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TB research is research to save the lives of people with HIV

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Why TB research matters

Next week, at the Conference on Retroviruses and Opportunistic Infections, one of the leading meetings on AIDS research, there will be over a thousand scientific presentations and posters describing cutting edge HIV research but, if previous years are any indication, only a couple of dozen abstracts will pertain to tuberculosis (TB) — the leading cause of death among people with HIV globally. This is not meant as an indictment of the conference organisers — who can only provide a forum for the research that is submitted to them — but it does reflect how little emphasis TB research and development (R&D) receives from the US National Institutes of Health (NIH) and other key funders of AIDS and medical research.

“The overall amount for TB [R&D] spent globally last year was only US \$455 million, which is less than a nickel for every dollar that NIH alone spends on HIV research,” said Mark Harrington of the Treatment Action Group (TAG), at the recent meeting of the Core Group of the TB/HIV Working Group of the Stop TB Partnership held in Addis Ababa last November. He was citing findings from TAG’s most recent analysis of TB research funding.¹

“NIH invested \$2.9 billion in HIV research last year compared to only \$157 million on TB research, despite the fact that TB kills almost as many people globally as HIV does [between 1 to 2 million people a year] and kills many of those of us living with HIV” he said.

The HIV research establishment and its funders seem to be ignoring one of the greatest consequences of the HIV pandemic: the resurgence of TB in areas of the world with a high burden of HIV — and seem to remain deaf to the growing chorus of voices from both the TB establishment and HIV community that TB research urgently needs to be given a much higher priority.

The latest bad news regarding HIV and TB

It is not hard to make the case that we are losing the fight against HIV-related TB. Much of the news on the HIV/TB front is going from bad to worse.

For instance, there’s more HIV-related TB today than ever before with an estimated 700,000 new cases of HIV/TB each year— and 85% of the cases are concentrated in Sub-Saharan Africa. Most cases are unlikely to be diagnosed and placed on life-saving treatment.

And now, according to Dr Christian Gunneberg of WHO, HIV/TB, data being reported suggest that current WHO estimates of the

actual burden of HIV/TB require substantial revision. About 18 sub-Saharan African countries have begun scaling up HIV testing in TB patients, and consistently, the proportion of TB patients testing HIV-positive is higher than the estimates — by a factor of 1.8, on average. And since TB is less likely to be diagnosed in patients with HIV in the first place, the proportion of TB patients who are HIV-positive may be even higher than data from testing TB patients suggests.

“Somehow these are gross under-estimates,” he said. “We expect the TB/HIV estimates to be higher in the next Global Report in March 2009. Watch this space.”

More than one in four TB cases are in one country alone: South Africa, with a WHO estimated case rate of 940 per 100,000 — which is higher than the TB case rate of 800 per 100,000 seen in Europe during the Industrial Revolution. In countries with a high HIV prevalence, TB incidence has been steadily increasing since the 1990s, with case rates rising two- to three-fold in a number of southern African countries, although in some countries the rates now appear to be stabilising.

“But in South Africa they continue to escalate,” said Dr Stephen Lawn of the Desmond Tutu HIV Centre in Cape Town and the London School of Hygiene & Tropical Medicine. “And off to the east of Cape Town, we have quite an extraordinary burden of disease. This study community where we are working has a very well run DOTS (directly observed therapy) clinic that serves the whole community and which has won lots and lots of certificates, which are proudly displayed. Despite that, rates have risen from about 500 per 100,000 in 1996, to over 2000 per 100,000 today. And that’s in the context of good DOTS.”

Dr Lawn noted that there’s also been a disproportionate increase in extrapulmonary and sputum smear-negative TB, which is difficult to diagnose and presents a huge challenge to a limited staff in this clinic. Over two-thirds of the TB patients in the cohort are HIV-positive. Cases requiring retreatment have increased from 3% to 24% — and 87% of those being retreated are HIV-positive.

Across Africa, up to a third of those diagnosed with HIV/TB who are not yet on ART die despite TB treatment. And even ART treatment does not entirely eliminate the risk of TB. In one of Dr Lawn’s studies in this cohort, the TB case rate was still 4.5 cases per 100 person years after three years on stable ART — much higher than the background rate in the community.²

On top of this, there is an emerging epidemic of multidrug-resistant (MDR-) and extensively drug-resistant (XDR-) TB in countries with a high burden of HIV. However, because of inadequate surveillance (due in part to the difficulty of getting a timely diagnosis of drug-resistant TB in resource-limited settings, particularly in people with HIV), the actual burden of drug resistance in these countries is unknown. But the cases already being detected [are more than South Africa can manage](#).

The TB R&D funding shortfall

And yet despite the failure of DOTS to control TB in countries with a high burden of HIV, and all of the hoopla around XDR-TB, between 2006 and 2007, the overall funding for TB R&D increased by just 6% or \$26 million, which Harrington remarked, “is hardly enough to keep up with biomedical inflation.”

Funding is nowhere near the \$9 billion that [The Global Plan to Stop TB: 2006-2015](#) said was needed for the development of new TB ‘tools’ (such as some of the diagnostics being rolled out). TAG went further, recommending that an additional \$11 billion be spent on basic science, infrastructure and operational research. Current

spending levels would have to increase by fivefold to reach the Global Plan targets.

“After documenting TB research investments for 2005-2007, we can now say with certainty that promises made by world governments and the private sector to supply the needed TB investment specified in the Global Plan are not being kept,” said Harrington at a press conference in Paris before the 2008 Union World Conference on Lung Health.

What’s worse is that much of the recent increase in funding comes from just one source: the Bill and Melinda Gates Foundation. But it would be a mistake if everyone assumed that they can keep going back to that well — according to HATIP sources, the foundation may wait a couple of years before making any further grants for TB research.

How to address the unmet HIV//TB research needs was a major concern of participants at the recent Core Group meeting, who recommended that “extraordinary actions be carried out by funding agencies, researchers and national governments,” according to a meeting summary. The Core Group devoted a special session to exploring ways to increase interest and investment in HIV/TB research — including updating and prioritising the HIV/TB research agenda.

Redefining the HIV/TB research agenda

An [HIV/TB research agenda](#) was developed four years ago, during a meeting held in Geneva to define the key HIV/TB research priorities as well as how to address them in the context of programme activities. According to the meeting report, much of the emphasis at the meeting was on operational research to support the implementation of the WHO’s [Policy on Collaborative TB/HIV Activities](#) which had come out the previous year, and to convince reluctant programme managers who wanted to see more data before they put these strategies into practice.

While many of the research questions highlighted in the report remain unanswered, clinical practice has changed dramatically in the last few years with the rollout of the HIV programmes in many countries. As [HATIP has previously reported](#), while operational research might help resolve some of the barriers to adopting some of the HIV/TB collaborative activities, including the Three I’s (TB intensified case finding, isoniazid preventive therapy and TB infection control) — some of the collaborative activities have been much easier to introduce than anticipated. For instance, several programmes have had great success scaling up HIV testing in people with TB, so perhaps all that was needed was the political will to do it, evidence from a couple of successful programmes, and a forum, such as PEPFAR’s HIV Implementers’ Meetings, where best practices could be quickly disseminated (See HATIP 88, July 2007, [part 1](#) and [part 2](#)).

But the 2005 consultation primarily focused on what could be done within the programmatic context.

The HIV/TB research agenda needs a bit of a makeover to reflect what has changed in the field, and to expand the scale and scope to include other types of research and engage more researchers — and also to stress its *urgency*.

“In Maputo in 2005, a WHO meeting of regional ministers declared this epidemic was a regional emergency requiring urgent and extraordinary actions. That makes the question: what are those urgent and extraordinary actions? The truth is we don’t really know. What we need to fuel this activity is urgent and extraordinary research,” said Dr Lawn in 2007, during a symposium at the

International AIDS Society meeting in Sydney where he provided a view from the field of what should be the HIV-TB research agenda.

By the time of his talk at the Core Group meeting in Addis, this agenda had evolved into a table with seven focused themes of research:

- Drug resistant TB
- Infection control
- TB prevention (including preventive therapy and vaccines)
- TB in the HIV and ART services
- The TB programme (and HIV activities there)
- Paediatric TB
- Large-scale community interventions

These themes are dissected by four methodologies of research:

- Epidemiology and disease burden
- Diagnostic tools and laboratory issues
- Clinical research and interventions
- Operational research (or as he put it in Sydney ‘health policy systems research to see how all this can be delivered within the confines of health systems in these developing countries’)

Dr Lawn and the meeting participants sought to identify some of the key research questions under each theme, though most of what follows are examples directly from Dr Lawn’s presentation (which can be downloaded [here](#)).

Drug-resistant TB

For instance, research on the burden and risk factors for MDR and XDR-TB is desperately needed. What is the actual burden and trend over time of drug-resistant TB in resource-limited countries? How much of the drug resistance is due to transmission in institutional settings (such as health facilities and prisons) versus transmission in the community? To what extent is drug-resistant TB undermining TB control? What exactly are the interactions between M/XDR-TB and HIV? Does HIV increase the likelihood of acquiring or developing drug-resistant TB?

Dr Annelies Van Rie noted out that these questions could be looked at in a number of ways: from an economic perspective (increased cost) from an outcomes perspective (decreased cure rates) or from a public perspective (increased stigma and reduced trust).

New diagnostic tools to detect drug resistance need to be developed and moved into the field. At the Core Group meeting, Dr Giorgio Roscigno of the Foundation of Innovative Diagnostics (FIND) mentioned current work to optimise the new line probe assays for drug resistance that are being introduced at the reference laboratory level in some countries such as South Africa. (Although WHO has approved these assays, the challenge is to get commitment to invest in the human and laboratory infrastructure needed to implement these in the field).

But FIND is presently trying to improve the test sensitivity of the line probe assays in people with smear-negative TB, and is also evaluating whether the test will work on dried spots (of sputum) — which would make specimen transport to the reference laboratory much simpler. FIND has other high tech diagnostics in development but the challenge will be to see whether these are affordable and practical at the peripheral lab level. Meanwhile, there are

non-proprietary methods of drug sensitivity testing, such as [MODS](#) and thin layer agar that need further field evaluations.

What are the optimum treatment regimens for MDR and XDR-TB? “MDR-TB treatment is difficult, toxic, and cure rates are not high so a very robust research agenda on MDR-TB treatment regimens is needed,” said Dr Lawn. Studies are also needed to show how to combine M/XDR-TB treatment with ART, looking at optimum drug concentrations, rates and management of overlapping toxicity, pharmacokinetic interactions as well as the optimal timing of ART.

What is the best way to deliver M/XDR-TB treatment? Can it be delivered to people where they live in the community, and if so how?

“In South Africa, 70% of the national TB programme budget is being spent on building MDR-TB hospitals. Hospitals are overwhelmed at the moment and will remain overwhelmed. We need to be able to decentralise care to the community. But how do we do that?” said Dr Lawn. “And how do we integrate that with DOTS and ART programmes? And very importantly, what do we do with contacts of MDR and XDR-TB patients?” In other words, what is the best preventive regimen to use for contacts of M/XDR-TB index cases?

Infection control

As mentioned in [the last issue of HATIP](#) (#129, January 2009), a recent scientific review of thousands of papers on TB infection control concluded that there’s not a huge evidence base demonstrating that specific TB infection control interventions work to prevent TB transmission in health facilities or in the community.

Research is needed to determine how to measure TB transmission and transmission risk in order to measure the impact of TB infection control interventions.

How can we protect patients in in-patient and out-patient facilities? How can we protect our healthcare workers? (As noted in the last HATIP, this will require a package of services including HIV testing, preventive therapy, personal protective equipment and antiretroviral therapy). At an infection control session at the Union World Conference on Lung Health last year, many healthcare workers voiced practical questions about N-95 masks, such as which one is best, how long can they be used, and how often should their fit be tested?

It remains unclear which interventions should be prioritised in the health facility setting. Which administrative interventions are more important and what are the most effective and practical physical interventions to introduce in in-patient or out-patient facilities: UV-radiation, modifications of airflow, or modification of natural ventilation?

Also, one of the chief challenges in infection control is making sure the interventions are put in practice – supplying N-95 masks for healthcare workers will do no good, if healthcare workers do not bother to wear them, UV lights won’t work if the bulbs aren’t changed regularly, ventilation won’t work when doctors, nurses, or staff don’t keep the doors and windows open.

“Monitoring infection control interventions – no one really knows how to monitor these and this is also a subject of operational research,” Professor Anthony Harries of the International Union Against Tuberculosis and Lung Disease told HATIP.

TB prevention

There is clear evidence that isoniazid or isoniazid in combination with a rifamycin can treat latent TB and prevent active disease. But what is, or could be, the impact of isoniazid preventive therapy or

other preventive therapy regimens when used on a wide scale within the community? How will this really affect TB control?

One concern that has slowed the implementation of IPT is the fear that it will increase the burden of isoniazid resistance

“There’s no evidence that IPT increases isoniazid resistance in controlled trials,” said Dr Lawn. “But what will happen when we roll this out in the community (especially communities where at least 30% of young adults have HIV infection?) When we give out IPT on that scale, and don’t have control of the drug, what will happen to isoniazid resistance within that setting?”

Preventive therapy should be given to people with HIV without signs of active TB. But research is needed to improve the ability to reliably exclude TB in those with very advanced immune deficiency.

What are the barriers to implementing IPT in each country and can operational research help address these? And do programmes keep track of their patients and monitor their adherence to IPT? Professor Harries reiterated that monitoring the performance of IPT programmes is another major area for operational research.

More recently there have been developments on the TB vaccine front, with [recent data from the DarDar study in Tanzania](#). However, many questions remain about the true degree of efficacy of the vaccine, and it needs to be evaluated in other settings. Other vaccines are also in development.

Further questions

HIV and ART programme

What is the true burden of TB in the HIV and ART programme and what are the best screening algorithms and diagnostic techniques to detect it?

How does ART affect TB control at the population level? Would earlier ART in people with HIV have a different impact on the burden of TB in the community?

What adjunctive interventions are needed to further reduce TB (such as IPT)? There are indications from one open label study that IPT further reduces TB rates in patients on ART, but this needs to be validated by controlled clinical trials.

Questions remain about how to optimally combine rifampicin-containing TB regimens and ART, especially second-line ART regimens. Rifabutin could be an alternative to rifampicin for people on protease inhibitor regimens, and there are moves to get the drug onto the Essential Drugs list in order to make the drug more widely available. But is it as effective in TB regimens as rifampicin?

How should TB immune reconstitution syndrome (IRIS) be diagnosed and managed?

How can ART programmes form tighter linkages with TB services and make TB diagnostic and treatment services more convenient for people with HIV and possibly TB?

The TB programme

As Dr Gunneberg pointed out, the true burden of HIV in people with TB in many programmes is still unknown.

Studies are obviously needed to improve the diagnosis of smear-negative and extrapulmonary TB and more rapidly detect MDR-disease, and to evaluate new diagnostic technologies.

Is the relapse rate among people with HIV on TB treatment truly greater or are most cases due to reinfection? How best can relapse be prevented? Is ART adequate or is longer TB treatment necessary? Would secondary IPT work? How best should retreatment cases be managed? What is the best retreatment regimen?

What is the best time to begin ART for people on TB treatment? [Recent data](#) have suggested that survival is improved in patients who start ART before completing TB treatment but more information is needed about the exact time to start ART. A number of studies with differing designs are now underway ([click here for details](#)).

"I am leading one study of "when to start" ART in TB patients in the AIDS Clinical Trial Group and also working with the HIV Prevention Trials Network to see if early ART (>350) reduces TB burden," Professor Diane Havlir of the University of San Francisco (and also Chairperson of the TB/HIV Working Group of the Stop TB Partnership) told HATIP.

Although TB programmes have demonstrated that they can scale up HIV testing, and offer cotrimoxazole to subjects who test positive, there has been less success getting people with HIV-related TB onto ART. Operational research is needed to develop optimal models for linking TB services to ART programmes to make sure that people aren't lost to follow-up.

Paediatrics

As our clinical review series on childhood tuberculosis demonstrated, paediatric TB is a neglected field, and much of what we know about the disease is based on research before HIV treatment became available. (See HATIP's recent three-part Clinical Review on childhood TB: part one, [Epidemiology](#), part two [Presentation and diagnosis](#), part three [Treatment and prevention](#)).^{3, 4, 5}

"Most of the questions we've been answering over the past two, three years in adults, still need to be asked in children," said Dr Lawn. Dr Mark Cotton of Tygerberg Hospital also gave a presentation at the Sydney IAS meeting on the HIV TB research agenda in children ([download a slide set in pdf form here](#)).

What is the true burden of TB in children in the community, and what is the burden of HIV-related TB in children? Diagnostic tools are desperately needed which don't rely on sputum, which young children have difficulty producing.

What are the optimum treatment regimens for both drug-sensitive and drug-resistant TB in children, and how can this be combined with ART? Pharmacokinetic studies are desperately needed to determine the optimal doses for TB drugs for children of different ages and sizes, especially for second-line drugs and new drugs in development.⁶

The BCG vaccine is not recommended in HIV-infected children but can it be safely given later after initiation of ART? Because of the difficulty excluding children with HIV when the vaccine is given (at birth) many children with HIV or who become HIV-infected post-natally will be vaccinated anyway. Some may develop life-threatening systemic BCG infections and BCG IRIS. How best should these conditions be managed?

How should programmes provide routine screening for TB contacts in children with HIV to make certain that TB-exposed children receive timely preventive therapy? How should the child contacts of MDR/XDR-TB patients be managed?

Large scale community interventions

The final theme in Dr Lawn's table is a call for the expansion of operational research beyond the confines of programmatic settings to find new ways to control TB.

"We shouldn't be small in our thinking. We know that DOTS is necessary but insufficient and we need more epidemiological data to understand why DOTS doesn't work and what is needed," he said.

He argued that researchers should consider "mass interventions." For instance, would it be possible, or advisable, to

provide mass TB treatment to ALL people with HIV with symptoms of TB (simply foregoing the laboratory-based diagnostic process) and then give mass IPT to everyone else? This could require working with partners outside of the health system — an idea that CREATE has piloted in its [ZAMSTAR study](#) (which is looking at intensified and enhanced case-finding within the community).

And what would be the effect on TB of putting everyone with HIV onto ART — as one notable paper has recently suggested? (see [HATIP 123, November 2008](#)).

"Granich's et al's model in *The Lancet* of annual universal HIV testing and immediate ART has the chance to considerably reduce the TB epidemic and this needs to be tested out (and in fact plans are being made to do so)," Prof Harries told HATIP.

Again, Dr Lawn stressed that urgent and extraordinary actions are needed to control HIV-related TB.

Expanding the TB research agenda and setting priorities

Although the list is quite extensive, it is by no means complete. For instance, in its present form, Dr Annelies Van Rie told HATIP, the agenda "clearly has a focus on clinical and epidemiological research, and does not pay attention to basic science, drug development, vaccine development, social science, etc."

Over the next several months a team from the Core Group will compile a more exhaustive list, prepare a final report and prioritise those questions that most urgently need to be answered. Clearly, issues of drug resistance, infection control — how to make health facilities safe — paediatrics (which is consistently neglected), and HIV/TB need to be at the top of the list.

A current and thorough assessment of the trials currently in progress or under development will be necessary to reduce duplication of effort. Dr François-Xavier Blanc gave a presentation at the Symposium in Sydney listing the major studies at the time ([see here](#) for pdf of slideset), but this will need to be updated and expanded to include country-specific operational studies.

Dr Lawn's agenda is very much focused on what can be achieved with what is currently going on in the field. Thus, it doesn't really address basic science, which is critically important according to TAG's report on [Funding Trends in TB Research](#):

"Aside from lack of funding, survey respondents attributed the lack of knowledge surrounding TB pathogenesis and appropriate biomarkers as the top barriers to accelerating and improving TB R&D. This highlights the importance of increased investment in the basic science of TB biology, immunology, pathogenesis."

Basic science would add a third dimension to Lawn's table because it affects the themes and methodologies of research. Basic science research could lead to a better understanding of the biology of TB and the life cycle of *Mycobacterium tuberculosis*: how does the microbe exist in droplets outside the body? How does the infection process occur? How does the immune system react and how does that affect the outcome of exposure, infection or the way the disease evolves? Basic science research forms the foundation upon which is based the development of new drugs, new diagnostics and vaccines that are so desperately needed in the field.

The overarching importance of better diagnostic tools

The holy grail: a point of care TB test

One priority area of research is the need to develop more sensitive and specific tests for TB that would work in people with

smear-negative TB (including children) and could be performed at least at the peripheral laboratory level. But a simple TB test that could be used wherever a person presents for care (point of care) (POC) would completely change the clinical landscape.

FIND has had some success bringing more complex but proven diagnostic technologies to resource-limited settings. Most of these technologies (MGIT, Line Probe Assays) only work at the referral laboratory or tertiary hospital facility level — though, the next technology FIND is moving forward, LED light microscopy, is a simple (though important) improvement on microscopy that can be battery-operated and used anywhere there is a microscopist trained to use it.

So far, however, FIND's track record has been less successful with more experimental technologies that might be useful in more peripheral settings, though Dr Roscigno reported some progress in this regard at the Core Group meeting ([see slideset here](#)). Unfortunately, he noted that POC TB tests still seems to be a long way off.

However, considerable activist pressure is mounting to apply resources to change this. Development of an inexpensive POC test was one of the issues addressed at 'TB: Dying for a Test,' a symposium sponsored by MSF prior to the 2007 Union World Conference on Lung Health in Cape Town ([download abstracts here](#)). At the meeting, Dr. Tido von Schoen-Angerer of MSF noted that the meagre pipeline is evidence that the potential market for "low cost" POC TB diagnostics is not incentive enough to stimulate commercial interest in R&D. He suggested that alternate incentives are needed, with one idea being that countries should pool resources to fund or reward the developers of new tools to combat diseases of high public health importance, such as a TB POC diagnostic test.

More recently, the AIDS Rights Alliance of Southern Africa and TAG co-sponsored a two-day workshop on how to expedite development of a POC TB test in Cambridge, U.K.

According to Mark Harrington, participants described an ideal test as having the following characteristics: requiring only one or two steps to perform; being sensitive and specific to *M. tuberculosis*; easily performed at rural health clinics; provides immediate easy-to-interpret results; able to diagnose pulmonary and extra-pulmonary TB; works in immunocompromised and HIV-positive patients, and [perhaps over-optimistically] would be able to identify resistance to at least isoniazid and rifampicin, but preferably also to fluoroquinolones and injectable anti-TB agents. They also concluded that the test should work on easily obtained specimens such as urine, saliva and bloodspots —but not sputum because it is a difficult specimen to work with (rarely available for children, for example) and it's not really collected for most other diseases.

"Diagnostic delays can last up to almost half a year with existing technology, to get people properly diagnosed and get them started on the proper treatment, and by the time their MDR is diagnosed many people, — especially if they are HIV-infected — are dead. So having a dipstick diagnosis of latent TB infection and active TB disease could revolutionise TB control efforts, and could save millions of lives enhancing access to TB services. And really, it's going to be essential to have such a test if we're ever going to be able to eliminate TB as a public health problem," said Harrington.

The participants at the Cambridge meeting proposed a multi-pronged initiative to focus scientific and financial resources on the TB POC test. Among the elements included would be a project-managed specification-based request for applications (RFA) for a TB POC test to be issued to academic and industry partners. Recently FIND announced that it's going to be releasing such an RFA, which is a positive step but more are needed.

"TAG's view is that the lack of investment in R&D reflects a fundamental lack of political will and a failure of leadership. The lack of basic science funding, in particular, is really crippling the search for new biomarkers, platforms and new scientists — who are very discouraged from entering the field because their funding is so anaemic," said Mark Harrington.

Engaging the community in research — and not just as an afterthought

"What is the solution to this? I think massive demonstrations," said Harrington who noted that activism had turned the tide in demanding increased funding in the fight against HIV. "We need a combination of top-down leadership and political will, and then we need from the bottom, massive mobilisation to demand much better diagnostic tests so that we can eradicate this curable disease."

However, it is important to stress that the community can't just be called on whenever a demonstration is needed for more funding. A respectful partnership between the research establishment, donors and the community needs to be developed much earlier on, according to participants in a meeting on engaging the HIV/TB community in TB research, which was organised and hosted by CREATE, just prior to the 38th Union World Conference on Lung Health in Paris.

"Meaningful involvement of the affected communities in TB research is paramount," said Carol Nawina Maimbolwa Nyirenda, a TB/HIV treatment activist working with the Treatment Advocacy & Literacy Campaign (TALC) in Zambia. "We are the ultimate beneficiaries of these services and our insights will be critical in improving service delivery and outcome measures."

The community is also, quite literally, where most of these large studies will be happening. Nevertheless, many community members at the CREATE meeting said that they felt excluded from TB research and that there is too little understanding between the community, researchers and funders (who generally seem to be setting the research priorities).

"Overall communities haven't been as well served by researchers in the past as they might be, and we would hope that CREATE and some of the other big studies ongoing now would be trying to learn the way forward," said Professor Peter Godfrey-Faussett of the London School of Hygiene and Tropical Medicine, and principal investigator of CREATE's ZAMSTAR study.

Changing this pattern will require political will, funding and effort to be put into capacity development of the HIV/TB community in the settings where research is going to be conducted. The community will be more effective partners if researchers and donors first invest in "research" literacy. But there are many advantages to developing this capacity: for instance, effective communication strategies before, during and after a trial are dependent upon community engagement. Community-led treatment literacy efforts are the most effective way to make certain that the community is aware of the research findings and how it should affect their options for care. Furthermore, activism will be necessary to translate research findings into policy change.

"Ultimately, having the donors, researchers and community at the same table helps the funder know that what they are funding is truly useful," said Dr. Lois Eldred of CREATE. "Also, involving the community early on, especially the local health infrastructure, increases the likelihood that positive research results will be sustainable." ([download the meeting report here](#)).

Other steps to increase investment and interest in HIV/TB research

To catalyse the HIV/TB research agenda, much greater political pressure will need to be applied to the major and private funders. TAG has set itself to applying pressure on the NIH to steer more investment funding towards HIV/TB research; and the Stop TB Partnership plans to encourage the UN Special Envoy for TB to visit heads of agencies that fund health research (e.g. NIH, Ford Foundation, Rockefeller Foundation) in order to request them to fund or increase their commitment to TB research.

The new political environment may offer new opportunities and Harrington called for a new US initiative under the new president Barack Obama to stop TB. He noted that there are various ways this could be done, for instance, the Office of the Global AIDS Coordinator could also start to manage the TB & Malaria portfolios, or they could set up a department for international development.

“The US president has to say the word “TB” and “U.S.” and “money” and “massive” in the same sentence. But I don’t care how it’s structured,” he said.

With the new administration, there could even be a silver lining for TB research in the economic downturn. There are efforts to increase funding for TB research in the stimulus package. At present, the Senate version of the bill includes \$2.7 billion for important medical research, with the following language: “In particular, the Committee recommends placing a priority on: short-term new grants that focus on specific scientific challenges; new research that expands the scope of ongoing projects; research on public health priorities such as influenza, tuberculosis and malaria; and stem cell research.”

Efforts are also underway to increase interest among investigators in HIV/TB research. One strategy recommended at the Core Group was the creation of awards to encourage young investigators to participate in HIV/TB research.

One small award was announced last year by the International AIDS Society (IAS): a TB/HIV research prize at the upcoming HIV Pathogenesis, Treatment and Prevention Conference to be held in Cape Town, South Africa (July 19-22, 2009).

The winner will receive a prize of US\$2000 for submitting the best TB/HIV research. [Online abstract submissions are now open.](#) The abstract submission deadline is 25 February 2009, midnight, Central European Time (CET).

Finally, a TB/HIV research meeting will be held in conjunction with the IAS meeting to draw more HIV researchers into the development and implementation of the HIV/TB research agenda. Dr Lawn will be one of the meeting’s organisers.

“I think the traditional model of research funding has been based on the level of interest (from pharmaceutical industry, interest

groups, advocates, media exposure and donors), how answerable are the questions and thirdly, how attractive are the data to the research community? Are they novel and are they publishable in high-impact journals?” Dr Lawn said in Sydney.

“But I think a novel approach is needed. What is the potential of reduction in disease burden? What is the impact on equity? Is it answerable? What is the likelihood of efficacious interventions being developed, and will it be deliverable? In the case of TB and HIV/TB, the answer to all these are yes. The burden of TB is huge and it’s impacting communities that are the most underserved and underprivileged communities on earth. These questions are answerable. We will, and can, find interventions if we put our minds to it, and these are deliverable on a large scale.”

HATIP would like to maintain an ongoing, moderated discussion, where our readership can post their ideas, needs or plans for HIV/TB research. [Join the discussion here.](#)

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about HATIP

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