ANCIENT ENEMY, MODERN IMPERATIVE: A TIME FOR GREATER ACTION AGAINST TUBERCULOSIS
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Tuberculosis (TB) is the second-biggest single infectious killer—after HIV/AIDS—on earth, causing the death of 1.3m people in 2012 (the latest year for which figures are available). This toll—2% of global mortality—continues despite a cure existing for nearly 70 years and heightened global efforts against TB going back two decades. Mark Dybul, executive director of the Global Fund to Fight AIDS, Tuberculosis and Malaria puts the issue bluntly: “we have the tools to end TB as a pandemic and public health threat on the planet, but we are not doing it.”

Now the World Health Organisation (WHO) has approved a new “Post-2015 Global Strategy and Targets For Tuberculosis Prevention, Care and Control”, which calls for the incidence of TB to be reduced to fewer than ten cases per 100,000 population by 2035 and for the number of deaths to be cut by 95%. Such a shift will require health systems to make dramatic progress that has so far eluded them. This Economist Intelligence Unit report, supported by Janssen, draws on interviews with 17 public health officials, funders, academic and medical experts, researchers, and activists as well as on extensive desk research to consider the state of the TB challenge, barriers to further progress, and how efforts need to evolve. Its key findings include the following.

**Despite important successes, progress against TB is still slow and significant weaknesses remain.** On the positive side, the WHO estimates that increased efforts against the disease have saved 22m lives since 1995 and helped to reduce the mortality rate from TB by 45% since 1990. On the other hand, nearly one-third of estimated new cases of TB went undiagnosed in 2012. More generally, prevalence and, in particular, incidence figures have been slower to come down than mortality, and much of the drop in the former may have resulted indirectly from economic development rather than directly from better TB control.

**Drug-resistant TB has become a public health crisis that is receiving too little attention and shows up failings in current efforts.** Drug-resistant TB accounted for 5% of all new TB cases globally in 2012 and 13% of deaths. In certain regions, especially Eastern Europe and Central Asia, the problem is particularly acute: in the Russian Federation, for example 23% of new cases and 49% of retreatments are for multi-drug-resistant (MDR) TB—strains that have immunity to the most common anti-TB drugs. Under one-quarter of people worldwide with these strains of the disease, however, are properly diagnosed and fewer still receive the necessary treatment. Largely a man-made problem, drug resistance is a sign of multiple failings in TB control. It develops initially because patients do not, for a variety of reasons, complete their course of medication successfully (an ongoing problem, with 13% failing to do...
so in 2012) or are given inappropriate drugs. The spread of the drug-resistant strains to new patients by direct infection, however, also reveals deficiencies in case finding and drug-susceptibility testing by TB programmes.

To date, TB efforts at various levels have often suffered from a lack of compelling ambition and interest. As Dr Neil Schluger, chief scientific officer of the World Lung Foundation and chair of the Tuberculosis Trials Consortium, states, there is “a tendency [among policymakers and the public] to think of TB as background noise. It still kills a lot of people but doesn’t seem to have a sense of urgency around it.” This affects efforts against the disease in a number of ways: national TB programme goals sometimes aim to treat only a proportion of those presumed to be ill; funding for TB programmes globally falls short by more than US$1bn annually and donor fatigue is a growing risk; moreover, research into new drugs and diagnostics has been slow, with funding in this area even declining. It remains to be seen whether the new WHO targets will galvanise efforts.

A high level of stigma still affects those with the disease and hampers efforts against it. Worldwide, the association of TB with poverty has created negative feelings towards those who develop the active form of the disease. Blessina Kumar, chair of the newly formed Global Coalition of TB Activists (GCTA), explains that “people don’t realise how bad the stigma and discrimination around TB is .... [they] are worse than the disease.” This not only exacts a high emotional cost from individuals, it can lead them to delay seeking treatment, allowing the disease to spread. Stigma can also negatively affect the way that patients are treated by care providers. Even some supposedly technical medical terms—such as “defaulter” for someone who fails to complete treatment—have negative connotations. More broadly, several experts interviewed for this study point to stigma as a likely explanation for the sometimes weak response to TB by health systems.

Efforts against TB remain overly provider-centred and set apart from health systems. The diagnosis and treatment of those with TB under the Directly Observed Treatment, Short Course (DOTS) strategy (long the core of anti-tuberculosis efforts) has been based on patients who feel ill coming to clinics for testing and, if found to have the disease, treatment. Although inexpensive, this approach misses a large number of cases and does not take account of the psychological and social needs of patients that might impede them from beginning or finishing their treatment.

Improved success against TB will require changes on a number of levels. Further progress against TB is essential, but will mean new strategies that address current weaknesses while not throwing away gains to date. These include the following.

- **Finding and treating people where they live.** To find the nearly-3m new cases of TB every year, health systems in countries with a high incidence of TB need to look across the entire population, and even those with a lower prevalence have to find better ways of going into, and working with, sometimes marginalised populations.

- **Taking TB control out of existing silos.** TB needs to treat the whole person, including addressing common co-morbidities such as HIV/AIDS, and co-ordinating public and private health provision.

- **Harnessing cost-effective technology.** Although progress in the field of TB remains frustratingly slow, new tools available today—both medical and non-medical—have the potential to transform treatment.

- **Raising the profile of TB.** Perhaps most important, activists and other stakeholders must find better ways to elevate national and global ambitions to deploy the tools at hand with sufficient intensity to make more rapid progress against this disease.
Ancient enemy, modern imperative: A time for greater action against tuberculosis is an Economist Intelligence Unit report, supported by Janssen, which investigates the health challenge posed by tuberculosis (TB) and ways to improve the effectiveness of the global response to it. The findings of this report are based on extensive desk research and interviews with a range of public health officials, funders, academic and medical experts, researchers, and activists.

Our thanks are due to the following for their time and insight (listed alphabetically):

- Dr Draurio Barreira, national co-ordinator, Brazilian National Tuberculosis Programme
- Dr Lucica Ditiu, executive secretary, Stop TB Partnership
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- Mark Dybul, executive director, The Global Fund To Fight Aids, Tuberculosis and Malaria
- Dr Paula Fujiwara, scientific director, International Union Against Tuberculosis and Lung Disease
- Dr Salmaan Keshavjee, associate professor of global health and social medicine, Harvard Medical School
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- Blessina Kumar, chair, Global Coalition of TB Activists
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- Dr Neil Schluger, chief scientific officer, World Lung Foundation, and chair, Tuberculosis Trials Consortium
- Dr KJ Seung, deputy director, Partners in Health, Lesotho Project
- Dr Joseph Sitienei, head, Division of Communicable Disease Prevention and Control, Kenyan Ministry of Health
- Dr Marc Sprenger, director, European Centre for Disease Prevention and Control
- Dr Shenglan Tang, director of the Global Health Research Centre, Duke Kunshan University in China
- Louie Zepeda, health and disability consultant, Philippines

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Tuberculosis (TB) is a disease caused by *Mycobacterium tuberculosis*, a widespread bacterium that typically travels between hosts in airborne droplets. When inhaled, in the majority of cases the infection is destroyed by the human immune system. Where it fails, two outcomes are common. In the most frequent, the bacteria spread to the lymphatic system, but there they are walled off and stopped from replicating by the host’s immune system. The result is called latent TB, in which the infected individual experiences no symptoms and cannot spread the disease. An estimated one-third of the world’s population has this condition.

In rarer cases, those infected develop active TB. It most frequently attacks the lungs and such pulmonary TB causes the persistent cough commonly associated with the disease. On occasion, though, TB instead affects other parts of the body, including the lymph nodes, bones, kidney, brain or the central nervous system. Non-pulmonary TB is not infectious, but may be harder to diagnose because of the lack of cough and because the sputum of those infected may not reveal the bacterium, making smear tests ineffective. Other symptoms of all forms of the disease can include pain, fatigue and fever. Pulmonary TB is the infectious form, as the cough allows the bacterium to become airborne.

Someone with active, pulmonary TB on average infects around one new person per month. In about two-thirds of active cases, if left untreated, TB is fatal. For pulmonary TB this is usually as a result of degrading the lungs to an extent that they cannot provide sufficient oxygen. Of those with latent TB, 10% go on to develop the active version of the disease at some point, in many cases as a result of their immune system having been weakened by other factors, such as malnutrition or co-infections like HIV.

Most TB responds to treatment with a six-month course involving a combination of so-called “first-line drugs”. This treatment can be physically challenging and in a small number of cases brings its own risks.

Drug resistance, meanwhile, is a growing problem: in 2012, although data are sketchy, the World Health Organisation (WHO) estimates that 5% of cases of TB, and 13% of deaths, resulted from multi-drug-resistant (MDR) TB which is defined as having an immunity to the most powerful of the first-line drugs.

MDR TB is treated with a range of second-line drugs. These are sometimes older medications replaced by first-line treatment. This therapy is invariably far less effective than first-line drugs on drug-susceptible TB, more expensive, and takes up to two years to complete. It is also far more toxic, causing in some cases, depending on the specific drugs used, everything from rashes, liver or eye damage, severe gastrointestinal upset, and depression sometimes to the point of being suicidal. Intolerance to side effects frequently makes adherence to the drug regime difficult. Moreover, in many countries the supply of these second-line drugs is irregular, making treatment less effective still. According to the WHO, for those beginning treatment with second-line drugs in 2010, only 48% were cured two years later. Overall, the only substantial advantage of second-line medication is that the TB bacterium is less likely to have developed a corresponding immunity to them.

In recent years, TB resistant to a number of these second-line drugs, so-called extensively drug-resistant (XDR) TB has appeared in over 90 countries and, according to the WHO, now makes up about 10% of MDR TB cases. The options available here are even more restricted, and include drugs of unknown effectiveness as well as recently approved medications that also involve substantial side effects. More concerning still, cases of so-called totally drug-resistant TB—a self-explanatory term with no formal medical definition—have been found in Iran, Italy and, more recently, India. Although susceptible to newly-introduced drugs, the presence of such highly resistant strains of TB, along with XDR TB, shows that even traditional second-line drugs are likely to be of less utility if not used properly.
An opportunity the world has so far missed

In May 2014 the World Health Organisation (WHO) set the goal of reducing mortality from tuberculosis (TB) by 95% by 2035. In 2012 TB killed 1.3m people, making it the world’s deadliest infectious disease after HIV/AIDS. Although not absent from developed states—especially large urban centres—the disease is largely one of developing countries [see map]. In particular, 22 so-called “high burden” states account for 80% of global cases and 83% of deaths. The disease’s toll has a marked economic impact as well. A 2009 World Bank analysis found that, even in the best of circumstances, TB was likely to drain over US$150bn per year from the high-burden countries as a whole between 2006 and 2015. Nor are relatively well-developed regions exempt: a 2013 academic study estimated that the disease costs EU countries over €5bn annually.¹

The tragedy, however, is that much of this hoped-for progress could have happened earlier. The vast majority of this loss—both human and economic—is entirely avoidable: the disease is preventable and has been curable with antibiotics since 1946.

A glass half full
This is not to dismiss substantial efforts against TB over the last two decades. A major turning point was 1993, when the World Bank’s World Development Report measured the impact of the disease using a then-new analytical tool, ¹ Ramanan Laxminarayan, et al, “Global Investments In TB Control: Economic Benefits”, Health Affairs, 2009.
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the disability-adjusted life year (DALY), which combines the number of years lost to a condition through ill-health, disability, or early death. Because TB most often attacks young adults or the middle-aged—and therefore kills people in their economic prime—the analysis found that treating the disease cost less than US$10 for every DALY reduced, making it by far the most cost-effective of a series of recommended, low-cost public health interventions in the report.

That same year, the WHO, noting the millions still dying from TB, declared it to be a “global health emergency”. Soon after, the organisation developed the Directly Observed Treatment, Short-Course (DOTS) strategy, based on emerging best practice in developing countries. Central to this is the diagnosis via smear testing—the microscopic analysis of sputum traditionally used for TB and still the most common diagnostic—of patients presenting at specialised clinics with symptoms. Those found to be infected then received a standardised six-month course of drugs under direct observation to ensure adherence. The strategy, however, went beyond diagnosis and treatment. It also included: sustained government commitment to TB control; maintenance of a regular supply of all anti-TB drugs; and standardised recording and reporting of the outcomes of individual patients and anti-tuberculosis efforts as a whole. DOTS quickly became standard practice for national TB programmes in high-burden countries as well as in most other states.

The strategy’s positive results include an estimated 22m lives saved since 1993. These efforts have also coincided with a drop in the prevalence of active TB per head of 37% between 1990 and 2012, and a decline in mortality of 45%. The Millennium Development Goals, a UN initiative, aim for both these metrics to reach 50% by 2015.

A glass half empty

Other data, however, paint a less optimistic picture. Even after the success of the last two decades, as noted above, this curable disease still kills over 1m people each year, indicating that the emergency is far from over. Moreover, while the long-term drop in mortality and prevalence may appear large as an aggregate, it is occurring slowly. Lucica Ditiu, executive secretary of the Stop TB Partnership—a multi-stakeholder group—notes that the annual drop of around 2% in recent years is actually small, given the current burden. Her organisation estimates that, at the current rate, it would take 180 years to reduce the global level of TB prevalence to the low levels currently present in the developed world.

Part of the problem has been that, just as DOTS was being introduced in the 1990s, the HIV epidemic began in earnest. The two conditions interact in numerous ways, but HIV, by weakening immune systems, makes its hosts more susceptible both to infection with TB in the first instance and to the activation of any pre-existing, latent TB. HIV also makes it harder for the body to fight the damage caused by the active form of TB. The result is substantially raised mortality: TB is the biggest killer of people with HIV and about one-quarter of those who died from TB in 2012 also had HIV. The synergy between the two illnesses, however, is predominantly an African issue: over three-quarters of the HIV-positive TB deaths are from that continent. It does not explain the slow progress on TB in other parts of the world.
Instead, although certainly saving lives, the extent to which anti-TB efforts have affected the incidence or prevalence of the illness is less clear. Indeed, new cases of TB have declined by just 17%, mostly in the last decade, according to the World Bank. TB is a disease of poverty, thriving in areas with poor public health provision where individuals live in close proximity, allowing easy air-borne transmission. Some transitions consistent with economic growth, such as rapid urbanisation and the development of slums, can therefore increase the spread of the disease. Overall, though, the health gains from improved standards of living in many parts of the world since the 1990s have tended to improve the TB situation. Accordingly, much of the drop in incidence at the global level, says Dr Michael Kimerling, senior programme officer, tuberculosis, at the Gates Foundation “is based on demographic change—by increasing the denominator when calculating the percentage of people infected—and economic development.”

A number of studies have even found that the reduction in TB prevalence over the years seems to be unrelated to the intensity of effort by national TB programmes. Rather, it correlates with measures such as a country’s score on the Human Development Index, a composite that includes national income and education levels, and general population health.  

Two likely explanations exist for this surprising outcome. One is the nature of the disease. Dr Draurio Barreira, the co-ordinator of Brazil’s National Tuberculosis Programme, points out that “TB is a multi-factorial problem, so the answer needs to be multi-factorial. You cannot separate specifically how much social protection, general health services and TB services would contribute to the decline.” Another reason for the results is likely to be an important weakness of current efforts against TB: they miss a substantial minority of new cases. WHO models indicate that in 2012, some 8.6m people probably developed active cases of TB, but of these only around two-thirds were identified. This leaves 2.9m newly ill or newly re-infected individuals spreading the disease. Consistent with this explanation, a 2012 academic analysis found that having a case-finding rate of over 70% in a given year brought down incidence, prevalence, and mortality in the subsequent year.

Evolving into a new crisis

The most worrying failure of current TB control efforts for the longer term is the growth of drug-resistant TB. The most basic multi-drug-resistant (MDR) TB against which standard, first-line antibiotics are ineffective [see box: Tuberculosis: The Basics] is estimated to have accounted for 5% of all new cases in 2012—3.6% of first-time patients and 20% of those who relapse. It also was responsible for 13% of deaths. In some countries, especially in central Asia and Eastern Europe, the numbers are much higher. In Kyrgyzstan, for example, 26% of new cases and 68% of relapses are multi-drug resistant, while in the Russian Federation the equivalent figures are 23% and 49%.

Because testing for the drug-resistant version of the disease is insufficiently widespread, under one-quarter of MDR TB patients are properly diagnosed and put on the correct treatment of second-tier drugs. Meanwhile, resistance even to these drugs is spreading, with one in ten MDR cases classified as extensively drug resistant (XDR) and over 90 countries reporting at least one case. As Dr Neil Schluger, chief scientific officer of the World Lung Foundation and chair of the Tuberculosis Trials Consortium, puts it, drug resistance “is out of control. The vast majority of people with it are not diagnosed or treated. We have to recognise that MDR TB is a real global public health emergency.”
development is a sign of poor prescribing practices and weak patient follow up in the face of non-adherence to medication. Moreover, Dr Eugene McCray, chief of international TB research and programmes at the US Centres for Disease Control and Prevention, explains that in the developing world the majority of new MDR cases are not the result of acquired drug resistance, but of direct infection from contact with a person with an MDR strain. “That means there

Countries that had notified at least one case of XDR-TB by the end of 2012

are failures in health systems in a lot of places—failures to make sure we find people, diagnose them, and treat them effectively.”

It is two decades since the World Bank showed the economic value of widespread tuberculosis treatment and the WHO labelled the disease a global health emergency. Nevertheless, despite laudable progress on mortality rates, TB remains a leading global killer. Moreover, it is showing a worrying potential for resurgence that leaves no room for complacency. Microbes are no respecters of borders. Although better public health infrastructure puts developed countries in a stronger situation than many others when it comes to TB, the outbreak of MDR TB in New York City in the 1990s shows that every country needs to be prepared for the risks presented by MDR and XDR TB. The WHO calls the situation a global health crisis.

The obvious question is why—what are the barriers to more effective TB control?
A complex disease many would rather ignore

The obstacles to better TB control begin with a lack of focus by key stakeholders. Dr Schluger sees “a tendency to think of TB as background noise. It still kills a lot of people but doesn’t seem to have a sense of urgency around it. Getting it into the consciousness of governments and ministries of health is a number one priority.” Dr Ditiu adds that TB “is like an orphan. It has been neglected even in countries with a high burden and often forgotten by donors and those investing in health interventions.”

Perhaps the strangest result of this attitude, Dr Ditiu adds, has been a common lack of ambition: “you have governments, for example, setting very low targets, especially for MDR TB patients, and saying we would like to treat a few hundred people even though the country is estimated to have thousands affected. Normally, you should have a plan to deal with all of those.” Dr Salmaan Keshavjee, associate professor of global health and social medicine at Harvard Medical School, has experienced the same problem. “A lot of people have limited vision when it comes to thinking about what we can do for TB in poor countries. That vision is not limited for HIV, or building airports, or putting people into outer space. It is only limited for TB.”

Part of the reason for such limited aspirations, says Dr Seung, is simply that addressing the epidemic “is hard. You have to train people, put in new systems, bring in new technology and drugs, and strengthen health systems to deal with a complex disease.” This kind of basic spending on healthcare, however, tends not to be attractive to policymakers, adds Dr Marc Sprenger, director of the European Centre for Disease Prevention and Control.

Adding to the complexity is a lack of knowledge about the full scope of the challenge. Although information on TB has improved markedly in the last decade, Mr Dybul, executive director of The Global Fund To Fight Aids, Tuberculosis and Malaria, believes that “we need stronger data everywhere, including data for smart investments, such as information strongholds of new infections geographically or key affected population.” At the highest level, this dearth affects ability to shape policy, in particular for MDR TB. “Most countries do not routinely test for drug resistance,” says Dr McCray. Even national figures on prevalence, therefore, may be inaccurate, and certainly may not be consistent across an entire country. Dr Seung explains that it requires different strategies if you rely on national or local data “when, say, the proportion of TB that is MDR is 2% [nationally] or 40% in the main centres. Part of the problem in using general country data is that you [don’t] know your epidemic. We are not putting our resources where the greatest burdens are.”

Information issues are also felt at the patient level. “Active case detection requires a lot of data,” says Mr Dybul, and “you need strong systems to follow people” as they go through care. In many countries, however, such tracking does not happen.

Another issue that increases the complexity of treating, and blurs health system understanding of, the disease is the unstable conditions in...
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The diverse effects of stigma

The impact of stigma operates on a variety of levels, starting with the individual. Blessina Kumar, chair of the recently-formed Global Coalition of TB Activists (GCTA), explains that “the stigma and discrimination are worse than the disease.” She likens it to being “excommunicated. Nobody wants to talk to you, to be in same room as you. It has a detrimental effect on your psyche.” The main driver of stigma is fear of transmission, but the association of TB with socially marginalised groups, and in Africa of those with HIV, adds to the negative perception. Although quantitative studies are few, some suggest what many experts assume: the shame associated with TB delays people seeking treatment, giving the disease more opportunity to spread.4

Clinicians are not immune to negative stereotypes. Health systems and those populations at risk of the disease traditionally have a problematic relationship. As Dr Seung says, “TB programmes tend to be weaker than other aspects of health systems because TB patients are viewed as dirty and capable of infecting you if you are a healthcare worker.” Such thinking percolates through the system in unconscious ways that unfortunately demean patients. Ms Kumar, for example, notes that those patients who are lost to follow up are referred to as “defaulters” and those thought to have the symptoms of the disease are called “suspects.” At an extreme, health professionals’ own negative attitudes towards the disease can even reinforce that in the wider community.5

These attitudes can also have a negative and painful impact on care at a human level. Louie Zepeda, a health and disability consultant active in the area of tuberculosis, notes that often TB patients say that professionals who oversee medication at DOTS clinics “are very rude. You are told to drink your medication and get out.” She adds that this may not actually be the case, but it is definitely how it is perceived and greater efforts are needed to make clinics seem more welcoming.

Perhaps ironically, stigma even affects the views of those who have been cured of TB, hampering activism. Albert Makone, Africa region representative for the GCTA, notes that because TB—unlike chronic conditions such as HIV, heart disease or cancer—can be cured, many of those affected “move on and no longer want to be associated with the disease or raise awareness of it.”

A potent barrier to improved results in tackling TB, according to many experts interviewed for this study, is an ongoing, extensive stigma. As Dr Kimerling puts it, “TB is associated with poverty at every level in the system. Why it is still a global disease has something to do with stigmatisation and association with the poorest of the poor—those who have no effective voice.” This has wide-ranging impacts, from the personal level [see box: The diverse effects of stigma] to questions of politics and funding.

Politics and funding

Medical professionals and politicians do not necessarily all share the common, negative views of TB, but prevailing attitudes and the low socio-economic status of many with the disease offer those in power little reward for promoting a more active approach. This is especially the case where doing so would require difficult choices to address policies that may cause marginalisation. Dr Shenglan Tang, director of the Global Health Research Centre at Duke Kushan University, notes, for example, that China has some 250m internal migrants who have gone from rural areas to cities. These individuals lack many aspects of

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5 See R. Zachariah, et al., “Language in tuberculosis services: can we change to patient-centred terminology and stop the paradigm of blaming the patients?”, International Journal of Tuberculosis and Lung Disease, 2012.

legal recognition in urban areas, including health insurance which, although nearly universal in China, is not portable outside of one’s registered location of residence. Moreover, even if they begin treatment, these individuals are not easy to follow from one area to the next as they frequently move in search of employment. Although different areas have taken some positive steps—Beijing and Shanghai, among other cities offer free first-line anti-TB drug treatment and limited TB testing to all—these can fall short; for example, the expense of drugs and testing that require out-of-pocket payment is beyond the means of most migrant workers. A comprehensive solution, however, raises the politically difficult issue of regularising internal immigration. The dangers of avoiding the question, however, are great. Mr Dybul believes that “MDR TB is a problem of lack of political will to address marginalised risk groups.”

Moreover, applying external pressure on politicians to encourage them to address these issues is equally ineffective. Ms Kumar comments that “TB activism is very limited”, adding that many activists have a background in HIV campaigns and even veterans of that movement, when moving on, seem to prefer to work in the field of other diseases, such as hepatitis C. Dr Kimerling adds “TB has not yet managed to find an effective, credible, unique voice among the advocacy community. People dying of TB are still dying in silence, with shame.”

The lack of political urgency helps to explain another difficulty for those working against TB: inadequate global funding. As Dr Kimerling puts it, one big difference between the response to HIV and TB is that “you don’t have people affected by TB lying in the streets demanding more funding for TB research”. As with prevalence and mortality figures, the glass is half empty. Total funds dedicated to anti-TB programmes more than doubled in real terms between 2002 and 2011.7 Most of this money came from domestic spending by BRICS countries (Brazil, Russia, India, China and South Africa), which collectively account for 45% of the world’s TB case load, and other middle-income Asian and Latin American states. The amount budgeted, however, is still less than necessary: the WHO estimates that in 2013 between US$7bn and US$8bn was required to run adequate TB treatment and control programmes in every country, but that only US$6bn was available.

Most of this shortfall is felt in low-income states that rely extensively on aid to fund their national TB programmes. There, says Dr Ditiu, “funding is a disaster.” Joseph Sitienei, head of the Division of Communicable Disease Prevention and Control in Kenya’s Ministry of Health, reports that in Kenya “funding provides only about 40% of the resources that are required. It means that a lot of interventions are not put in place. For example, we don’t have enough money to make sure that [public health] messages are always out there and we don’t have adequate staff.” Meanwhile, donor fatigue is growing. Ms Kumar notes that “with donors, one has to really lobby to ensure that TB gets a minimum share of the pie, even though TB results in a much higher burden and economic loss [than many other diseases].”

Funding for research and development (R&D) is also problematic. In its latest annual survey of TB R&D expenditure, the Treatment Action Group (TAG), an HIV and TB activist organisation, and the Stop TB Partnership estimated that in 2012 total global spending on every aspect of TB R&D declined from US$658m in 2011 to US$627m in 2012, of which only US$237m went into the development of new drugs.

When DOTS don’t fully connect

The difficulty, however, will be tackling poor TB control, which blunts the effectiveness of existing tools. In certain countries, there is cause for concern. Dr Schlüter’s thoughts on the situation in Eastern Europe could describe the global picture: “delivering new things does not necessarily mean they will be used properly. Country programmes really need to get their act together. Some do it well, some are doing improving, but many are failing”.

MDR TB is a problem of lack of political will to address marginalised risk groups.

Mark Dybul, executive director, The Global Fund To Fight Aids, Tuberculosis and Malaria

it like 30 years ago.” Of the 22 high-burden TB countries, for example, six still detect only around half or fewer of estimated TB cases.

Policy can go a long way: Kenya, despite its funding difficulties, identified 79% of expected new TB cases in 2012; Nigeria, with more than double the GDP per head, found only 51%. Mr Dybul notes that with “leadership and resources, you can do almost anything with a health system. Ten years ago people said antiretroviral therapy would not be possible because of weak health systems. Now there are 10m people being treated.”

Although poor implementation brings obvious problems, the way that TB control has been pursued over the past decades also creates barriers to success. Indeed, just as the tens of millions of lives saved shows the potential strengths of a large-scale, supplier-driven, vertical health programme, its inadvertent effects also show the limitations of such an approach.

To begin with, the diagnosis and treatment elements of the DOTS system as originally conceived—with patients needing to present at treatment centres—was heavily provider-focused. Ms Kumar says that much TB prevention and control remains organised around clinicians and is highly “paternalistic. The patient is expected to go to a centre, open their mouth, have pills thrown in, and is then sent home. We look at TB as only a medical problem and not a public health one that affects the community and people.” Efforts to deal with it in this way inevitably fall short. Dr Ditiu agrees. Care “remains very medicalised. Patients are not empowered, or considered like real partners.”

A supposed strength of DOTS is better drug adherence than would occur if individuals took their medication at home, although recent research in fact suggests that there is little, if any, benefit observed compared with self-administered therapy.8 On the other hand, a notable weakness of a clinic-centred approach is that, as Dr Keshavjee says, “it has relied on passive case finding: patients coming when they feel sick. Active case finding has not been stressed under DOTS.” This remains the norm. The ill often need to come in to a facility for a test. This passive strategy therefore leads to lower levels of case finding and delays in the discovery—and therefore treatment—of many cases that are found, allowing higher levels of transmission.

Another problem with the way that many countries address TB is that national programmes set up with WHO encouragement have tended to create vertical, self-contained structures rather than integrate with healthcare in general. Although ensuring that TB remains the focus of programme efforts, this approach brings a variety of complications. One has been a lack of co-ordination between national efforts and the private healthcare providers who play a substantial role in many developing countries. The quality of private TB care, though, varies greatly and is often problematic. A recent analysis of the private market for TB drugs in 11 high-burden countries found a wide range of dosages available rather than just the few, standard ones. This supported earlier studies indicating frequent ignorance among these providers about the correct amount to prescribe.

In different ways in India and China, failures to bring private practitioners fully on board has impeded effective care and increased the danger of drug resistance. The Indian government has identified the country’s huge private sector in medicine—with its varied, non-standardised diagnostic and treatment practices and poor adherence monitoring and follow-up—as the leading challenges to improving the country’s TB efforts. The government has, accordingly, begun to regulate private TB care more carefully by requiring, for example, practitioners to notify the government of every case. Meanwhile, in China, Dr Tang notes that hospitals, which derive their income largely from pharmaceutical sales

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and diagnostic tests, tend to overprescribe more costly second-line anti-TB drugs even when there is no indication of drug resistance in order to extract greater revenue. They also frequently prescribe additional “liver protection pills”, for which there is little evidence of medical value in treating TB.

Even within publicly provided care, a lack of integration can weaken the response to TB. Dr Fujiwara notes that even HIV and TB care—despite the link between the two conditions—has “traditionally been very vertical and fragmented.” Mr Dybul adds that “barriers to alignment are multiple” and run from important medical questions about how best to treat a co-infected patient to unabashed political turf wars. However, the Global Fund’s recent policy change requiring countries with high levels of HIV and TB co-infection only to make funding proposals that involve unified care may speed the integration of services.

Finally, the dynamics of an effort led by an international organisation and funded by global donors can slow reaction to emerging dangers. According to Dr Seung, this helped give MDR TB a chance to grow more rapidly than it otherwise might have. About ten years ago, he says, “even at the highest levels there was a lot of wishful thinking and modelling showing that MDR strains would disappear on their own. That trickled down to national TB programmes. These programmes are so dependent on external funding that when the WHO is saying one thing it is hard to get funding for what you are really worried about.”

More generally, pursuit of a single, broad strategy seems increasingly out of step with the distinct regional attributes of the global TB epidemic. Central Asia, for example, needs to focus more on MDR TB than much of the world, while for African states addressing HIV co-morbidity is a higher priority. Even within countries, more nuances may be needed. Ms Kumar says that “what we see in Mumbai is very different to what we see in Delhi. The way you address TB in Mumbai has to be totally different.”

To make progress in the fight against TB, then, countries will need to overcome not just a lack of weapons—a slowly diminishing impediment—but a range of political and social obstacles even while rethinking basic questions around how TB care should interact collaboratively with patients, the rest of the health system, and international actors. Failure would not just mean that the TB epidemic would continue as is, but rather it would allow it to worsen—in particular the MDR and XDR TB strains. The need is for approaches that address the current TB challenges while maintaining progress.

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Dr KJ Seung, deputy director, Partners in Health, Lesotho Project

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The broad lines of where change needs to occur have been clear for some time. In 2006 the WHO published its Stop TB Strategy, which went beyond DOTS to include a variety of other inter-related elements, including: addressing vulnerable populations, MDR TB and the link between HIV and TB; strengthening health systems with a focus on primary care; engaging all care providers; empowering people with TB and communities through partnerships; and promoting research. These additions all show a common direction of travel, namely paying necessary attention to specific medical issues while moving towards greater co-operation between those working against TB and at-risk populations, patients, and other healthcare providers.

However clear the need, such a shift has not been, and will not be, straightforward and will take time. Dr Keshavjee recalls that although many states became convinced of the need to address MDR TB in the middle of the last decade, “these countries are like big ships. It takes two or three years of planning. A lot of [MDR TB] programmes did not start until 2009 or 2010.” Substantial cultural changes among healthcare workers may take even more time. Nor is there any globally applicable model to copy—one of the strengths of DOTS—in a world where the TB epidemic now has marked regional variations.

What follows, therefore, is not a comprehensive plan of TB control. Instead, it uses specific examples to show how different countries and other stakeholders have been addressing, in ways appropriate to their circumstances and resources, deficiencies in efforts against TB.

Finding and treating people where they live

One-third of estimated active TB cases were missed in 2012. Some may be in private care in countries where TB is not a notifiable disease, but most simply are not receiving treatment and, as a result, the disease is spreading. Almost by definition, these individuals are unwilling or unable to turn up at standard clinics. Meanwhile, more than one in ten of those found, and over half of those with MDR TB, do not complete treatment. One crucial element of improving both case finding and treatment success is to reach beyond medical silos and find ways to operate in affected communities. Dr Kimerling says that “we have to find creative ways to find people sooner in a targeted manner in order to test and then link them with care.” Dr McCray agrees: “Our approach to TB control globally has to be more patient-centered, where we actively engage the patient and community in their care. That is the only way to reach marginalised communities where TB is not being diagnosed.”

The best specific approach for finding more of the people who have developed TB depends on circumstances, but innovative strategies can produce good results.

In Kenya, this has included different efforts to use the broader health service to look for TB and sending volunteers and health workers out into the community to look for infected individuals. “Cough Monitor” programmes in areas with high TB are one way that the Ministry of Health has engaged in active case finding. A typical effort, based in the country’s Rift Valley, involves 50 health centres and local clinics.
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A comprehensive strategy for TB means more than population-wide measures. It also requires a targeted approach to search out and cure the disease in those sub-groups at greatest risk. That these are almost inevitably of marginal socio-economic status only adds to the challenge.

In Western Europe, Dr Sprenger explains, even “in low-prevalence countries, in big cities such as London, Rotterdam, and Barcelona TB is prevalent in vulnerable groups. You should therefore transfer efforts [in those countries] to detect TB there.” London currently has the largest TB problem of any west European city, with high prevalence among people who use drugs and the homeless in particular. University College London’s “Find and Treat” service literally goes in search of cases among these marginalised populations in the city, provides medication and seeks to address other needs of these individuals that may impede treatment. The scheme’s mobile unit, equipped with digital x-ray facilities, visits places frequented by these groups such as hostels, annually tests about 10,000 high-risk individuals, and finds around 16 cases per year. It hands out referrals to TB clinics and accepts referrals from them to provide treatment-adherence support for patients in its target group.

Cough Monitor is part of a broader community outreach effort by Kenya’s health ministry, which includes a long-range project for community health workers to visit every household in the country and, based on questionnaire results, to screen for TB. This has already reached large parts of Kenya and led to over 30,000 tests, of which 6% were positive. Moreover, Dr Sitienei notes that the country already has a policy of following up all home contacts of those with TB and its Hygiene in the Home programme provides advice on preventing transmission to other family members. Such a wide range of activities helps sensitising patients to the dangers of TB and providing tests to any with a persistent cough. Community workers also visit villages with a health questionnaire and collect sputum samples from those whose symptoms are consistent with possible TB. Between 2008 and 2013 this local programme tested around 2,000 people annually with roughly 16% testing positive for TB.

Seeking and treating TB in marginal populations

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Another population that frequently has high levels of TB is prisoners. Azerbaijan’s prison service has been able to reduce the mortality rate of those with the disease in its detention system from 45% in 1995 to just 3% in 2011. The success has come from an integrated approach run out of the prison system’s single Special Treatment Institute. All new prisoners are screened for TB and those within the system are rescreened annually. Any found with TB are sent to the Institute, where all treatment takes place. There, after further screening and tests for drug susceptibility, all patients are assessed individually and assigned a course of treatment. Finally, for patients who leave prison before their treatment is complete, an NGO takes over the monitoring of their care, and this has greatly reduced non-adherence among former convicts. The Institute’s cure rate for drug-susceptible TB is a respectable 71%, but for MDR TB it is an impressive 75%, well above the global average of under 40%. An International Committee of the Red Cross report on the programme stressed that its success derives from many factors, which include not just high-quality care, but political commitment to the programme and individual, personalised attention. As with London’s Find and Treat, success with marginal populations involves a multi-faceted approach that looks at their particular requirements.

to explain why Kenya already has a 79% case-finding rate, one of the highest among high-burden countries.

Countries should not only be finding cases in the community, they should also be treating them there wherever possible. Dr Seung notes that “Lesotho is an interesting case study but it is small, so it gets passed over.” This low-income country faces a high burden of TB and HIV. Since 2006, however, not only has it been able, by working with non-governmental organisations (NGOs), to refurbish an existing general clinic into an MDR TB treatment facility with a 70% survival rate, it has created an effective community-based treatment programme for those with drug-resistant TB who are well enough to leave hospital. Using a principle called accompaniment, community health workers in remote towns and villages oversee medication of patients. This is equally helpful for the health service, since the high number of beds occupied by TB patients in hospitals can create a bottleneck. It is also very positive for the patient, who can be supported by family members during care. In a pilot programme, of the 134 MDR patients enrolled, of whom 70% also had HIV, only one stopped taking their medication—well below the 20% often found in Southern Africa—and 53% were cured,11 showing the effectiveness of working with patients and families even in difficult conditions.

Integrating TB control with broader healthcare provision

A vertical TB programme flies in the face of two realities about patients: the health of a particular individual frequently involves a range of needs rather than a specific medical requirement and, if given the choice, not everyone will wish to receive care from the same providers.

(I) One-stop shops for patients

The best example of multiple patient needs with TB is its high level of co-morbidity with HIV in Africa. The International Union Against Tuberculosis and Lung Disease (The Union) has developed a robust approach. Beginning in 2004, says Dr Fujiwara, it focused on creating a “one-stop shop. We started from the TB patient side to integrate TB and HIV care. We wanted to build a model, so that a person can come in and get everything at the same time.” Since then, in 59 urban and rural clinics in Benin, the Democratic Republic of Congo (DRC), and Zimbabwe, The Union has tested and refined this approach and expanded it to provide HIV services regardless of TB status.

Central to the project has been an almost experimental approach with ongoing, comprehensive data gathering and analysis to determine and update best practice. Riitta Dlodlo, TB-HIV programme co-ordinator for The Union, thinks that this component of the programme was “one of, if not the most important for providing quality services, be it for TB or TB-HIV.” It has also allowed understanding to accumulate to such an extent that The Union was able to issue a detailed manual, distilling evidence-based practice, in late 2012.12

The programme has shown—through providing integrated testing, counselling, and care for both conditions in one facility—that TB clinics can become important entry points to HIV testing and care. The experience has also demonstrated that the laboratory capabilities needed for the two diseases often overlap, saving resources for low-income countries, and that the integrated approach leads to high adherence levels for antiretrovirals even after TB has been cured.

Dr Dlodlo believes that the benefits work the other way as well: multi-skilled nurses are able to recognise and begin testing and treatment for known HIV patients with undiagnosed TB. Furthermore, the thorough data analysis has also had a positive effect, with the Congolese National AIDS Programme considering adopting the project’s AIDS patient documentation as the national standard. Now, notes Dr Fujiwara, the Zimbabwean Ministry of Health has rolled out The Union’s model at 23 sites across the country with USAID/Pepfar support in an effort to scale it up.
(II) Co-ordinated public-private services
Silos organised around types of healthcare provider can be as problematic as those based on medical conditions. In many high-burden countries, private practitioners are important, or even leading, providers of TB care: the Indian government estimates that they treat just 30-50% of TB patients. Often, however, the quality of private care varies widely.

One way to address this is to create a system where the public sector is effectively the only provider and can standardise care. Dr Barreira notes that in Brazil “we don’t have the private sector treating TB. They send the patient to the public health system.” Part of this is regulatory: he explains that TB drugs are available in the country only through public health clinics. Dr Barreira adds, however, that such an approach also relies on Brazil having a universal public health system that provides a basic level of care. This includes the provision of TB medication at no cost, which takes away any incentive to seek non-standard, potentially less expensive treatment.

In a number of other countries the role of private practitioners, and sometimes low confidence in the public system, make Brazil’s approach impossible. Finding effective ways to work with the private sector is therefore essential. This needs to go beyond simple regulation which, on its own, may lead to only slow progress. In May 2012, for example, India made it a legal requirement for private practitioners to notify the government of TB cases—bringing it into line with practice in most countries. Over the last year, however, only 50,000 notifications occurred out of the hundreds of thousands of cases estimated to be privately treated. Media reports indicate that often the issue is a lack of trust between private providers and the government.

A Bangladeshi project, which proved so successful that it was scaled up across three urban areas covering 10% of the country’s population, shows the potential for public-private co-operation. The scheme involved training private, for-profit, medical providers in the national TB programmes guidelines. At the same time, it adjusted certain national programme processes to facilitate interaction with the private sector. An analysis of the project found that success depended on overcoming initial scepticism on both sides through dialogue and creating good relationships. The results justified the effort. Two years after the full scale up, in 2010, some 47% of identified TB cases in the areas covered by the programme resulted from private-sector referrals. This is consistent with experience elsewhere. A global review of literature on public-private co-operation found that in general it increases both case finding and the care of those patients treated by private physicians.

Integrating public and private care, then, is an important goal, but requires finding the appropriate mix of regulation and co-operation.

Adopting cost-effective technology
Although progress on TB research is slow, countries should, as much as they are able to, consider adopting any new tools that become available. The most important recent development is a new DNA-based testing technology—Xpert MTB/RIF or GeneXpert—that the WHO endorsed in December 2010 and that Dr Seung calls “a game changer.” Although it still requires a laboratory rather than being a point-of-care test, within two hours the system can identify not only TB, but resistance to one of the major first-line drugs.

Cost is an important issue, even after a group of funding agencies agreed in August 2012 to cover 40% of the price for 145 developing countries. Dr Barreira explains, however, that a pilot study in Brazil found that the technology uncovered 34% more cases than existing tests and allowed immediate second-line treatment for those who were found to have MDR TB. This made GeneXpert cost effective in centres where more than 2,000 tests are run per year. As a result, his country’s TB programme is buying enough machines and cartridges to provide such tests for facilities.


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covering about 60% of the population.

Medical machinery, however, is not the only kind of technology able to help improve TB care. The Kenyan Ministry of Health, along with Safaricom, one of the country’s major mobile-phone companies, and a number of other partners have developed a data management system called TIBU, which means “cure” in Swahili. Since November 2012, this has allowed the direct entry of details on new TB infections, using tablet computers at the point of diagnosis, into a national database that currently holds details on around 90,000 patients. The information can then be used in a wide variety of ways. At the national level, it enables the monitoring of trends, as well as indicating if any districts are performing poorly and need support. Local clinicians can use it to determine in real time if drug stocks are able to meet local need and to order new medication where required. It allows the treatment of individual patients to be followed even if they migrate to a different part of the country, and sends SMS messages to anyone who does not attend a clinic, reminding them to take prescribed their pills. Finally, TIBU is linked with Kenya’s mobile payments system, M-Pesa, to allow faster dispersal of support payments to those with MDR TB who continue to adhere to treatment. Although data concerning the effect of the system on outcomes is not yet available, Dr Sitienei is confident. With the system, “we can make sure patients are being taken care of.”

The TB movement has been centred on the huge WHO efforts, which led to significant achievements over many years. Now, though, is the time to multiply the voices.

Dr Lucica Ditiu, executive secretary, Stop TB Partnership

Raising the profile, raising ambitions

Strengthening the response to TB, such as in the ways described above, is essential to addressing the challenge presented by the disease. Just as important over the long term, however, will be to raise the social and political profile of TB and thereby to increase the likelihood of an ambitious response to it. This requirement points to the need for stronger advocacy. The effort against TB has always been more of an inter-governmental project than a popular cause. Dr Ditiu explains that “the TB movement has been centred on the huge WHO efforts, which led to significant achievements over many years. Now, though, is the time to multiply the voices. We need to engage all those affected, including government sectors other than health.” Ms Zepeda adds that the power of a social movement is required to get governments to address the needs of TB patients.

One new coalition is intent on making sure those voices include those most affected by the disease—the patients. Launched in 2013, the Global Coalition of TB Activists (GCTA) grew out of the Stop TB Partnership’s Community Task Force and aims to unify TB activists with representatives at the national and regional level.

Ms Kumar, the GCTA’s chair, sees several practical benefits to such a coalition. One is the need for a common voice. She believes that one reason that policymakers pay so little attention to TB “is that the TB community talks in so many different languages. We should have some basic sentences about TB that are the same.” She also says that TB activists currently lack important institutional support. She notes, for example, that after taking part in a demonstration against a failure to supply TB drugs, she was removed from a number of government expert committees. “There are repercussions to activism. Without global support, it is not going to happen. People will get scared and keep quiet.”

The organisation is still finding its feet, gathering data in order to understand the situation of patients making decisions about treatment, with the aim of introducing them to and involving them in the Coalition. It is also fostering regional organisations. Mr Makone reports that the African Coalition on Tuberculosis (ACT!) currently has seven country chapters and activists in other African states, and hopes to expand.

The first important test of strength for this potential new movement is fast approaching. The WHO has historically always welcomed such TB activism as has existed.15

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15 Mark Harrington “From HIV to Tuberculosis and Back Again: A Tale of Activism in 2 Pandemics,” Clinical Infectious Diseases, 2010.
however, the organisation approved the adoption of major goals, including a 95% reduction in TB deaths and a 90% fall in the incidence of TB by 2035. If health systems are going to cure 95% of active cases, they will need to find at least that many. The WHO scheme envisages not just improved medical care but “bold policies and supportive systems” that involve better community engagement as well as poverty alleviation to address the social determinants of TB. The question is whether TB activists can help persuade governments to take on this substantial challenge both officially and in practice.
Essential next steps

The story of efforts against TB in recent years is not one of failure but of underachievement. Millions are alive today because of existing TB programmes, but many are still dying unnecessarily because better ways have not yet been found to uncover cases in hard-to-reach populations and bring them appropriate treatment. The growth of drug resistance is not only making the task more difficult, it is revealing failings in basic TB control. As Mr Makone puts it, “we need new drugs, vaccines, and diagnostics, but with the tools that we have we can achieve much more than we are achieving currently.”

Moreover, new tools are becoming available—albeit slowly—in the fight against TB. These need to be deployed in ways that do not repeat the problems with earlier efforts, but make inroads in the fight against TB.

Accordingly, TB strategies need to move in practice beyond medical silos to work in and with communities on finding cases and improving treatment outcomes. This involves a range of changes, including those listed below.

- Seeking and treating the ill in new ways, where they live. Clinic-based efforts alone will not reach the nearly 3m undiagnosed TB cases. In high-burden countries, the search will need actively to look for TB across the population as a whole. Even in lower burden ones it will involve finding effective ways to target and treat the disease in sometimes challenging marginal populations.

- Integrating care to take account of the whole human being. Those with TB frequently have co-morbidities and lack the social or economic resources to be able to complete their treatment—especially of MDR TB—over the long term. Effective TB care means finding ways to overcome these barriers.

- Taking advantage of the resources of health systems as a whole. National TB programmes are an effective way to focus attention on the disease, but they should not become a TB care silo. The whole health system needs to be involved in finding TB, and medical facilities—including HIV clinics and private care providers—are proven ways to help address the disease.

- Harnessing new technology (both medical and non-medical). Medical advances in TB are still frustratingly slow, so those that come along need to be applied in the most useful way. The WHO has encouraged the use of GeneXpert and such a test will be essential in rapidly diagnosing and defeating MDR TB. Health systems need not rely solely on medical technology, however. Mobile information technology and integrated
databases show great promise in being able to understand the challenge that TB poses at both national and local levels, as well as in tracking patients and helping to avoid issues with drug stocks.

Most important, however, is ambition and focus. The WHO has set ambitious targets, but TB is a complicated disease. As experts interviewed for this study repeatedly stressed, we still have much to learn about how best to apply the basic elements of TB control. Those answers will not come by accident. They will require the kind of effort at all levels—international and national—that can only come from raising the profile of TB to a level proportional to the damage that it still causes.
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