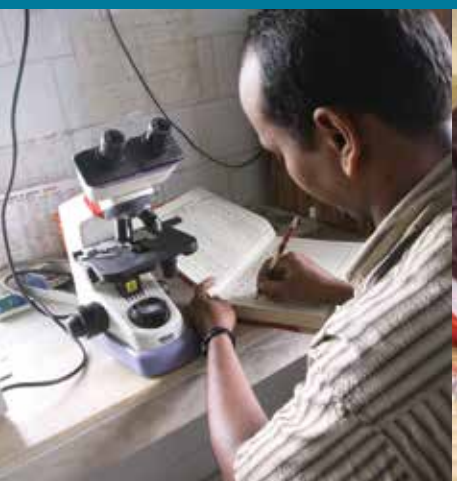
THE LOOMING CO-EPIDEMIC OF TB-DIABETES:
A CALL TO ACTION





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About the World Diabetes Foundation

The World Diabetes Foundation was founded in 2002 with the vision of being a catalyst for change. Our objective is to open a window of hope in developing countries by supporting prevention and treatment of diabetes.

We seek to bring diabetes higher on the global agenda through our partnerships. It is our hope that increased global awareness will increase the resources to address and limit the diabetes epidemic.

The Foundation is governed by a seven-member Board of Directors under the chairmanship of Prof Pierre Lefèbvre. Day-to-day operations are vested in the WDF staff under the management of Dr Anders Dejgaard, Managing Director. See more at: http://www.worlddiabetesfoundation.org.

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About the International Union Against Tuberculosis and Lung Disease (The Union)

For nearly 100 years, The Union has drawn from the best scientific evidence and the skills, expertise and reach of our staff, consultants and membership in order to advance solutions to the most pressing public health challenges affecting people living in poverty around the world. With nearly 17,000 members and subscribers from 156 countries, The Union has its headquarters in Paris and offices in the Africa, Asia Pacific, Europe, Latin America, North America and South-East Asia regions. Our scientific departments focus on tuberculosis and HIV, lung health and non-communicable diseases, tobacco control and research.

The Union works with stakeholders from every sector, including governments, international agencies, civil society, and the private sector. We provide stakeholders with a full range of services and products that span from generating evidence to taking action to improve public health.

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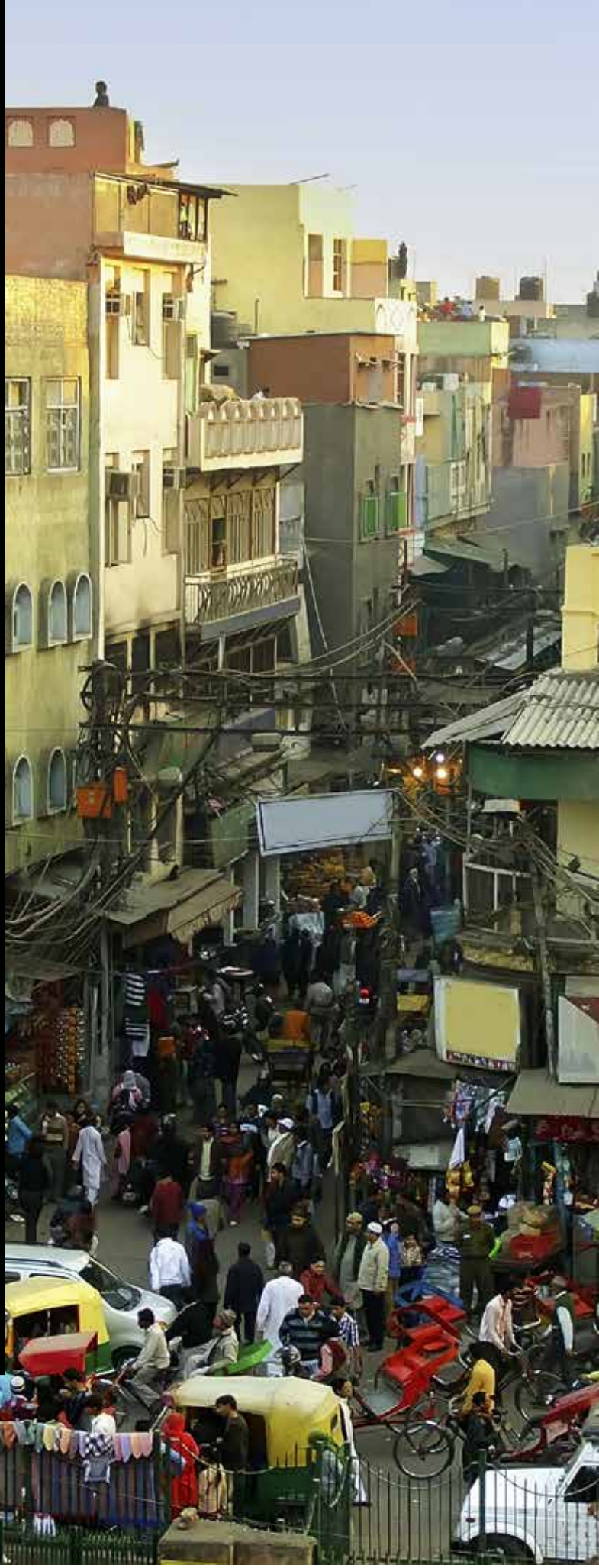


Knut Lönnroth, WHO
FORWARD

Diabetes is rampant in low- and middle-income countries, affecting the poor and rich alike, and increasing the risk of TB across all population segments.

When The Union and the World Health Organization began developing guidance for addressing TB and diabetes back in 2009, the magnitude and importance of the double burden had not quite sunk in among public health practitioners and clinicians, let alone the public. Diabetes was seen as a disease of the rich world, which had started to affect also the better-off in poor countries—a perceived sign of development. With TB mainly affecting the poor, the two epidemics where assumed to be only marginally overlapping. That assumption was wrong. Diabetes is rampant in low- and middle-income countries, affecting the poor and rich alike, and increasing the risk of TB across all population segments.

The growing burden of TB-diabetes is changing the landscape of TB care and prevention. Increasing prevalence of non-communicable diseases and aging populations are increasing the relative importance of different risk factors for TB. While classical TB risk factors and comorbidities—like undernutrition and HIV-infection—remain crucial to address, chronic conditions that impair people's defence against TB, such as diabetes, have emerged as additional important factors.

There is now abundant evidence of high rates of diabetes in people with TB, and often diabetes is only discovered if actively screened for. The same is true for TB rates among people with diabetes. Strategies to improve health care access, diagnosis, clinical care, financial risk protection, and prevention need to be adapted to this reality. Coordinated efforts for planning and implementation across public health programmes are required. The essential approaches are succinctly outlined in this unique report.

The *Collaborative Framework for Care and Control Of TB and Diabetes*, published by WHO and The Union in 2011, sparked actions on several fronts, as summarised in this document. It stimulated pilot projects, national policy dialogue, and new research. It also influenced the discourse on global TB care and prevention. In May 2014, the World Health Assembly endorsed WHO's new, post-2015, global TB strategy (WHA resolution A67/11), which incorporates all essential elements of TB and diabetes collaborative activities. The post-2015 sustainable development goals are more clearly highlighting the importance of addressing chronic diseases as part of the broader health and development agenda. Shared health systems bottle necks, clinical challenges and determinants require a joint response. Documents such as this will help bridge the conceptually dubious divide between communicable and non-communicable diseases.

The collaborative work on TB and diabetes has only just begun. Many actors need to become more actively involved, from the highest political levels to civil society and patient organizations. It is my hope that this document will spur more engagement and actions to improve prevention and care of both conditions.

Knut Lönnroth, World Health Organization

Executive SUMMARY

If we fail to act, the consequences could prove catastrophic for healthcare systems in areas that are impacted.

Diabetes mellitus is quietly fueling the spread of tuberculosis (TB). The purpose of this report is to demonstrate to policymakers, public officials, health program managers, clinicians and activists that the world faces a looming co-epidemic of TB-diabetes, and that this is a serious public health risk we need to urgently address. If we fail to act, the consequences could prove catastrophic for healthcare systems in areas that are impacted.

Diabetes is a chronic, noncommunicable disease that weakens the immune system, making people with diabetes three times more likely to get active TB. Diabetes is escalating, especially in countries where large numbers of people are infected with TB. Diabetes affected 382 million in 2013 and will increase to a projected 592 million by 2035. As diabetes spreads, it will cause more and more people to develop TB.

TB is an infectious disease that spreads from person to person through the air. TB kills more people than any other infectious disease except HIV/AIDS: 1.5 million people died from TB in 2013. These cases of "active" TB disease emerge out of a massive pool of latent TB infection. One in three people around the world—two billion people—hold a latent TB infection somewhere in their body, where it can remain dormant through one's whole life. Every person infected with TB faces about a 10 percent chance that the infection will activate and spread in the body, giving them the telltale symptoms of TB: gradual but severe weight loss, night sweats, and the famously bloody cough. At this stage, the infection can spread to people nearby. People who have weak immune systems are more likely to develop active TB.

We must learn from history. When HIV/AIDS—another illness that weakens the immune system—escalated in the early 1990s, it caused TB rates to skyrocket. Eighteen African countries saw TB rates quadruple. But the world was slow to act, despite clear evidence that HIV was fueling the spread of TB. We have an opportunity now to head off TB-diabetes, before we see the worst of its impact.

This report is a call to action to address this threat before it takes a larger toll in death and disability as well as economic impact—and before we see the gains made against TB in the past decade rolled back by diabetes. The report also identifies where knowledge gaps should drive a research agenda, and how evaluation should be used to gauge progress and shape policy.

Tuberculosis-Diabetes
INTRODUCTION

Diabetes is fueling the spread of TB.

Diabetes is fueling the spread of TB. This is largely because diabetes rates are skyrocketing around the world, and having diabetes increases the risk that a person will become sick with TB. Diabetes is also more difficult to manage in people who have TB. And a person sick with both diseases is likely to have complications that do not typically exist when either is present on its own.

Successfully addressing TB-diabetes therefore requires a coordinated response to both diseases at all levels of the health system—from the crafting and implementation of national policies, to the management of disease control programs, to the delivery of services to individual patients.

TB and diabetes are two of the world's leading causes of death and disability. TB is an infectious disease caused by a bacteria that spreads from person to person through the air. TB is contagious and can be cured in most cases with antibiotics. Diabetes is a chronic, non-communicable disease that has various causes associated with diet, behavior and genetics. Unlike TB, diabetes is not contagious, and there is no cure in the vast majority of cases; patients must manage the illness over the course of a lifetime.

Policymakers, public officials, health program managers, clinicians and activists must recognize that the looming co-epidemic of TB-diabetes is a serious public health threat—and work together to mount a concerted response. The report is a call to action to address this threat before it takes a larger toll in death and disability as well as economic impact—and before we see the gains made against TB in the past decade rolled back by diabetes. The report also identifies where knowledge gaps should drive a research agenda, and how evaluation should be used to gauge progress and shape policy.

The recommendations in this report will not require establishing new global health agencies or mobilizing vast new sums of money. They are practical, actionable steps, based on evidence compiled to date, that can be implemented largely through current public health programs and allocated funding. As with most other effective public health measures, we expect these actions to quickly become net cost-savers. And as chronic diseases like diabetes escalate in developing countries, those countries can apply lessons from addressing TB-diabetes to the management of other chronic illnesses, creating further cost-saving opportunities.

A Brief history of efforts to research and describe TB-diabetes

Anecdotes about the deadly interplay between TB and diabetes have existed since ancient times. Avicenna the Greek recorded around 1000 A.D. that TB—then known as pthisis—caused complications among people with diabetes, and diabetes was responsible for increasing a person's risk of developing pthisis. The Indian saint Yugimahamuni described the symptoms caused by TB and diabetes as a syndrome he called "meganoikal".[i,ii]

New data demonstrating the important public health links between TB and diabetes have re-emerged within the last decade.[iii] In 2007, researchers from the Medical Research Council, the World Health Organization (WHO) and Britain's Newcastle University carried out a systematic review of previously published research into the increased risk that people with diabetes have of developing TB.[iv] Using a different methodology, in 2008 researchers from Harvard University published a second systematic review of all previously published studies that had attempted to quantify the increased risk of developing TB among people with diabetes.[v] These landmark studies, along with three additional systematic reviews published by researchers in 2009, 2010, and 2014.[vi,vii,viii] Taken together, this body of research has clearly shown that diabetes makes a person two to three times more likely to develop TB—and that the interaction between the two diseases constitutes a worldwide health threat.[ix]

Diabetes makes a person two to three times more likely to develop TB.

In 2009, experts on TB and diabetes gathered in Paris to review the available evidence and determine whether it was strong enough to justify and inform the creation of international guidelines for the care and control of the dual disease. As an outcome of this meeting, in 2011 the International Union Against Tuberculosis and Lung Disease, Paris, France, and the World Health Organization released The Collaborative Framework for Care and Control of Tuberculosis and Diabetes. This document provides evidence-based guidance for policymakers and health program implementers to begin addressing the growing epidemic of diabetes and TB.[x]

With a thoroughly reviewed body of research and international guidelines, we now have the evidence and the guidance needed to move forward with a global response to TB-diabetes.

Learning lessons from the slow response to another co-epidemic: TB and HIV/AIDS

Between 1990 and 2005, countries across sub-Saharan saw the number of people falling ill with TB each year quadruple. This led the WHO and African ministers of health to officially declare TB an "emergency" epidemic.[xi]

Why did TB skyrocket? Nobel Peace Prize Laureate Archbishop Desmond Tutu—himself a TB survivor and outspoken advocate—explained in an op-ed in 2012:

Imagine TB as kindling. Two billion people — one-third of humanity — carry a latent TB infection. The vast majority of those infected live their whole lives without becoming sick with TB or spreading the infection. The body's immune defenses seal the invading TB germs within a tiny capsule at the infection site — preventing the germs from multiplying.

Now picture HIV as a match.

HIV destroys the immune system. When this happens, the capsule containing the TB germs weakens and breaks. The germs spill out and multiply. The person becomes sick with tuberculosis, transmitting the germs to others through a telltale cough.[xii]

In countries where TB and HIV are fueling each other's spread, the norm is now to fight the diseases together through "collaborative activities". These include an integrated public health strategy, as well as health services that screen people with HIV for TB, test people with TB for HIV, and provide appropriate care to people affected by both infections.[xiii]

But it took far too long to get here—and the cost of delay has been prohibitive. The first reports on the interactions between TB and HIV were published in the late 1980s, and warnings were sounded in the early 1990s about an impending dual epidemic. It wasn't until 2004 that the first global "interim" strategy for addressing TB-HIV was developed.[xiv] Driven by HIV, TB was declared an official emergency in Africa the next year.

When it comes to addressing TB-diabetes, we must not let history repeat itself. Just as sub-Saharan Africa bore the brunt of the TB-HIV epidemic, South Asia now faces a looming co-epidemic of TB-diabetes. In some high-burden states in India, an estimated 20 percent of sputum smear-positive TB cases[1] are already found among people with diabetes.[xv] And as of the time of this writing, it is estimated that there are more people in the world living with TB-diabetes than there are living with TB-HIV.[xvi]

[1] Sputum-smear positive TB cases are those in which TB bacteria are visibly present within a person's sputum.

Tuberculosis-Diabetes
THE CHALLENGE

TB-diabetes is a looming co-epidemic.

We are witnessing an unprecedented transformation in the global burden of disease. Throughout history, most people died from infectious diseases—illnesses that are contagious and caused by germs. In the past few centuries, industrialization and economic development, lifestyle changes and the advent of modern medicine have induced a fundamental shift toward non-communicable diseases—primarily heart disease, cancer, diabetes, and chronic lung diseases.

These changes were seen first in advanced market economies like the United States and Europe, but they are now sweeping through rapidly developing countries like India, China, Nigeria, and Brazil. Today, about two-thirds of deaths worldwide each year are caused by non-communicable diseases—and eighty percent of them occur in low- and middle-income countries.[xvii] Furthermore, the number of people living with diabetes—and particularly Type 2 diabetes—is rising rapidly, and projected to increase from 382 million in 2013 to 592 million by 2035.[xviii] Of those, 80 percent will live in developing countries and nearly half will be unaware that they have diabetes until they develop a complication from the disease.[xix]

TB kills more people every year than any other infectious disease except HIV/AIDS. An estimated nine million fell ill with TB in 2013, and 1.5 million died. About one in three people worldwide—an estimated two billion people—live with a latent TB infection. In most cases this infection will remain dormant for one's entire life, never making the person sick. However, the risk that this latent infection will progress to active TB disease increases significantly if a person's immune system is compromised—for example by diabetes.[xx]

With diabetes on the rise globally and many unaware that they're at risk—and with enormous pools of latent TB infection and high burdens of active TB disease in many countries—TB-diabetes is a looming co-epidemic.[xxi] Furthermore, in countries where diabetes is escalating and TB rates are already high, diabetes will increasingly impede efforts to control TB.

An emerging body of evidence has shown that where rates of TB-diabetes have been carefully measured, they are significant—and higher than researchers previously believed. A study in the Indian state of Tamil Nadu found that nearly half of all patients with TB had either diabetes (25.3%) or pre-diabetes (24.5%). Among 8,886 TB patients screened in China, 1,090 (12.4%) had diabetes.[xxii] Of 1,262 patients with TB in Southern Mexico, 29.6% were also found to have diabetes.[xxiii] Generally, prevalence rates tend to be higher among older populations and among people living in urban versus rural areas. More epidemiological research is needed to determine how much of the global TB disease burden can be attributed to diabetes.

Prevalence of Diabetes in TB Patients: Recent Studies

Region	TB Patients w/Diabetes	Year Published
Karnataka State, India	32%	2011
Kerala State, India	44%	2012
Tamil Nadu State, India	25%	2012
Texas, USA	39%	2011
Mexico	36%	2011
Tanzania	17%	2011
Pakistan	16%	2012
South Pacific	40-45%	2013

TB-diabetes is projected to hit South Asia particularly hard. Countries with high TB burdens and rapidly growing rates of diabetes—such as India, Peru and the Russian Federation—are likely to see the most significant impacts of the co-epidemic.[xxiv] By 2030, India, China, Indonesia, Pakistan and Brazil together are projected to have half of the world's people living with diabetes.[xxv] WHO classifies all of these countries as "high TB burden" countries, meaning that without concerted efforts, they are poised to face epidemic levels of TB-diabetes.[xxvi]

How TB and Diabetes Work Together

TB and diabetes interact with each other on a number of levels, with each disease exacerbating the other. Diabetes triples a person's risk of developing tuberculosis.[2,xxvii] The likelihood that a person with TB will die, or that they will get TB again after they have been successfully treated for it, is also significantly higher among people with diabetes.[xxviii] Research also shows that among people who are being treated for TB, those with diabetes remain contagious longer than those who do not have diabetes. [xxix]

TB can temporarily increase the level of blood sugar, a condition known as "impaired glucose tolerance," which is a risk factor for developing diabetes.[xxx] Impaired glucose tolerance is also known as "pre-diabetes," because it often precedes the onset of diabetes. Moreover, some drugs used to treat TB (especially rifampicin) can make it more difficult to control diabetes due to the way that they interact with oral diabetes medications.

There are growing concerns that oral diabetes medicines can decrease the effectiveness of TB medicines. While controlling glucose levels likely reduces the risk of developing TB among people with diabetes, not enough research has been done to know if it's enough to reduce the risks of developing TB or dying from it. It's also not yet clear how to optimize glucose control in people who have both TB and diabetes.[xxxi]

Diabetes increases the general risk of infection, but we do not actually know the precise cellular or molecular mechanisms that cause diabetes to predispose a person to developing TB; this is an important area for further research.[xxxii] What we do know is that diabetes impairs cells within the immune system that play a critical role in fighting the TB bacteria within the body, similar to what we see with HIV infection.[xxxiii]

[2] It is currently unknown whether diabetes increases the risk that a person will develop a latent TB infection after being exposed to the germ.

What is Tuberculosis?

Adapted from World Health Organization: What is TB? How is it Treated?[xxxiv]

TB is an infectious disease caused by the bacterium Mycobacterium tuberculosis. While it typically affects the lungs, it can affect virtually any part of the body. TB spreads from person to person through the air when someone sick with the disease coughs, sneezes or spits. Another person needs only to inhale a few of these germs in order to become infected. Key symptoms include cough, fever, night sweats, and weight loss, sometimes which can occur over many months. While TB is treatable and curable in most cases, without proper treatment up to two thirds of people with TB will die. TB is treated with a cocktail of multiple antibiotics taken over the course of at least six months, though multidrug-resistant cases require treatment for up to two years. About a third of the world's population carries a latent TB infection. Typically, each person infected with TB has a 10 percent chance of progressing to TB disease within his or her lifetime. People with compromised immune systems—often caused by HIV, malnutrition, age or diabetes—or who use tobacco regularly have a much higher risk of developing TB disease.

What is Diabetes?

Adapted from The Diabetes Atlas 6th Edition[xxxv]

Diabetes is a chronic, non-communicable disease that, if left unmanaged, can lead to early death and a number of other serious health conditions. Diabetes occurs when the body either cannot produce enough of the hormone insulin, or it is not able to use insulin effectively. Insulin allows the body's cells to absorb glucose and use it as an energy source.

There are three main types of diabetes: type 1, type 2, and gestational diabetes. For the purposes of this report, we will focus on Type 2 diabetes, a condition where the body does not use insulin properly, resulting in elevated levels of glucose in the bloodstream. It is a lifelong chronic condition and the most common form of the disease. Type 2 diabetes is almost exclusively the type that interacts with TB in the body, and to which we refer in this paper concerning the TB-diabetes co-epidemic. This form of the disease can go undetected for years, but nevertheless leads to long-term damage to the body during that time.

Diabetes can cause people to suffer from a number of other serious health conditions, including cardiovascular disease, kidney disease, eye disease, nerve damage, the loss of extremities, and a variety of infections—including TB.

Economic Impact

Both TB and diabetes exact significant economic costs on society, including both the direct costs of healthcare and indirect costs of disability, lost productivity, forgone investment in human and physical capital, and death. No assessments have been carried out to date on the economic impact of TB-diabetes, though assessments have been conducted on the economic impact of each disease individually.

An estimated 75 percent of people who develop TB are between the ages of 15 and 54, which tend to be their most economically productive years.[xxxvi] A 2007 study commissioned by the World Bank found that had it not been for the implementation of the DOTS TB control strategy, the economic burden of TB between 2006 and 2015 for the world's 22 "high-burden countries," would have ranged between $1.18 billion to $3.33 billion for each country.[xxxvii]

Diabetes treatment and care is not yet widely available in developing countries, and when treatment is available it is rarely free. For individuals in developing countries, the out-of-pocket costs to treat diabetes are significant, commonly leading households to sell their possessions to pay for treatment.[xxxviii] These household costs add up to significant impact. According to modeling conducted by the Harvard School of Public Health and the World Economic Forum, high-income countries currently pay most of the costs of diabetes. In 2010, this amounted to $376 billion in direct costs globally, with high-income countries paying 90.8 percent, middle-income countries paying 9.1 percent, and low-income countries paying 0.1 percent. This trend is projected to change dramatically, however, as diabetes escalates in middle-income countries. By 2030, the direct costs of diabetes are projected to increase to $486 billion globally. By that time high-income countries are projected to face 25.4 percent of the cost, with middle-income countries facing 72.1 percent and low-income countries facing 2.5 percent.[xxxix] These costs do not include additional indirect costs due to disability and death.

The enormity of these costs, and mounting evidence of a TB-diabetes co-epidemic, underscore the urgent need for a robust economic assessment that accounts for the pernicious interaction of TB and diabetes in patients.

An interview with TB–diabetes expert Dr. Anthony Harries

Professor Anthony David Harries is Senior Advisor at The Union and Director of the Department of Research. He is a physician and a registered specialist in the United Kingdom in infectious diseases and tropical medicine and spent over 20 years living and working in sub-Saharan Africa. He is an honorary professor at the London School of Hygiene and Tropical Medicine and the author of hundreds of published papers on TB, HIV/AIDS, tropical medicine and the impact of operational research. In Malawi he served the Ministry of Health as National Advisor on both TB and HIV, with responsibility for scaling up antiretroviral therapy there. In 2002 Professor Harries was appointed Officer of the Order of the British Empire for services to work in TB in Africa.

Q. Why are you so concerned about TB-diabetes?

The dual problem of diabetes and TB is similar to TB-HIV, another major public health dilemma I've spent a lot of my career working on. In the case of TB-HIV, which started in the 1990s, the world had enough evidence to show that a co-epidemic had emerged, but it took several years to focus the attention of people outside of the public health community. A lot of people died. In Swaziland, the country in Africa where it's most common for people to be affected by both TB and HIV at once, average life expectancy was cut in half in a decade. So now that we're watching diabetes escalate in areas where it's prime for fueling a TB-diabetes co-epidemic, it's crucial that we get ahead of the problem while we're able.

Q. What's happening in these early stages of a response?

Well, the focus for TB-HIV started with screening TB patients for HIV and screening HIV patients for TB. We're starting to use a similar approach to tackle TB-diabetes. If you have diabetes and live in a country with a high burden of TB, it's important that you find out if you also have TB. If you have TB, then you can get treatment. Now, if you have TB and you don't know whether you have diabetes, it doesn't matter where you live—you should find out if you have diabetes. This is important. Half of people who have diabetes are totally unaware that they have it.

Q. What aspects of the looming TB-diabetes co-epidemic set it apart from TB-HIV?

One obstacle that was not a factor in the TB-HIV case is that, while TB and HIV treatments are both free for patients, diabetes treatment usually isn't free. Oftentimes people living where TB is common simply can't afford the medicine and care they need to manage their diabetes. And in a lot of countries, diabetes treatment isn't available, period. So we need to make diabetes treatment widely accessible and affordable. We are grappling with a diabetes epidemic that is growing year by year. In order for us to stop it, people need to be able to be tested for diabetes and begin receiving treatment and care as early as possible.

Q. So what needs to happen now?

With diabetes growing at an incredible rate, it poses a large problem for the response to TB. Curbing the global diabetes problem is vital to eliminating TB. Those of us studying these diseases can provide the evidence. But my experience working to respond to TB-HIV has taught me that we can provide all the evidence in the world, but we also need to proactively convince and inspire others who we need to act. It takes time to direct resources and train health workers, build supply chains for medicines, set up robust data monitoring systems and do the things necessary to respond to a modern epidemic. We're witnessing a convergence of two terrible diseases. We need to move quickly.

Tuberculosis-Diabetes
THE WAY FORWARD

We have a framework in place to guide a response to TB-diabetes

A Framework For Action

In 2011, The Union and WHO released the Collaborative Framework for Care and Control of Tuberculosis and Diabetes.[xl] Like the WHO Policy on Collaborative TB/HIV Activities, which was launched first as an "interim policy" in 2004, updated to a definitive policy in 2012 and has provided guidance during this whole time for responding to TB-HIV, the framework lays out the key features of a public health response to TB-diabetes.

The framework identifies three broad challenges for responding to TB-diabetes:

- **Providing regular bi-directional screening for the two diseases (i.e., screening diabetes patients for TB and screening TB patients for diabetes)**
- **Administering quality-assured treatment to patients suffering from both diseases**
- **Preventing TB in people with diabetes**

To address these challenges, the Collaborative Framework provides a series of recommendations for public health policymakers, health program implementers and care providers (see Box 2). The recommendations are most relevant for countries that have high burdens of TB, and high or rising rates of diabetes. While the specifics will vary depending on country contexts, responsibility for implementing the recommendations sits largely with TB programs and programs responsible for preventing and administering care for people with diabetes. In principle, where strong public health programs are already in place, the bulk of the work required to implement the recommendations will involve coordination between programs, initiating basic screening activities, and putting in place effective referral services. Implementing the recommendations will be most straightforward in settings where TB and diabetes services are being offered through primary health care services.[xli]

The framework is intended to guide activities until 2015, after which progress needs to be evaluated and the latest research used to develop a revised framework that will guide activities in the next phase of the response.

CASE STUDIES

Recommendations from the Collaborative Framework for Care and Control of Tuberculosis and Diabetes[xlii]

Establish Mechanisms for Collaboration

The bodies and processes for joint coordination for delivering TB and diabetes services should be established at regional, district and/or local levels, depending on country-specific factors, with representation of relevant stakeholders. These stakeholders should carry out activities from a shared plan that reflects national plans for TB and non-communicable diseases.

Surveillance (i.e., collecting and analyzing relevant data on cases) of TB should be conducted among diabetes patients in settings with medium to high burdens of TB.

Surveillance of diabetes should be conducted among TB patients in all countries.

Where collaborative activities are being established, national programs should agree on a core set of indicators (i.e., data points to measure) and tools to collect data for monitoring and evaluating activities to improve care and prevention of both diseases.

Detect and manage TB in patients with diabetes

At a minimum, people with diabetes should be screened for chronic cough, night sweats and fever at the time of their diagnosis with diabetes and, if possible, during regular check-ups for their diabetes. People with TB symptoms should be examined in line with national guidelines. Other diagnostic procedures (e.g., for TB that occurs outside the lungs) should also be pursued according to national guidelines.

Screening for TB disease more broadly (e.g., for all people in whom diabetes is diagnosed, regardless of their symptoms) should be explored as part of the research agenda to improve the diagnosis of TB among people with diabetes and to determine whether screening is in fact cost-effective.

A referral system should be established so that patients suspected of having TB are promptly referred to TB diagnostic and treatment centers. They should also be evaluated according to national guidelines of the national TB control program.

Case-finding for TB should be intensified by increasing awareness of and knowledge about the interactions between TB and diabetes, including joint risk factors, among both healthcare workers and the people they serve.

Healthcare facilities, including diabetes clinics, should have in place an infection control plan (i.e., a plan for reducing exposure to TB infection among both patients and health workers) that includes administrative and environmental control measures. These measures should follow WHO's established guidelines for TB infection control.

Treatment and case management of TB in people with diabetes should be provided according to existing TB treatment guidelines and international standards. Currently, the same TB treatment regimen is recommended for people with diabetes as for people without diabetes, but research is needed to find the most effective way to treat patients with diabetes and TB.

Detect and manage diabetes in patients with TB

Patients with TB should be screened for diabetes at the start of their treatment, where resources for diagnosis are available. Until better evidence is available to inform the best screening and diagnostic approaches for diabetes among people with TB, the type of screening and diagnostic tests should be adapted to the context of local health systems and the availability of resources. Until research tells us the best way to help people with TB manage their diabetes, in TB patients diabetes should be managed in line with existing WHO guidelines.

Screening People for Tb and Diabetes in India is Feasible, But What's the Most Effective Way to Do It?

India has the highest burden of TB of any country in the world, with 1,000 people dying from the disease every day.[xliii] As the country has been developing rapidly, India has also come to have one of the highest burdens of diabetes in the world. There were approximately 61.3 million adults with diabetes in India in 2011.

In response to these high rates of TB and diabetes, the healthcare system in India has been exploring a standard way of screening people who have one disease for the other, and vice versa—a process known as "bidirectional screening."

A study conducted by the India Tuberculosis-Diabetes Study Group examined results and challenges of screening patients with diabetes for TB within clinics. After receiving training, healthcare workers screened patients for TB by asking them a series of questions. Those who reported experiencing symptoms typical of TB were referred for TB testing. Those diagnosed with TB received treatment, and all patients were referred back to the diabetes clinic for continued diabetes care.

The study produced important lessons. First, the specific questions asked during the screening process and the type of diagnostic tests used are important considerations. The researchers used two tests that are inexpensive and widely used but not the most sensitive available.[3] As a proportion of the total number of people tested, few were diagnosed with TB and those who were tended to be very infectious. So the study therefore demonstrated that it is feasible to institute a process where people with diabetes are routinely screened for TB and referred for testing. At the same time, it showed that the questions asked during the screening process and the specific type of diagnostics used will affect how many patients are actually diagnosed and whether the process is likely to be cost-effective.

The India Tuberculosis-Diabetes Study Group also assessed the screening of TB patients for diabetes in eight hospitals and more than 60 clinics across India.[xliv] After receiving training, health workers asked TB patients whether they had a known diabetes diagnosis. Those who reported having diabetes were referred for care to control blood glucose levels. Those who did not report having a known diabetes diagnosis received blood glucose tests (RBG) at random, followed by fasting blood glucose (FBG) if RBG was above a certain level. Patients diagnosed as having presumptive diabetes were referred to a clinic for diagnosis confirmation and care.

The study found that the screening process was feasible and worked well. Thirteen percent of the more than 8,000 TB patients screened had diabetes. Using these results, if similar rates of diabetes exist among TB patients nationwide, this screening process could identify people with 286,000 diabetes. This is an important and hopeful finding, because diabetes is believed to be undiagnosed in over half of individuals living with the disease.

These pilot studies have shown that it is feasible to conduct bidirectional screening for diabetes and TB in India, but more research is needed to determine the most effective way of doing it. Done effectively, given the high rate of both diseases in India, bidirectional screening should lead to earlier detection of both TB and diabetes, and earlier and better treatment of both diseases.

[3] It is currently unknown whether diabetes increases the risk that a person will develop a latent TB infection after being exposed to the germ.

CASE STUDIES

Recommendations from the Collaborative Framework for Care and Control of Tuberculosis and Diabetes

China is another country experiencing high rates of both diabetes and TB. The country accounts for nearly 14% of the world's TB burden, with nearly one million people developing the disease and 30,000 dying from it each year.[xlv] As a result of rapid industrialization, urbanization, and changing lifestyles in recent years, almost one in ten people in China have diabetes.[xlvi]

S. J. Tang and colleagues studied the rate of diabetes and pre-diabetes in people who were newly diagnosed with TB in a rural community in China and compared it to the rate of diabetes among people who didn't have TB. Among 6,382 patients, those diagnosed with pulmonary TB were more than three times more likely to have diabetes than those without TB. People with diabetes were also more likely to have a variety of TB that was more infectious. In rural China, diabetes awareness is low and screening is rare. The researchers found that only a little over half of people they diagnosed with diabetes had been diagnosed previously. They concluded that the TB-diabetes link is significant even in this rural setting where diabetes was thought to be uncommon.

Another study conducted in TB clinics in Guangzhou, China, a major city, found a high rate of TB treatment failure in patients who also had diabetes. This suggests that TB treatment might need to be lengthened for patients who have diabetes, and/or diabetes needs to be aggressively controlled at the time when TB treatment starts.[xlvii] It also reinforces the importance of integrating screening and treatment for the two diseases.

Based on the 2011 "Collaborative Framework for the care and control of Diabetes and Tuberculosis", the healthcare system in China has also piloted routine bi-directional screening of TB and diabetes.

The pilot project was carried out in five diabetes clinics throughout China. After receiving training, health workers screened patients for TB each time they visited the diabetes clinic. Screening involved asking five questions about TB symptoms or possible exposure. If a patient answered yes to any of the questions, he or she was referred for TB testing, and those diagnosed with the disease were treated. Regardless of the TB diagnosis, all patients were expected to be referred back to the diabetes clinic for further care.[xlviii]

The pilot project improved TB detection among diabetes patients. In these five clinics, TB case notification rates were significantly higher than among the general population. Case notification improved as clinic staff became more familiar with the procedures. One of the hospitals had especially high TB notification rates due to well-conducted training, clear roles and responsibilities, special staff allocated for screening and data recording, and easy referral for TB services because of close proximity to the diabetes clinic. The project's outcomes suggest that screening diabetes patients for TB results in increased and earlier detection, better and earlier treatment of TB, improved outcomes for TB treatment and diabetes care, as well as a reduced risk of TB transmission. This kind of system, which included routine data recording and analysis, may also improve data collection on diabetes and serve as a model for other non-communicable diseases.

This pilot project shows that it's feasible and effective to screen diabetes patients for TB in China. With the danger that TB and the increasing burden of diabetes pose to public health in the country, bi-directional screening could benefit the treatment and detection of both diseases.

A TB–diabetes Research Agenda

While researchers have published vital new studies on the links between TB and diabetes in recent years, critical knowledge gaps remain.

The following questions must be urgently answered to inform the successful treatment, management and control of TB-diabetes. Answering these research questions will be critical for providing an evidence base that informs the next iteration of the Collaborative Framework after 2015.

Screening and diagnosis

- What are the best tools and strategies for screening for and diagnosing diabetes among people with TB and vice versa—including approaches within resource-poor settings?
- Among people with tuberculosis, when is the best time to screen for diabetes: at the start of treatment or a few months after treatment has started?
- Among people with diabetes, what is the most effective approach to screening for TB? How often should screening be conducted? What are the most appropriate screening tools?
- Should people with diabetes be screened for latent tuberculosis infection and, if found, treated for it?

Treatment

- Is the standard TB treatment regimen adequate, appropriate and of long enough duration for treating TB among patients with diabetes?
- What is the best treatment protocol to use to treat diabetes in patients who are also taking anti-tuberculosis medicines?
- What can we do to reduce the likelihood of death and recurrent TB (i.e., when a patient is successfully treated for TB and yet develops TB again) in patients who also have diabetes?
- What are the short- and long-term effects of glycaemic control on latent TB infection, active TB disease, and TB treatment outcomes?

Case management

- What is the benefit and what are the operational issues related to more intensified diabetes monitoring and treatment in TB patients? What is the respective role of insulin versus metformin?
- How does poor management and control of diabetes impact the likelihood that TB patients will die from TB or develop TB again after they complete treatment?
- Does quarterly cohort reporting of new cases of diabetes, tracking health outcomes of patients being treated over time, and analyzing complications and survival rates lead to 1) better management and care provided to people and 2) improved forecasting and more reliable supplies of medicines?
- What models of health service delivery can best contribute to the integration and sustainability of care for people with TB-diabetes in low- and middle-income countries?

Disease surveillance, response, and monitoring & evaluation

- What are current and projected future rates of TB-diabetes in key countries and regions, i.e., those with medium and high burdens of tuberculosis and those experiencing increasing rates of diabetes?
- How well does the DOTS model of tuberculosis control apply to the large-scale response to diabetes?
- What is the feasibility and effect of using joint indicators for the monitoring and evaluation of TB-diabetes efforts?

Research and development

- There is a need to develop a better, simpler, and cheaper point-of-care test (i.e., a test administered wherever the patient is and delivers results during the same visit) that can diagnose diabetes and TB in resource-poor settings.

Costing

- Projections of the cost of implementing the Collaborative Framework and the research agenda are needed, both for individual countries that need to implement the framework as a priority as well as global cost projections that can be used to mobilize resources from global health donor and financing agencies.

TANDEM

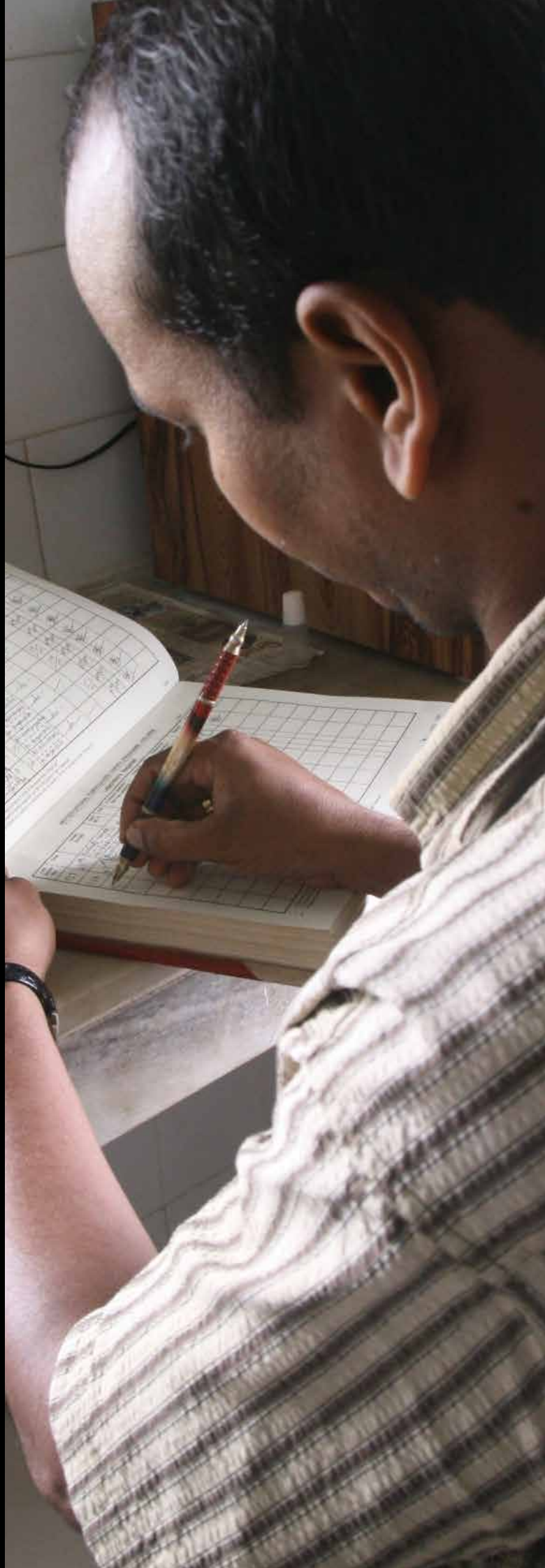
Addressing knowledge gaps in policy, patient management, and underlying causes of TB–diabetes.

TANDEM is a four-year collaborative research project that aims to address the link between diabetes (diabetes) and tuberculosis (TB). The project looks to improve knowledge and data on important aspects of this relationship. This goal is critical, as greater understanding of the interaction between the two diseases is necessary to improve care for TB-diabetes patients and create effective control strategies.

TANDEM is working to test two central hypotheses: 1) that screening and management of diabetes in TB patients can be improved and will impact control of TB-diabetes co-morbidity, and 2) that diabetes influences TB susceptibility in part through hyperglycemia and genetic variation common to both diseases. To investigate these hypotheses, TANDEM is integrating innovative expertise in clinical, epidemiological, and laboratory sciences. The project's multi-disciplinary consortium links field sites in 4 TB endemic countries facing a rapid diabetes increase (Romania, Peru, South Africa, Indonesia) with leading laboratories in 4 European countries (Germany, United Kingdom, Netherlands, Romania).

TANDEM's objectives are comprehensive and multifaceted, ranging from issues of screening and management to the cellular and molecular aspects of the diseases. The project intends to identify feasible and effective screening methods, and determine the prevalence of co-infection. TANDEM will also assess the required level of diabetes management during and after TB treatment, and the effect of glucose control on TB treatment outcome. Another goal includes pinpointing what accounts for TB-diabetes susceptibility and poorer treatment outcomes. Finally, the project aims to establish the basis for the causal link between the two diseases, particularly examining the effects of hyperglycemia and genetic variation.

For more information about TANDEM, see "TANDEM: understanding diabetes and tuberculosis" in The Lancet Infectious Diseases.[xlix]



Tuberculosis-Diabetes RECOMMENDATIONS

The following recommendations provide practical action steps, based on the evidence accumulated to date, for policymakers, public health financing bodies, program implementers, clinicians and advocates. They are intended to spur progress toward implementation of the recommendations within the Collaborative Framework for Care and Control of Tuberculosis and Diabetes.

Policy:

1. Where necessary, national (and where relevant, state-level) policymakers should establish policies that call for and enable coordination between public health programs currently tasked with controlling TB and responding to diabetes. Countries with a high burden of TB and escalating rates of diabetes should institute such policies as a priority.
2. Funding should be made available to implement a robust TB-diabetes research agenda, including both in the research and development of new tools as well as in operational research (see above).

Program implementation:

3. Ministers of Health should oversee implementation of the recommendations within the Collaborative Framework, including assessing the cost of implementation. Where it is not currently feasible to implement the recommendations at scale, pilot projects for dual screening should be established along with time-bound, costed plans for scaling them up.
4. Ministers of Health should convene to share plans and lessons learned from efforts to address TB-diabetes to-date. They should work with their counterparts in bordering countries in order to provide a "continuum of care" for clients who travel across borders during the course of treatment.

Financing and technical assistance:

5. Bodies that provide financing for public health activities should make resources available for implementing the recommendations within the Collaborative Framework and advertise the availability of this funding to applicants. They should also develop guidance for including TB-diabetes activities within funding proposals that they solicit, with a priority placed on regions with a high burden of TB and rising rates of diabetes. Guidance that the Global Fund to Fight AIDS, Tuberculosis and Malaria has issued for the inclusion of coordinated TB-HIV activities within its funding proposals could serve as a good precedent for similar guidance for TB-diabetes activities.[1]
6. Technical assistance agencies should develop core competencies to advise health programs on effectively implementing the recommendations of the Collaborative Framework and advertise the availability of this assistance.

Health service delivery:

7. Clinicians who treat clients for TB and/or diabetes should familiarize themselves with TB and diabetes screening protocols. They should educate patients about risks and provide referrals to services as appropriate based on local context.

Advocacy:

8. Global health activists should educate policy-makers, large-scale public health program implementers and international development agency leaders about TB-diabetes, and work to both shape policies and mobilize resources to implement the Collaborative Framework.
9. Advocates in low- and middle-income countries where TB-diabetes is a growing challenge should wage campaigns to educate decision makers and the public, and call for the implementation of the Collaborative Framework within their countries.

Tuberculosis-Diabetes
CONCLUSION

It is within our power to respond to the looming TB-diabetes co-epidemic and forestall its most harmful consequences.

Diabetes is rising rapidly worldwide and is increasingly fueling the spread of TB. In people being treated for TB, diabetes is associated with their remaining contagious for longer than usual, and it increases the risk that they will die from TB or become sick again after they have finished treatment. Successful TB control programs are undermined by rising rates of diabetes in many rapidly developing countries. The Collaborative Framework for Care and Control of Tuberculosis and Diabetes provides practical guidance for a coordinated response to both diseases. The framework is informed by the latest evidence and builds on existing public health infrastructure.

The legendary Canadian ice hockey player Wayne Gretzky is famous for his playing strategy, which was "to [skate] where the puck is going, not where it's been."[li] This strategy applies just as well to the public health response to TB and diabetes. We have witnessed how HIV caused TB to skyrocket in sub-Saharan Africa. The response to that co-epidemic was slower than necessary, leading to enormous and avoidable loss of life plus economic costs. We must avoid repeating this mistake. It is within our power to respond to the looming TB-diabetes co-epidemic and forestall its most harmful consequences.

The Looming Co-epidemic of TB–Diabetes

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