one aspect of the clinic and another? Is one test discarded in favour of another? This is where coordination is required, and, where the protocol fits in (cf Berg 1998; Dodier 1998).

This algorithm had to be adapted, and was considerably more complex by late 2014, by which time five algorithms had been developed for different categories of suspect: “Algorithm 1: New PTB suspect case where CXR is available and accessible; Algorithm 2: New PTB suspect case where CXR is NOT available /accessible; Algorithm 3: Symptomatic vulnerable groups during targeted campaigns or Active case Finding (Vulnerable groups were defined as refugees, IDUs, slum population, migrants, prisoners, factory workers, diabetics, symptomatic contact cases, Others e.g. alcoholics, cancer patients, health workers, Monks, kids in hostels, etc.); Algorithm 4: Treatment Failure, Relapse, loss to follow up; Algorithm 5: Symptomatic contact of MDR TB index case and PLHA with TB symptoms”.[xviii]

These new algorithms also create new diagnostic categories. Staff involved in TB control in Nepal were struggling with where on the existing forms to place the new diagnostic outcomes. Does a smear negative, but Xpert positive outcome get categorised under the existing smear positive category of patient? Initially this was felt to be the easiest thing to do, but as was pointed out at early meetings with TB reach evaluators, the invisibility of the diagnosis by the Xpert meant that the impact of the technology on diagnosis, and thus the capacity to evaluate its impact becomes immediately lost. A new category had to be created. But this was not the only new category created. In addition the category of resistance to rifampicin also was created. The case notification protocols also had to be revised in light of these to include smear negative / Xpert positive, but also for the additional Xpert positive / rifampicin negative or positive outcome. The new case notification results generated were immediately fed back to the NTP, and the results were constantly being poored over. Meetings we attended with the WHO, and NTP were mediated by powerpoints of the results projected onto walls, analysed and discussed. What are the implications of these findings: just as with the editorial written for the Cochrane group by a group from the Liverpool School of Hygeine and Tropical Medicine, so too were the implications for Nepal. The latest, and updated figures were constantly mulled over.

After nine months from the introduction of the technology, the results were published on the IOM website:

> By the end of September 2012 it had achieved many goals, A total of 5,300 tests had been performed, detecting 914 additional MTB cases (877 Rif- and 44 Rif+ cases). Many cases among smear negative samples, which would have gone undetected without the intervention of GeneXpert technology, have been diagnosed as positive.

As well as for local consumption, a poster presentation was prepared for the IUATLD World Lung Health Conference in Paris of 2013 (“Experience after one year of GeneXpert technology implementation in Nepal”). By then these figures had increased: 7,755 tests performed; 1,376 MTB+/RIF-, 108 MTB+/RIF+ (and another 13 cases of “Rifampicin indeterminate result”). The overall positivity of the results was 19% of all tested, ranging from 30% to 9% in differing centres. Amongst MDR suspects, 24% demonstrated Rifampicin resistance. However, these were not the only outcomes demonstrated by the technology, and a significant percentage presented as “test failures”. Of these 899, 546 were “error”, 198 “no result”, 156 “invalid” with the reasons stated as “power interruption, improper specimen processing and faulty modules and cartridges”. The technology proved a lot less reliable than had first been assumed, and 50% of the modules failed their remote calibration tests, and some needed to be replaced (this had not been budgeted for, and involved reordering from outside of the country).

The discussion section of the presentation echoed some of the discussions that had been conducted in the halls of offices of the IOM, NTP, WHO and other REACH funded NGOs. Firstly, it was soon apparent that there was a considerable incremental increase in case finding of bacterial positive cases (24% up). But the high number of test failures was a surprise, and clearly a major challenge for both the project and potential rollout. Confirming the RIF+ cases was an issue, because, as we have already seen in the section on available laboratory services there is extremely limited culture facilities in the context of Nepal, and all these had to be sent to the GENETUP clinic in Kathmandu for confirmation. The discussion session also mentioned that the incentive payment scheme was effective, but that sustainability will be an issue. This issue of incentives was a major issue for the rollout of Xpert, and to which we now turn.

Integration NGO and Government services, and the question of incentives

The installation of the Xpert machine required meetings, letters and considerable coordination. As the programme manager for the TB REACH project stated: "*December 2011 was a hectic month as it took all the month to install the machine in the health facilities. We had to check for electric supply. We provided UPS and generators. Normally, microscopic centres are not spacious. Even though the GeneXpert doesn't take much space we had to make space for it in the existing labs".* However, these initial preparatory meetings and installation processes were not enough.

On the wall in the Rajbiraj clinic is pasted a printout of the incentive scheme. IOM Nepal, TB Reach Project the paper proclaims, "Performance based overtime payment for GeneXpert Centre Staff". It outlines the amount payable with incentives for the number of tests performed per month. For the two module machines this starts at 4000 rupees for 40 tests per month, rising to the maximum of 9000 for the performance of over 71 tests; and for the four module machines it starts at 5000 rupees for the up to 70 tests, rising to 10000 for over 100 tests performed. Cash in an envelope is handed over later by the visiting IOM TB Reach supervisor, to both the laboratory worker in charge and to the DOTS supervisor, because as was explained by the supervisor, their workload also increases with the increase in case finding.

While this incentivisation scheme assisted in the achievement of the targets set for the TB REACH funded IOM programme, as per the terms of their funding agreement, it fed into a longstanding issue around the coordination of NGO and Government services, namely the payment for service delivery. Government laboratory staff saw this as an increase in their work load and were frequently reluctant to engage in the programme. As an IOM supervisor told us, they didn't have the budget for co-ordination initially and started without giving any incentives, and little work was achieved. He said, "You can compare the results and performance from here [IOM site] and government institution....We installed Gene Xpert in Chandranigapur in September [2013] but there has not been any tests so far [December, 2013]." Similarly another programme manager from IOM gave details of the incentives provided by IOM, "The tests were few in number and therefore after May, 2012, we had to start performance based incentive scheme. Initially, we used to give Rs. 5000 to each institution per month till May but after that, we maintained that institution that tests more than 100 people per month would be provided incentive of Rs. 10,000." He also stated that they provided incentives to other workers in the DOTS system, the Regional Tuberculosis and Leprosy Officers (RTLOs), District Tuberculosis and Leprosy Officers (DTLOs) and others and maintained that on an average, they spent Rs. 22,000 per district per month on this alone. These incentives are given in cash as we witnessed. (Cash incentives are also paid by drug companies to health workers as incentives for prescribing their products (Harper et. Al 2011), so the practice is widespread). The TB

REACH team has to meet certain targets as detailed in their proposal and their decision to introduce the performance related reward system set the benchmark for other organisations who also were awarded TB REACH grants. The introduction of additional work loads into the government system was to be paid for.

As we have shown, the Xpert is installed in government labs and is operated by the government staff in the lab. The capacity to run the machine draws on other additional resources to the ones provided with the grant (tubes and cartridges), in particular Government resources including slides, reagents, microscopes, staff etc. So when the government has agreed to use its infrastructural, material and human resources for a programme that has been introduced within its system, the demand of incentives from lab staff and others is understandable. The question remains, however, that if the programme is entirely the responsibility of an NGO, on what authority are they allowed to mobilize these additional government resources? As Timmermans and Berg have suggested, the development of guidelines (here associated with the introduction of a new technology) is drawn upon to advance other context specific goals and professional trajectories. "For all those involved, the guideline is not a goal in itself but a *means,* acted upon in terms of their own aims and the local constraints structuring the situation in which the guideline happens to be placed" (2003: 70). These become more clearly visible when a new technology is brought in from outside.

In conclusion

[i] http://who.int/tb/laboratory/mtbrifrollout/en/

"The technology is based on the GeneXpert platform and was developed as a partnership between the Foundation for Innovative New Diagnostics (FIND), Cepheid Inc. and the University of Medicine and Dentistry of New Jersey, with support from the US National Institutes of Health. WHO recommended use of the technology in December 2010 and is monitoring the global roll-out of the technology to promote coordination"

[ii] http://www.bd.com/ds/productCenter/BC-Bactec.asp

[iii] From the website

"Detail overview of Resettlement Process:
IOM assumes responsibility for all aspects of resettlement after the UN High Commissioner for Refugees (UNHCR) refers a case to IOM for third country resettlement consideration.
IOM Nepal resettlement activities include:

- File Preparation/ Organization of Selection Missions/ Case Tracking,
- Cultural Orientation,
- Health Assessments,
- Movement

IOM Damak Operations is responsible for the organization and support of selection missions for, Australia, Canada, New Zealand, Norway, Denmark, the Netherlands and the UK.

File Preparation / Organization of Selection Missions / Case Tracking:
The Resettlement Support Center (RSC) in Damak is responsible for these activities. Once the In-processing staffs in RSC receive files from the UNHCR in Nepal, they interview cases for the United States and Australia and complete the country-specific forms for these countries.
They organize selection missions for the US, Australia, Canada, New Zealand, Norway, Denmark, the Netherlands and the UK. Out-processing staff direct and monitor post-selection activities: Health Assessments, Cultural Orientation, Sponsorship Assurances and Exit Permits. The RSC also produces the US travel documents. In addition, the RSC handles activities related to case processing in Sri Lanka, India and Pakistan for the United States.

More on Resettlement Support Center (RSC)...

Cultural Orientation (CO). IOM conducts 3-5 day Cultural Orientation courses in eastern Nepal for refugees accepted for resettlement in the US, Australia, Canada and Norway. The course, based upon the curricula provided by the country of resettlement, focuses on the primary resettlement concerns of refugees – Housing, Employment, Education, Social Services and Legal Rights. In addition, IOM conducts a 2-hour course on the flight/transit process at the IOM Transit Centre in Kathmandu on the day prior to the commercial flight to the country of resettlement.
Health Assessments. Based on the specific protocols of the resettlement countries – US, Australia, Canada, New Zealand, Norway and Denmark – IOM's Migration Health Department (MHD) conducts health assessments to ensure that refugees are fit to travel to the country of resettlement. In addition, MHD

coordinates diagnostic tests/treatments and specialist appointments. Furthermore, MHD conducts pre-departure exams in Damak (prior to the charter flight to Kathmandu) and Kathmandu (prior to the commercial flight to country of resettlement) to ensure that refugees are fit to travel. MHD also arranges escorts for refugees that require medical assistance during the resettlement flight.

Movements. This activity is the responsibility of the Operations (OPS) team, which works from Damak and Kathmandu. In Damak, the team's responsibilities include transporting (using 15 IOM buses) 500-700 refugees daily between the seven camps and the IOM office for interviews and medical appointments, and organizing transportation of 300 refugees per week on charter flights from eastern Nepal to Kathmandu.

In Kathmandu, the Operations team receives refugees transported through charter flights from eastern Nepal and arranges accommodation for them at the IOM Transit Centre. The team also arranges commercial airline bookings for approximately 1,000 refugees per month, and facilitates airport formalities for all departing refugees. OPS-Kathmandu provides operational flight escorts on an as-and-when required basis. It also handles flight movements for cases ex-Sri Lanka and India.

Other Resettlement Activities of IOM-Nepal

Transit Center (TC). IOM Kathmandu operates a Refugee Transit Centre which has the capacity of accommodating 400 people a night. This 24-hour facility provides clean water, hygienic food, comfortable beds and a children's playground for the refugees. Typically, Bhutanese refugees from eastern Nepal spend 2-4 nights at the Transit Centre in Kathmandu prior to their commercial flight to the country of resettlement. During this time, refugees undergo a final fitness-to-travel examination, and a final Cultural Orientation session as a part of the transit process.

Exit Permit (EP). 3 representatives from the Government of Nepal conduct exit permit formalities at the IOM Damak office immediately after the countries of resettlement have accepted to resettle refugees. This is a significant improvement over the previous process that involved a lengthy, cumbersome series of clearances from different hierarchies within the government. IOM provides air transportation and accommodation facilities for the representatives of the Nepal Government to IOM in Damak."

[iv] https://www.gov.uk/government/publications/tuberculosis-test-for-a-uk-visa-clinics-in-nepal/tuberculosis-testing-in-nepal

[v] http://nepal.iom.int/jupgrade/index.php/en/component/content/article/18-topic-details/80-harmonization-of-the-tuberculosis-management-protocols

"Under this project, more than 3,000 refugees with suspicion of suffering from TB were tested bacteriologically and 437 were found to be culture-positive. More than 40 of them with drug resistant TB benefited from individualized treatment. 24 cases with MDR TB and complex TB cases got treatment in isolation facility. Five AMDA laboratory staff received on-the job training in IOM laboratory and more than 30 AMDA medical staffs (doctors, paramedics and DOT workers) received training on laboratory method of TB diagnosis, interpretation of laboratory tests, TB treatment, management of side-effects of TB treatment, chest X-ray reading, TB epidemiology and infection control. The project is being implemented in coordination with AMDA, UNHCR and the government of Nepal".

[vi] http://amda.org.np/

[vii] http://www.finddiagnostics.org/programs/tb/TB_and_diagnostics.html

[viii] http://www.who.int/tb/publications/tb_framework_checklist3.pdf

[ix] (See McNerney 2011, Prospects for a point of care test (POCT)

[x] http://who.int/tb/laboratory/GeneXpert_rollout_large.jpg?ua=1

[xi] http://www.stoptb.org/wg/new_diagnostics/assets/documents/PressRelease_Xpert_Review_31Jan13.pdf

[xii] http://www.cochranelibrary.com/editorial/10.1002/14651858.ED000051

[xiii] http://www.nepalntp.gov.np/index.php?view=page&id=66

[xiv] http://www.stoptb.org/global/awards/tbreach/

[xv] Housed in Geneva, the STOP TB Partnership now has over 1,300 partners, and is organised in a way that seeks to be representative of the broad constituencies of those involved in the global control of TB. The particular projects with which this complex assemblage is involved are expansive, and given the nature of its organisation, ever expanding. These currently include diverse activities and funding within the following categories: Challenge Facility for Civil Society; Global Advocacy; Global Drug Facility (GDF); In partnership with the Global Fund; the Kochon Prize; National partnerships; TB Reach; and a number of Working Groups and Task Forces (including the Global Laboratory Initiative). See: http://www.stoptb.org/

For more on the formal history of the STOP TB Partnership see:

http://www.stoptb.org/about/history.asp

[xvi]

http://stoptb.org/assets/documents/global/awards/tbreach/List%20of%20PSG%20Members%20August%202013.pdf

Members as of 2015 include: NTPs of Ghana and Cambodia, Centers for Disease Control and Prevention (CDC), TB ACTION, International Union Against Tuberculosis and Lung Disease (The Union), Department of Foreign Affairs, Trade and Development (DFATD), Partners In Health, Bill and Melinda Gates Foundation, World Health Organization, US Agency for International Development (USAID).

[xvii] http://nepal.iom.int/jupgrade/index.php/en/aboutus/18-topic-details/81-tb-reach-project-with-genexpert

[xviii] Document used by IOM, developed with NTC, and WHO: RATIONALE AND PRACTICAL DIRECTIONS FOR THE USE OF XPERT MTB/RIF IN NEPAL