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hiv & aids treatment in practice

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Three I's to reduce the burden of TB in people with HIV

Key activities that are critical to continued success of ART-scale up

This year, approximately 750,000 people with HIV will develop TB, mostly in sub-Saharan Africa. About 230,000 of them will die. Needlessly.

But TB is both a preventable and treatable illness so it does not have to be a death sentence in people with HIV.

There are three essential activities that all HIV programmes should be doing that could protect people with HIV from TB infection, help prevent active disease from developing, and identify active TB disease early and improve the chances of cure — the 'Three I's. These are:

- **Intensified case finding (ICF) for active TB**: aggressive screening can lead to the early diagnosis of TB — improving the response to treatment and reducing the likelihood of it spreading to others. It also offers an opportunity to protect people with HIV who don't yet have TB by:
- Giving them **Isoniazid preventive treatment (IPT):** an antibiotic that could reduce their risk of developing active TB by 33-62%; and
- By practicing **TB infection control (IC)**: which involves measures that can reduce the spread of TB to vulnerable people with HIV, health care workers and the community.

Since World AIDS Day last year, HATIP has published special issues supported by the Stop TB Department of WHO that address each of Three I's [HATIP's # 96 on IPT, 104 and 105 on intensified case finding, and 109 on infection control]. In those articles, we noted some of the operational challenges involved in implementing these interventions in order to get our readers thinking about how to tackle such issues in their own setting. But challenges should not be seen as barriers — there have also been challenges scaling up HIV care and antiretroviral therapy (ART) in resource-limited settings but now ART is reaching over 3 million people, and HIV care is available for millions of people and families impacted by HIV.

And yet, HIV programmes have been failing to take advantage of the key strategies to manage TB in people with HIV — and it is undermining those very HIV/AIDS services we have been working so hard to establish.

"The Three I's need to be viewed as an essential and integral component of ART scale-up, and an integral part of universal access," said Dr Kevin De Cock, the head of WHO's HIV/AIDS Department. "You cannot leave these aspects out of all this, any more than you can patient monitoring or dealing with drug resistance for ARVs or some other essential component of the ART scale-up programme."

He made these comments at the conclusion of a meeting on the Three I's held in Geneva in early April, where treatment advocates, community representatives, HIV programme managers, HIV caregivers, and international and national policy makers and HIV CBO/NGO representatives from around the world put out a call to action to start implementing the Three I's now.

This issue of HATIP reviews that three-day meeting, with brief summaries of the presentations made by experts in the field, and some of the challenges to scale-up identified by meeting participants during group discussions. But our primary focus will be on the meeting's key outcomes, and the participant's insights about how to speed implementation of the Three I's, and the proposed concrete steps that can be taken to move this agenda forward on the global and local fronts.

Opportunities for HIV/TB collaboration

Opening the meeting, Dr De Cock stressed that the link between HIV and TB was first noted in the mid-1980s, "and between 1988 and 1993, I was working in West Africa and the association between these diseases just sort of hit you over the head," he said. But, it took the outbreak of drug-resistant TB in New York in the early 1990's to renew interest in TB as a global health issue.

Similarly, the outbreak of extensively drug resistant TB (XDR-TB) at an ART clinic in Tugela Ferry, South Africa has brought to the world's attention the fact that HIV and TB is a particularly dangerous combination

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— jeopardising TB control efforts worldwide. The risk of XDR-TB to people with HIV is especially grave, as data suggest a greater than 95% mortality rate.

“This issue of XDR-TB and MDR-TB can be interpreted in a couple of ways,” said Dr De Cock. We can either say, ‘this is really quite serious,’ or you could interpret it as one of the most important events in public health in recent times. My own bias is toward that latter interpretation. If there’s one thing that can turn the AIDS epidemic into a pseudo-SARS epidemic, it will be the more visible spread - particularly to the Western industrialised world - of XDR-TB”

Urgent action is thus required to prevent, diagnose and treat TB in PLHIV, their families and communities — and with the ongoing scale-up of HIV services, it should be possible to address HIV/TB in a manner that is convenient for patients with or at risk of both infections.

Clear suggestions for how to better integrate TB and HIV care and treatment are presented in the *Policy on Collaborative TB/HIV Activities*, released in 2004 by the WHO Stop TB Department and Department of HIV/AIDS.

The policy recommends twelve key activities divided into four “policy-making level” actions required to set up, plan and monitor TB/HIV programme collaboration; five activities that TB programmes can perform to reduce the burden of HIV disease among people with TB (including providing them with HIV testing and counselling, HIV prevention services, and either directly providing or making certain that people with HIV/TB receive adequate and appropriate HIV care including cotrimoxazole prophylaxis and ART, when needed). Recently, national TB programmes (NTPs) have begun to make great strides towards the implementation of activities to reduce the burden of HIV disease in TB patients.

However, national AIDS programmes have not made as much progress adopting the remaining activities that are focused on people accessing HIV care and treatment services: the Three I’s.

The Rwandan example

But several countries have demonstrated that scale-up of these activities is possible. One country that serves as a model is Rwanda, and Dr Greet Vanderbriel of the International Center for AIDS Care and Treatment Programs (ICAP) gave a presentation on that country’s progress on behalf of Dr Jules Mugabo, MD of the Ministry of Health (MoH).

After consultations with key stakeholders, Rwanda’s TB/HIV policy was drafted and approved by the MoH in October 2005. Guidelines, training, TB screening tools and information education and communication materials were soon developed. Importantly, the HIV testing policy was modified to include provider-initiated testing and counselling for TB patients, TB and HIV recording and reporting tools were revised to include information on TB/HIV, and a system for monitoring and evaluation (M&E) of TB screening was developed and implemented.

The programme offers one-stop services so that TB patients who are identified as being HIV-positive can receive all their basic HIV services, including CD4 cell monitoring, cotrimoxazole and ART through their TB clinic while they are on TB treatment. Once the TB treatment is concluded they are referred and/or accompanied to the ART clinic where their care will continue.

Meanwhile, TB screening is offered to all HIV patients at programme entry and at each six-month follow-up visits. TB screening and HIV testing and counselling services are also offered to family members of index patient through home visits by peer educators.

By the end of 2007, 89% of TB patients were being screened for HIV, 61% of those with TB/HIV were receiving cotrimoxazole and 39% ART. TB screening is also high (88% in 25% of the national ART clinics) at enrolment into HIV services, with steady improvement in screening performance at follow-up visits as well.

Clearly access to ART must be improved, but another finding of the programme was that TB detection through ICF has been lower than expected, indicating a need to strengthen diagnostic capacity at health services and perhaps to adjust the TB screening tool to increase its sensitivity (see *ICF* below).

Another issue is that, at present, Rwanda is not routinely offering IPT to people who screen negative for TB — something that Dr Vanderbriel said they would have to revisit soon.

ICF— experiences in the field and challenges in the community

"ICF is the gatekeeper for everything else [IPT and IC]," said Dr Wafaa El-Sadr, of ICAP and Columbia University, "what happens next is the problem." See *HATIP 104 & 105).* In addition, Dr El-Sadr said, ICF that leads to early diagnosis (and treatment) of TB could help reduce immune response inflammatory syndrome and improve outcomes on ART.

"We have clear reasons to intensify case finding," agreed Ezio Santos-Filho, member of the Stop TB Coordinating Board and an HIV/TB treatment advocate. "It should be common sense — but it's not."

The Brazilian activist speaks from experience: he has had TB twice.

Even though ICF is policy in most countries, so far that policy has not been translated into operational guidelines or standard operating procedures. Screening tools have not been standardised and screening is not occurring in all the appropriate settings — wherever people with HIV congregate or come into contact with health services. According to meeting participants, programmes want more clarity on the best symptom complex to include on a TB screening tool that could be easily administered by trained lay healthcare staff.

One persistent question in some countries is whether chest x-rays should be required to exclude TB — in fact, in some Asian countries, clinicians rely upon them exclusively — although studies suggest that they miss a lot of TB cases. Studies where they have been added to symptom screens have yielded mixed results, some suggesting that they do not greatly improve sensitivity for TB, others suggesting that they do. But chest-x-rays are rarely possible in most settings.

"I find it hard to imagine a chest x-ray as a screening tool —it's overwhelming if not impossible requiring it in most settings where we work because of the huge numbers of patients involved and because of the lack of availability of chest x-ray even for diagnostic purposes; as well as the need for repeated screening in individuals in HIV care and treatment," said Dr El-Sadr.

Family contacts also need to be screened since TB can spread in the home. "TB is a family disease," said Dr El-Sadr. "If you have one person in a household with TB, you'll have others with TB infection." However, screening in children is particularly difficult and existing history/symptom scoring systems perform poorly, especially in children who are malnourished or living with HIV. More research is desperately needed to improve TB diagnosis in children.

Another issue is that many programmes have resisted updating their standard TB screening tools that rely on questions about chronic cough (for 3 or more weeks) despite the fact it has been shown to be poorly sensitive as the single gatekeeper symptom for TB in people with HIV.

More sensitive screens that capture up to 90% of the patients with TB would be preferred, but they will dramatically increase the demand on laboratory services to diagnose TB. And, unless diagnostic services are co-located, or specimen transport systems are arranged, patient must be referred to another facility — which isn't always effective.

"Referral systems are mostly on paper," said Mr Santos-Filho. "When people have a positive screen, what do we do? If they are referred somewhere else for diagnosis, are they properly encouraged? Do they have the means? People do not have money to go the TB clinic that may be far away. For instance, in Mexico City, the brand new HIV centre doesn't do microscopy so people have to travel two hours by bus or do a culture."

And yet there are models where ICF has been scaled up successfully, such as in India's voluntary testing and counselling clinics, which Dr Puneet Dewan described to the Three I's participants (a similar presentation was covered in HATIP 105). In addition, Dr Dewan described a more recent collaboration between the national TB programme and Avahan — a Gates Foundation-supported network of NGOs, in which STI clinic staff, outreach staff and peer educators have been trained to perform routine symptom screening.

One of the meeting participants, Dr Kudur Prakash, Deputy Director of the SANKALP Project in Bangalore, works with this network, and said that the outreach workers bring patients into clinics for TB screening, and then there will either be an accompanied referral to the nearest microscopy centre, or the sputum can be collected in the clinic and transported to the lab.

"There's beginning to be an effort to try to reach beyond the walls of the facilities to reach people at home," said Dr El-Sadr. "There's a lot of potential to use the systems for support, care and treatment for HIV for case finding in households — there are lots of motorcycles and bicycles out there, peer workers going out to the homes, outreach workers trying to ensure that people are brought back in for services. It is potentially possible to layer case-finding within the community using this incredible workforce."

IPT to prevent active disease and the further spread of TB

IPT is currently recommended by WHO for all people living with HIV (PLHIV) in areas with a prevalence of latent TB infection >30%, and for all PLHIV with documented latent TB infection or exposure to an infectious TB case, regardless of where they live. More recently, evidence has shown that the combined use of isoniazid preventive therapy and antiretroviral therapy among people living with HIV significantly reduces the incidence of TB; and the use of IPT in patients who have successfully completed a course of TB therapy has been shown to markedly reduce the risk of subsequent TB cases.

But when Dr Paul Nunn of the Stop TB Department asked meeting participants whether they thought that IPT was official WHO policy, there was confusion in the crowd — and later many participants said that there are mixed messages coming from within WHO and from other technical advisory groups about IPT. Dr Nunn also noted that currently only 82 countries have IPT policies — and that "there's clearly a disconnect between policy and implementation, as a result of which implementation is low."

The only country which has implemented its IPT policy in people with HIV is Botswana, and Ntukunu Makubate, of the BotswanaNational IPT Programme gave a presentation on that country's experience. As described in HATIP #96, the large programme had challenges with problems with recording and data entry and high levels of incomplete data. Large numbers of patients never came back for their final clinic visit, so it is impossible to say whether they completed treatment. Makubate believes that many did — it's just that Botswana's population is so highly mobile that people are often in a different part of the country at the end of the treatment course. "Batswana often have 4 homes: one in the city, in the ancestral village, the kraal where they keep their cattle, and then at the fields that they plough," she said.

Her colleague, Dr Ndwapi Ndwapi, Operations Manager of Botswana's ART programme said that the electronic database and monitoring and evaluation system "should be in place from the start." He also believes that IPT should be integrated into the HIV treatment guidelines, joint planning and training and supervision "rather than trying to fitting this into an already crowded training field."

"I'd like to point out that lack of adherence or falling off with prophylaxis is not a disaster for public health, like the lack of adherence to HIV treatment is, because people have latent disease or no disease and so they can't get resistant or fail," said Mark Harrington of the Treatment Action Group, who gave a presentation tackling some of the excuses against IPT implementation. But first he talked about his personal experience.

"I look forward to my annual TST because it gives me the opportunity to find out if I need INH. I've been on a protease inhibitor-containing regimen since 1996, and if I had gotten active TB, I'd have to switch regimens. So I would much rather be on INH for 9 months or even a year because I wouldn't have to switch my ART regimen."

He acknowledged that community activist groups and PWA groups have not done enough to educate their peers about IPT and create demand. But he took TB programmes to task for deriding IPT and said that most of their excuses against IPT implementation had little scientific basis.

"One of the major areas of resistance to adoption of IPT policy, is the fear of drug resistance - particularly by TB programme managers and/or those with control over the INH, but usually it's the TB programme managers," Dr Nunn said. "So they've got their hands on the INH tap and they don't want to turn it because of fear of drug resistance - a fear which has never actually been proven to be an issue."

Mark Harrington pointed out that there was a greater risk of resistance in people with active disease — and "concerns about excluding active disease before using IPT could be addressed by scaling up ICF and WHO's algorithm for the diagnosis of smear-negative and extrapulmonary TB," he said.

Indeed failure to roll out IPT is directly linked with the failure to implement ICF, and insecurity about the reliability of screening tools and algorithms to exclude active TB at the primary care level — and quite often, whether the use of chest x-rays is required to detect some cases of active TB. There are fears that if cases of active TB are missed, suboptimal treatment could lead to drug resistance. But Mark pointed out quite accurately that most breakthrough cases respond to standard treatment, although that data set is small.

In addition, people have called for more guidance on technical issues such as how to manage toxicity; how to ensure adherence and retain patients in care (particularly well patients that HIV programmes have yet to effectively target).

But Harrington stressed that standard TB treatment is more toxic, and yet it is used, and that ART programmes could adapt ART adherence support mechanisms to help people finish their IPT course.

In general the sense of the meeting participants was that the benefits of IPT far outweigh its potential risks. Also, since IPT is targeted towards 'well' patients, who are also frequently given cotrimoxazole, many participants thought that co-formulations or co-packaging the two drugs might be beneficial.

"There is absolutely no reason why cotrimoxazole and isoniazid cannot be co-formulated," said Dr Charlie Gilks of the HIV Department. "And programmatically, there are a lot of advantages in putting the two together."

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Infection control

TB infection control (IC) measures are essential to prevent the spread of *M. tuberculosis* tovulnerable patients, health care workers, the community and those living in congregate settings. Fundamentally, TB infection control is about safety — people receiving or offering HIV care should not have to worry about being exposed to TB in the process. In light of the crisis of drug-resistant TB in countries with a high burden of HIV, establishing facilities that are safe from TB has become an emergency situation for health services, prisons and other congregate settings, in general, but especially for HIV programmes.

Guidance on TB IC measures, including administrative controls (good workplace practicing such as triaging coughing patients), environmental (good ventilation) and personal respiratory protection have been produced by WHO and the CDC (see Resources).

However, Phillip Mokoena of the Treatment Action Campaign in South Africa said awareness of TB IC is very low in the community and that treatment literacy efforts were urgently needed to create awareness in the community about the importance of infection control.

The group discussions about TB IC were particularly involved.

“TB IC is a health systems issue that nobody clearly owns; and within public systems there are often multiple or unclear lines of authority to enact and enforce policies and standards. In some settings there may be multiple ministries involved who would be responsible for the healthcare facility,” said Dr Puneet Dewan.

“Most of the engineering solutions are outside of the area of expertise of most people working in healthcare; and there is a short supply of technical experts particularly in resource-limited settings,” said Dr Bess Miller of USAID.

Dr Liz Corbett of the London School of Hygiene and Tropical Medicine noted that “few countries have any concept of TB as an occupational safety hazard” and that the facility-level administrative controls are neglected, without dedicated accountable staff. In addition there is a lack of clear simple operational guidance on basic TB IC for those working in existing health settings, especially small facilities or community based organisations servicing people with HIV/TB. Other technical issues such as commodity/supply chain issues, waste management, and laboratory safety must also be addressed.

Key recommendations of the meeting participants

However, the meeting created new impetus to integrate the Three I’s as part of improved healthcare delivery services for people living with HIV. There was clear consensus on several key outcomes:

As Dr De Cock emphasised, the Three I's (ICF, IPT, IC) need to be promoted and adopted as an essential part of the HIV treatment and care package just like the provision of cotrimoxazole. The WHO 1998 IPT policy should be re-conceptualized and updated by the end of the year to recommend implementation of the Three Is with an emphasis on TB screening with a standardised WHO screening tool as an essential part of HIV care. Whenever people with HIV are screened for TB, they should either be identified as someone needing diagnostic evaluation for TB or other HIV-related conditions, or they should get IPT.

The policy must make it clear that the HIV programme is responsible for the Three I's and in particular IPT and ICF implementation. Policies should also be developed for the Three I's in congregate settings, including households, prisons, mines and the community, and targets should be set for implementation.

The key policy outcomes are described by the official meeting report (see http://www.who.int/entity/hiv/pub/meetingreports/WHO_3Is_meeting_report.pdf). The following section describes more of the meeting participants’ discussions concerning how those outcomes may be put into operation.

Recommendations on Three I's implementation

ICF policy and implementation

To correct perceptions that TB screening is the responsibility of TB programmes, the revised policy and guidance must make it clear that TB screening (and IPT) is a basic part of opportunistic infection management in people living with HIV. The policy should make it clear that TB screening can and should be performed wherever people with HIV come into contact with HIV care or services (including HIV testing and counseling sites), or are found in congregate settings or communities. Guidance should also make it clear that ICF is also an important first step in TB infection control.

Develop a simple standardised TB screening tool

An essential part of the ICF/IPT package will be the promotion of a WHO-sanctioned screening tool that is sensitive enough to detect most (80-90%) cases of culture-positive TB (including extrapulmonary) in people with HIV. In order to do this, WHO's team needs to quickly perform a systematic review of available data from the best-designed studies of ICF to identify the most appropriate signs and symptoms to include on the screening tool. The resulting tool has to be simple and practical for use by trained community healthcare workers or lay counselors in low resourced settings.

Although the tool will be standardised, the meeting's participants acknowledged that 'one size may not fit all.' In other words, the tool can be adapted to suit the local settings (cultural differences in symptom reporting, etc). In addition, some settings might have more capacity and resources to do more aggressive investigations. It is expected that ongoing research will continue to refine the tool (see *Operational research*) but that's no reason not to start using a good tool now.

"We need to agree on the basic screening tools or methods for now," said Muhamed Mulongo of The AIDS Service Organisation. "I know that the current methods have limitations. But if we can start somewhere and go on refining within time to get closer to 100% case detection in the future."

And having a standardised tool should help convince reluctant programmes to stop relying on the old TB screening tools designed to detect TB suspects before the HIV epidemic — which has changed the clinical presentation of TB. In particular, not all people with HIV and TB have a chronic cough, so it should no longer be the single gatekeeper symptom for TB screening in people with HIV. "Cough" will of course be part of any standardised tool, since it remains one of the most common symptoms of TB — and of other important illnesses such as pneumonia in people with HIV that also require diagnostic attention. Chronic cough may continue to be an especially important symptom to note for purposes of triage and fast tracking, however, since it is more likely to be due to TB than other causes.

The tool should also clarify the role of chest x-ray as part of TB screening. Although in well-equipped health facilities, chest x-ray might pick up some additional asymptomatic cases of sub-clinical TB (without other symptoms yet), requiring chest-x rays would limit the scale-up of ICF in most resource constrained countries or in settings such as HIV counseling and testing sites.

A way to screen for (and diagnose) TB in children also has to be devised.

"Not only HIV-infected, but in general, diagnosing TB in children is tricky," said Dr Anand Date of the CDC. "So there should be more operational research and emphasis given on how do we tackle that issue."

A key but often overlooked place to start is contact tracing since it will often lead to TB-exposed children in the home. "We should review and enforce the policy of contact tracing as an opportunity for intensified case finding and IPT," said Dr Angélica Sálomáo of the WHO AFRO region.

Strengthen laboratory/diagnostic capacity

"If intensified case finding is done by all HIV care providers from tomorrow, it's going to put an enormous workload on the existing lab services," said Dr Date, "so there should be attention paid to the assessing and improving the quality of the existing lab services."

To be certain that ICF leads to timely and reliable diagnoses, TB diagnostic laboratory infrastructure and capacity will need to be strengthened. This will require increased coordination and harmonisation with groups working on laboratory issues.

“It’s going to be the weak link overall,” said Dr Bess Miller, “so it will be important to work with the Global Laboratory Initiative on strengthening lab diagnostic capabilities at all levels — including external quality assurance, and developing the human capacity to perform more smear microscopy as we’re scaling up.”

She also suggested promoting the use of HIV resources (such as PEPFAR funding for laboratory infrastructure) to enhance TB diagnostic capacity and improve laboratory turn-around (see resources section).

Likewise, to be certain that people with smear-negative and extrapulmonary TB get properly diagnosed and treated, there needs to be greater promotion and implementation of WHO’s guidelines on the diagnostic algorithms for smear negative and extrapulmonary TB, along with greater access to timely TB culture.

To help countries implement ICF, policy will need to be translated into clear operational guidance addressing the following areas:

- **How to integrate ICF into the range of different HIV-related services:** HIV counselling and testing sites, support groups, ART clinics, PMTCT clinics, home based care, etc) congregate settings, including mines, prisons and military barracks, and communities (including displaced people).
- **Staffing.** The roles and responsibilities for performance, supervision, training and program monitoring for ICF need to be delineated — especially when programmes have moved to task shifting.
- **Integrated TB infection control**. Since screening may lead to sputum collection, guidance must emphasise good infection control practices for TB screening and sputum collection by staff, volunteers, and peer workers — particularly those who may have HIV.
- **Frequency of screening** — especially given that there may be more than one setting where a person with HIV might be screened. How will screening and referral be coordinated across multiple service providers? Also, each referral for TB evaluation at another facility could cost the client time and possibly money for transport. However, if people who screen negative for TB are immediately put onto IPT to prevent TB, the odds of requiring a subsequent diagnostic work-up for TB should decrease substantially.
- Another area that must be addressed is **how to manage people who screen positive when they turn out to be negative for TB** on laboratory investigation. Such cases will be more common with a sensitive screening tool in people with advancing HIV disease since there is an overlap between the symptoms of advancing HIV disease and TB.
  “If you think about the symptoms that could trigger intensified case finding, if the patient with HIV and has symptoms of TB but hasn’t got TB — they must have something else. People with HIV, when they get sick, need to have access to services that can identify TB, among other opportunistic infections such as pneumonia, because they want the most appropriate and correct treatment,” said WHO’s Dr Charlie Gilks.
- **Standardised recording and reporting, and monitoring and evaluation systems.** “There is a need to include screening as a core activity for universal access reports,” said Dr Haileyesus Getahun of WHO, “and this, ideally, will be done by improving the existing pre-ART and ART registers.”
- **Recording practices should be simple** to that overworked healthcare workers don’t perceive ICF as an additional service but as a routine part of HIV care. Other mechanisms need to be put in place to monitor ICF outside of healthcare delivery settings (eg, VCT clinics).

Operational research: Concurrent with implementation of the standardised guidance and tool, operational research should be promoted too identify the best models of implementing ICF in HIV settings, and to optimise the screening tool for the local setting.

Next steps at the country level for ICF implementation

International policy and guidance will have no effect until it is adopted and implemented at the national and local levels. One aspect of this will be getting the Ministry of Health to mandate that the national AIDS

programme (NAP) is responsible for ICF in HIV care settings, and to encourage improved collaboration and joint planning between the NTP and the NAP.

“We pretend quite often that [HIV and TB programmes] have collaborate activities,” said Dr Sálomáo, “but eventually what we see is that we are not even talking.”

Higher levels of government will also have to become engaged to make certain that ICF happens everywhere it should, i.e., to make certain that the ministries responsible for services in congregate settings (Defence, Justice, Mining, etc) participate in the scale-up of ICF.

National policies, and international operational guidance will need to be adapted into detailed operational protocols that taking into account the local logistical challenges:

- The priorities for healthcare and support settings in which ICF should first be scaled up, should be based upon local TB epidemiology. Clearly, however, TB symptom screening must be integrated into the routine physical examination and follow-up visit checklists for all people receiving care from HIV/AIDS programmes.
- The coordination of training and supervision in the range of settings where ICF will be performed — again, taking into account that community based health workers may be involved in ICF implementation. These TB elements should be integrated into existing training and mentoring activities for new health workers and staff, particularly HIV staff but refresher trainings for existing health staff will also promote implementation.
  “Even though TB is included in most of the HIV trainings, I have seen training packages and when you actually look at the content of TB component of the HIV training, it’s really not that emphasised — it will be usually be just on two slides on opportunistic infections,” said Dr Date. “So it’s really important that AIDS programme, TB programme and the training institutes - which are involved in developing these training materials, make sure that TB is comprehensively included in the training packages.”
- Integrate TB elements into recording and reporting systems.
- Establish effective linkages for diagnosis and treatment, working out the logistics in order to minimise losses during referral. Programs must make diagnosis more convenient for the patient. One possibility is to develop TB diagnostic capacity (microscopy) onsite at the ART clinic or within the general health services. But when TB diagnostic capacity is not co-located at the same facility where TB screening is being performed, effective referral mechanisms (possibly escorted referrals) should be developed to retain TB suspects in the diagnostic process and make certain those found to have TB get onto treatment. Another option is to collect sputum samples from TB suspects where screening occurs and to establish reliable systems to transport specimens to the diagnostic facility and to return the results to the patient/and their care provider.

Global next steps for IPT policy and implementation

The new IPT policy must settle, once and for all, the issue that HIV/AIDS programmes are responsible for delivering IPT in HIV settings — it is not the NTP’s responsibility.

In settings with a high burden of HIV/TB, people with HIV who screen negative for active TB should automatically be prescribed IPT, unless isoniazid is contraindicated (e.g, in heavy drinkers).

This means there will have to be better cooperation between HIV and TB programmatic areas to improve the supply chain for universal access to isoniazid. The Global Drug Facility and other supply chain stakeholders, including the AIDS Medicines and Diagnostic Service (AMDS), Global Fund to Fight TB and Malaria (GFATM), and the PEPFAR Supply Chain Management System (SCMS) should be engaged and a UNITAID proposal for isoniazid should be developed to facilitate large-scale procurement.

Additionally, strategies could include co-packaging and co-formulating isoniazid with cotrimoxazole (IPT and CPT. These strategies must also address paediatric dosing and formulations.

Address operational concerns by backing up IPT policy with clear operational guidance: Many programmes are reluctant to scale up IPT because there has been so little programmatic experience with IPT. So to increase uptake, clear operational guidance should be developed that confronts the perceived barriers to delivery of IPT, informed by a systematic scientific review of the available IPT experience. This

operational guidance can also be used for advocacy purposes (see *Advocacy push*). It should address such key issues as:

- **Excluding active TB**. Most suspects for active TB cases can be excluded from an IPT programme by using a very sensitive TB screening tool — even at the primary healthcare level. The issue of whether to use chest-x rays should be addressed in a way that reflects the constraints in different settings and does not impede IPT implementation.
- **Resistance**: Even with a sensitive TB screening tool, some sub-clinical cases of active TB will be missed, and possibly develop resistance to isoniazid —though there is little evidence that this happens frequently. Nevertheless the guidance should review management of such cases (again, evidence suggests that the standard TB regimens to manage TB cases that break through on IPT). Plus, "we need to do surveillance for resistance," said Harrington, "including in IPT programmes among those that develop the disease."
- **What is the role of tuberculin skin testing** (TST) or other tests to determine TB exposure, and how could this could vary by setting and local risk of exposure to TB?
- **Who is eligible for IPT?** Programmes remain unsure whether they can use IPT in previously treated TB patients, pregnant women with HIV, exposed households and particularly, exposed children. WHO's Dr Siobhan Crowley made a case for considering "the infant and the young child who's always born without TB but always lives in very close proximity to TB. Because of people's fears about not being able to diagnose TB — we wind up sitting there and waiting until they develop disease —which we then have to treat before we give them ART, leading to huge mortality. So we've got to be thinking about these infants and young children."
- How can IPT be delivered to marginalised/at risk populations, e.g. prisoners, refugees, migrants, etc?
- **Safety**. Although IPT has been safely used in many settings, healthcare providers need to be reassured about the safety of IPT in resource-constrained settings. Pertinent questions include how to avoid liver toxicity: how best should people with pre-existing liver problems be recognised and excluded? How frequently and how should patients on IPT be monitored? How safe is IPT in pregnant women? What is the safe level of alcohol consumption? What should be included in safety information and education for patients?
- **How to use IPT in combination with ART .** Data suggest IPT and ART may be synergistic against TB. However, guidance will be needed in order to avoid peripheral neuropathy in people concurrently on d4T-containing ART regimens. For instance, should programmes consider recommending a switch from d4T to AZT or tenofovir *before* peripheral neuropathy occurs?
- **What is the optimal duration** (six months, nine months, indefinitely?) and frequency of IPT in people with HIV (keeping in mind that this may vary by setting and local TB exposure rates)?
- **Adherence:** Highlight best practices supporting adherence, for example, CREATE studies successfully adapted lessons learned from successful ART adherence and cotrimoxazole prophylaxis programs such as the use of trained peer supporters. "Look at HIV infected people that have amazingly high - over 90 to 95% adherence to ART," said Mark Harrington. "Why don't HIV treatment programmes use HIV adherence training and support methods to increase uptake and adherence to IPT?"
- **Monitoring and evaluation guidelines and indicators.** Norms need to be established for recording and reporting (integrating TB elements into pre-ART and ART card and existing registers), monitoring and evaluation to demonstrate the progress and impact of IPT. For instance, there should be standardized reporting of the proportion of new clients accessing IPT, and programs should be able to assess the impact of IPT as part of package of care, as well as additional qualitative and quantitative benefits (including cost-benefit analyses).

One important aspect of IPT delivery that several meeting participants emphasised in the scale-up of HIV services, is that there has been inadequate attention paid to how to deliver pre-ART care, where IPT fits best. In most health systems, the capacity of staff and infrastructure is limited where clients with HIV enter into care. Guidance should be provided to help crowded clinics and health systems better provide essential care including IPT to "well" patients, such as working with community-based partners to develop a basic package of wellness services and delivery of IPT through home and family-based care.

Operational research on IPT

While it should not delay IPT implementation, there is limited experience using isoniazid in programmatic settings in resource-limited countries. An operational research agenda on IPT should be developed, which should include:

- Setting up operational research and demonstration projects in districts and countries to increase programmatic experience and strengthen the evidence base on IPT (perhaps comparing methods of delivery, including home based care, etc).
- Evaluation of different adherence support practices and IPT delivery models.
- Establishing the optimal TB preventive regimen: Should shorter 2 drug IPT regimens be considered in some settings (particularly in people who are less likely to be re-exposed to TB) or conversely should IPT be continued indefinitely to prevent TB re-infection in countries with a high burden of TB?
- Measuring the impact, if any, on drug-resistant TB: It is unclear whether scale-up of IPT will lead to an increase in isoniazid resistance (brought about through sub-optimal treatment of undetected active cases of TB) or whether the decrease in the incidence of active TB on IPT could actually lead to a decrease in the total number of drug-resistant TB cases (including rifampicin-resistant and MDR-TB).

Country-level next steps on IPT policy and implementation

But in order to get IPT happening on a wide scale national, clear endorsement and direction from high levels in government and Ministry of Health will need to be secured. Again, joint HIV/TB planning and monitoring should be strengthened but the HIV programs should ultimately be responsible for implementation of IPT on patient and programmatic level. This means that HIV programme resources must also be leveraged to ensure adherence, treatment completion.

Action plans: Policy and guidance will need to be translated into country level action plans, including integration of ICF/IPT into opportunistic infection prevention and care guidelines. WHO and other partners should provide technical assistance at regional and country level. Key issues to address are:

- Isoniazid procurement and supply logistics. There must be an agreement on procurement, distribution mechanisms, stocking and reordering logistics. Access to IPT must be free, but in order to truly accomplish universal access, there must also be free access to TB screening and diagnostic services.
- Monitoring and evaluation, which is essential from the start. Experience from the IPT program in Botswana has demonstrated that unless recording and reporting/monitoring and evaluation systems are in place when the program is launched, it will be difficult to document completion of treatment or the full success of the program. Standardised TB prevention indicators should be incorporated into existing HIV care and treatment recording and reporting documentation.
- Establish and/or reinforce routine TB drug resistance surveillance.
- ICF/IPT training and supervision must be integrated into existing HIV programs to avoid multiple training programs in an already crowded field
- Information education and communication efforts need to be launched immediately targeting the community, patients AND healthcare workers: “The acceptance by the community, the patients, clients or end-users as well as the service delivery staff themselves is critical to ensuring the success of any IPT program,” said Cynthia Eyakuze of the Open Society Institute (see *Advocacy*).
  “Many of the folks who are running ARV clinics, don’t really know much about IPT,” said Reverend Edward Phillips, Managing Director of the Eastern Deanery AIDS Relief Program in Nairobi Kenya. “So there really has to be an education in general, on both sides, whether it’s the TB side or people running ARV clinics.”

Global next steps: TB infection control policy and implementation

Given the nosocomial spread of TB (including drug resistant TB) in HIV-related care settings, TB infection control needs to be recognised as a health systems emergency. There should be a clarion call for high-level commitment and political will to implement TB IC — positioning TB IC as an essential human right for anyone accessing health services (see advocacy push).

Since TB infection control cut across so many disciplines, there is a greatly increased range of stakeholders who must be engaged in the process to reduce the spread of TB in health facilities, including:

- Advocates for health systems strengthening;

- Those working on other infection control issues, particularly those working on other airborne infections (such as the pandemic containment and response cluster/ groups working on SARS, avian influenza). TB IC should be integrated into universal precautions (infection control guidelines designed to protect workers from exposure to diseases spread by blood and certain bodily fluids) — although, at the same time, there should be recognition that TB IC must be treated as distinct and an emergency.
- International groups working in occupational safety and promoting legislative protections for healthcare workers. TB IC must be seen as a matter of occupational safety and there must be increased access to employee healthcare services, including HIV and testing for TB exposure.
- Technical specialists. There is a clear need to build more capacity to provide technical assistance, and address the shortage of infection control experts and specialists (architects, engineers, industrial hygienists).
- The Global Laboratory Initiative. Safety in the laboratory and for laboratory technicians must also be prioritised — recognising that in clinical facilities, laboratory technicians often have little power to improve the safety of their work environments.

However, since TB infection control puts the HIV community (both people living with HIV, their families and their healthcare providers) at greatest risk, the HIV community must drive the process to establish TB IC in settings providing care to people with HIV and where people with HIV congregate, and immediately implement TB in ART settings. In fact, it must be recognised that TB IC is a key aspect of the scale-up efforts for ART so TB IC should be better integrated into HIV programmatic guidance such as the "Essential Prevention and Care Interventions for Adults and Adolescents living with HIV in resource limited settings."

In addition, as part of the process to strengthen the HIV community's participation, the "STOP TB Partnership" Infection Control sub-group should be add more people from the HIV community.

The updated WHO HIV Dept and Stop TB Department TB IC framework is in development, and meeting participants felt that its development should be accelerated. It will provide normative guidance on the priorities of the interventions; assessments of facilities, ventilation standards; recommended elements for accreditation or certification, and develop standardised indicators for monitoring of administrative measures (one critical measure of TB IC success could be the regular assessment of the TB prevalence among healthcare workers). It should also include a standardised assessment tool to assess the risk of TB transmission at the facility level that can be applied across the countries.

But it is important that programmes do not to wait for the new framework to come out — guidance already exists describing good TB Infection control practice (see Resources). But to help countries and programmes prioritise the scale-up of TB IC interventions, at the meeting, representatives of the the STOP TB Infection Control Group committed to produce, within two months, simple concrete TB IC guidance, based on the existing policies, "Ten Essential Actions for Effective TB Infection Control. Safety without stigma."

These have already been released:
http://www.stoptb.org/wg/tb_hiv/assets/documents/10%20Essential%20Actions%20for%20Effective%20TB%20Infection%20Control.pdf

Similarly, simple guidance should be developed or adapted targeting community-based groups and organisations, such as HIV support groups, to reduce TB transmission within the community.

As there aren't enough equipped facilities to isolate people with drug resistant TB — guidance must also be developed for management of MDR-TB and XDR-TB within the community. The alternative is to leave those people untreated and more likely to transmit resistant TB.

Strengthening the supply chain: Supply chain management for IC related products also needs to be improved. WHO should develop clear specifications for IC procurement, while the Stop TB Department should develop and put forward a UNITAID IC proposal.

Operational research: Concurrent with implementation, demonstration countries/districts could be set up to strengthen the evidence base for TB IC and to help prioritise IC interventions.

"While it's clear that the whole package of TB IC interventions works, as was shown in New York City, to reduce nosocomial transmission, it's unclear what is the most effective part of it," said Dr Puneet Dewan. "Whether it's ventilation and airflow, index of suspicion and triage, cough hygiene and patient education or even how important the screening and education of health care workers regarding TB and HIV can be."

Country level TB IC policy and implementation

High-level government commitment will be required in order to make TB IC, in all settings, a national priority. Clear lines of authority need to be established to enact and enforce TB IC policies and standards. Besides the Ministry of Health, the Ministries of Defence, Justice, etc must also be engaged to provide TB IC in prisons, military barracks, hospitals and other congregate settings.

The national TB IC policy must be established or updated, along with national accreditation or certification standards and enforcement mechanisms. In addition, countries must develop local technical capacity in IC.

There was some debate among meeting participants about whether facilities that do not pass TB IC facility assessments should perhaps not be permitted to practice medicine. However, given that an assessment conducted by Dr Liz Corbett and colleagues showed that the majority of facilities in sub-Saharan African settings would likely fail (see HATIP 109), this may not be a practical solution — although it was suggested that HIV/TB activists might use assessments to draw attention to the failure of their public health systems to adopt TB IC.

"This is actually something that was discussed at a meeting in Southern Africa that brought together activists, policy makers and scientists to discuss the issue of IC," said Dr Alasdair Reid of UNAIDS. "One of the things that came out of that was some sort of accreditation — a big rubber stamp on the outside of the clinics saying, "TB safe" or something along those lines — where they had to fulfill a set of simple guidelines. And then the community would know that and might boycott the facility if it wasn't fulfilling those criteria. It's fairly straightforward to organise if it's a big campaign."

"The community does have to be engaged - they are the best sort of policeman for TB IC implementation," said Dr Corbett.

Operations manuals and standard operating procedures need to be developed adapting currently existing international guidance (with assistance from WHO and other technical partners) for the range of facilities where TB IC may be an issue within a country. Some participants felt that emphasis should first be on developing an interim plan for immediate improvement of TB IC implementation in existing facilities (adopting good work practices and measures such as outdoor waiting rooms etc…) — before considering expensive engineering and architectural measures.

At the facility level, programmes need to find ways to empower those who are made responsible to TB IC. "The type of people who are often allocated that responsibility at the facility level tend to be of a lower cadre who are not that good at pushing people," said Dr Corbett.

Some meeting participants felt that for now the primary focus of efforts should be on making health facilities safer. However, others argued that there should also be campaigns directed at preventing TB transmission within the community.

"If you get down to the communities where TB transmission takes place, these messages are not there," said Muhamed Mulongo of TASO. "I think we need to think how best can we get to those homes, to those small crowded huts where much TB transmission takes place, because communities are not getting that message."

At the very minimum, community groups and community-based organisations where people living with HIV/AIDS meet must also be educated about basic TB IC and encouraged to practice basic TB IC (see *Advocacy*) wherever they meet, teach cough hygiene, and so on.

Advocacy

Global advocacy for all the Three I's: "Push"

"Advocacy has to happen at all different levels," said Cynthia Eyakuze. "At the global level, within the national level — the policy makers, the providers and the patients themselves. And there's very different types of advocacy, including campaigns going onto demand creation, etc."

A 3 I's communications strategy should be developed to generate the pressure and demand globally. Immediate steps include distributing the report on the meeting's outcomes to WHO staff at all levels, discussing the meeting's outcomes at upcoming STAC and STAG meetings, WHO regional technical advisory group meetings, and to plan regional or country level 3 I's meetings.

The meeting outcomes are already being promoted at all major upcoming meetings (UNAIDS PCB, PEPFAR, the June 9th UN meeting, World AIDS Conference).

"We need to promote the dissemination of successful and best practices. There are good things happening in some parts of the world; we have to communicate and disseminate them," said Dr Getahun. "There must also be scientific advocacy, using existing scientific literature and enlisting major medical journals to promote TB prevention, diagnosis and treatment in general for people living with HIV."

Technical experts from other agencies (KNVC, Union, JICA) should be engaged — champions and skeptics alike. In particular, an advocacy and communication strategy to tackle the misconceptions/perceived obstacles to IPT implementation is crucial.

Advocacy "Pull"

Donors and global community groups need to work together to generate grass roots demand for the Three I's.

"This is the first time that I've actually heard the "push and pull" mechanism being applied to clinical services and I think it is important because the "pull" from the community of TB patients, has historically been lacking in the TB programme, compared to the HIV programme, where I think it was very effective in getting a lot of changes made," said Dr Alwyn Mwinga of the CDC Global AIDS Program in Zambia.

"Community activist groups and PLWA groups have not yet done enough to educate their peers and create demand," said Mark Harrington. "This is related to the fact that TB is still a stigmatised disease."

But that is changing, as evidenced by the first-ever activist march for TB during the World Union on Lung Health in Cape Town which involved over 5000 people. And more and more HIV activists are being trained to become HIV/TB activists.

HIV/TB activists at the Geneva meeting are clearly taking on the Three I's as part of their own agenda.

"We [TAG] recently did a training for 45 activists from 25 different countries on TB science literacy — they were really excited about it and people do want to know the science behind all of this. There are now some really professional activists operating at a very high level. So when you are developing policy… I really urge you to engage with the community because they're your greatest advocates in terms of helping to push your research and your programs into policy into programs and implement action," said Claire Wingfield of TAG.

"We should empower people living with HIV/AIDS to understand symptoms of TB and ask for care, ask for screening for TB," said Dr Alyssa Finlay of the CDC. "TB stigma can be addressed through education and awareness. Community, national leaders and role models should promote TB screening and address the issue of TB stigma. There should be simple, clear, positive messages that intensified TB case finding is part of the package that gives you the best care possible."

This positive spin is crucial — rather than the usual negative messages about TB.

"We've got to make sure there's a very positive message about TB because it empowers action," said Dr Gilks.

Human rights activists should be engaged as well by putting TB prevention in a human rights-based context. For example, Mark Harrington described the failure to implement IPT as a clear human rights problem.

“Failure to provide IPT which prevents TB, which causes the most deaths from HIV, is a violation of human rights. IPT could help 10.3 million people with TB/HIV co-infection right now. And the fact that we’re not doing it is a grave violation - I believe - of their rights to life and [treatment] with a cheap effective drug,” he said.

Likewise, people with HIV have a human right to safer healthcare facilities. Reverend Phillips suggested legal action might even be in order:

“I really believe a couple of great malpractice lawsuits would do well for a few ministries of health! It may never happen in the world, but I really think a few great lawsuits would wake up the Ministries, and then maybe they’d do something!”

Large-scale information education and communication campaigns for TB prevention, diagnosis and treatment need to be launched targeting HIV and TB in the family. “Health providers should ask patients about family members when they come to their clinic visits,” said Dr Finlay, “and screen them as well.” In addition, she suggested that education about TB should be integrated into schools to mobilise children.

Dr Ndwapi Ndwapi of Botswana suggested using the interaction with clients in ART clinics as an opportunity for public education — because while they in the waiting room, they are a captive audience.

The community of healthcare workers also needs to be engaged. Demand for TB IC and prevention also needs to created among the healthcare workers, who often initially see implementation of the Three I’s as “extra work.”

“Most of our workers are overburdened so when we look at this approach, we should make some room to say, ‘How are we going to support our workers?’” said Dr Sálomáo.

At the same time however, healthcare workers need to be convinced that implementation of the Three I’s is in their own best interest.

“I would suggest that all the 3 I’s activities are in support of the workers because the workers are at risk for TB, many of them are infected with HIV and many of them will develop TB,” said Dr Reuben Granich of WHO. “So I think that this effort is very much about worker safety and worker rights and supporting these overburdened healthcare workers.”

Dr Dick Chaisson of Johns Hopkins Medical School pointed out that in the US, an outbreak of TB in a health facility in Florida “led to a huge demand from healthcare workers for safe environments. If you’re talking about community mobilisation for IC, the healthcare worker community has to be mobilised and just as the patients have to demand IPT, they have to demand IC. It’s an untapped source of incredible power that needs to be utilised to address the issue!”

Resource mobilisation

Implementation won’t happen without resources — additional human resources will need to be recruited and trained to work on this issue as part of raising HIV care, standards and implementing the 3 I’s. Finally, the meeting participants called for the 3 I’s should be prioritised in the upcoming GFATM round 8/9 proposals, and in the upcoming PEPFAR country operational plans. Funding partners should be urged to direct funding toward infection control activities, including renovations and refurbishments.

Even before the Three I’s meeting concluded, many of the meeting participants made commitments to promote the Three I’s agenda — including representatives from many of the funding partners. These can be read in full at the end of the official Three I’s meeting report:
http://www.who.int/entity/hiv/pub/meetingreports/art_hivtb_meeting_april2008/en/index.html