



TACKLING TUBERCULOSIS

Recent progress and challenges

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ABOUT THIS REPORT

Tackling tuberculosis: Recent progress and challenges is a report by The Economist Intelligence Unit (EIU), commissioned by Janssen. It is intended to be an update of The EIU's 2014 report, *Ancient enemy, modern imperative: A time for greater action against tuberculosis*. The report will first examine the socioeconomic and political dimensions of tackling TB and then look at policy and progress in the areas of prevention, diagnosis and treatment.

In August-September 2016 The EIU conducted interviews with six global TB experts. The insights from these in-depth interviews appear throughout the report. The EIU would like to thank the following individuals (listed alphabetically) for sharing their insight and experience:

- Michael Kimerling, director, Technical Services Division, KNCV Tuberculosis Foundation
- Lovett Lawson, chairman of the board, Nigeria Stop TB Partnership
- Mario Raviglione, director, Global TB Programme, World Health Organisation
- Kseniya Shchenina, co-ordinator, Tuberculosis: Support and Answers
- Fanny Voitzwinkler, head of EU office, Global Health Advocates
- Eliud Wandwalo, senior disease co-ordinator for TB, Global Fund to Fight AIDS, Tuberculosis and Malaria

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INTRODUCTION

As countries strive to reach the UN Sustainable Development Goals for 2030, tuberculosis (TB) continues to challenge policymakers around the globe, with developing countries bearing a particularly onerous burden.

Although TB was responsible for around 1.5m deaths in 2014, down from nearly 1.8m in 1990, it is now the leading infectious disease killer worldwide, surpassing HIV/AIDS.¹ According to Mario Raviglione, director of the Global TB Programme at the World Health Organisation (WHO), incidence of the disease has been falling by around 1.5% annually for around a decade, but meeting the WHO's goal of reducing TB by 90% by 2030 would require a reduction in incidence of 10% per year over the next decade—a goal that looks increasingly precarious, especially with an estimated 3m cases going unreported.

In its 2014 report *Ancient enemy, modern imperative: A time for greater action against tuberculosis* The Economist Intelligence Unit (EIU) identified a number of factors that were undermining efforts to tackle the disease, including a slow, insufficiently ambitious and frequently ineffective response; the increasing public-health crisis of multidrug-resistant tuberculosis (MDR TB), highlighting the failings of existing efforts; a high level of stigma faced by patients; and overly provider-centred efforts.²

Although there is an increasing awareness of the particular burden posed by MDR TB, it is nevertheless expected to account for around one-quarter of the 10m annual deaths likely to be associated with drug resistance by 2050, according to the final 2016 *Review on Antimicrobial Resistance*, commissioned by the UK Government in collaboration with the Wellcome Trust.³ Improving diagnostic and treatment regimens for MDR TB remains a key challenge. In addition, the experts interviewed for this report say that closer links between TB and HIV programmes could help to identify those in need of treatment.

This update report will assess the progress made in the global response to TB since The EIU's 2014 study. We will first consider the socioeconomic and political context of tackling TB and then look at policy and progress in the areas of prevention, diagnosis and treatment.

¹ World Health Organisation (WHO), *Global Tuberculosis Report 2015*. Available at: http://www.who.int/tb/Global_TB_Facts.pdf

² The Economist Intelligence Unit, *Ancient enemy, modern imperative: A time for greater action against tuberculosis*, 2014. Available at: <https://www.eiuperspectives.economist.com/healthcare/ancient-enemy-modern-imperative>

³ *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. The Review on Antimicrobial Resistance, chaired by Jim O'Neill, May 2016. Available at: https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

CHAPTER 1: THE POLITICAL AND SOCIOECONOMIC CONTEXT

The prospects for improving TB prevention, diagnosis and treatment efforts are intrinsically linked to socioeconomic and political factors. For a start, a country's level of development has a strong influence on its response to the disease. "As you build up primary health infrastructures, the stronger these become, the better TB can be managed," says Michael Kimerling, director of the technical services division at the Netherlands-based KNCV Tuberculosis Foundation, which works to strengthen health systems in the fight against TB. "It's such a classic disease of public health. Development is important for overcoming TB."

Furthermore, the lack of significant progress towards universal access to health coverage in many developing countries and the gaps in social safety nets create significant inequities between countries. In many developed healthcare systems, although a patient with MDR TB might be unable to work for as long as two years due to the treatment regimen, they would be eligible for financial compensation, according to Mario Raviglione, director of the Global TB Programme at the World Health Organisation (WHO).

"The vast majority of endemic countries for TB have neither universal medical coverage nor social protection mechanisms," says Dr Raviglione. "We are making strong recommendations to governments that they have to embark on social protection mechanisms for people receiving treatment." A related challenge involves the financing needed from donor agencies to compensate for health systems that lack the funds for sufficient TB control—a gap estimated to be around US\$1.6 bn a year.⁴

Raising the profile of TB

As far as the political will to tackle TB is concerned, the disease continues to receive relatively less attention than other higher-profile diseases, the experts interviewed for this report say. The UN Sustainable Development Goals (SDGs) group TB together with other diseases, including HIV/AIDS and malaria, for which it aims to end the "epidemic" by 2030. "Fundamentally, what needs to be recognised is a lack of political commitment," says Dr Raviglione. "As we mentioned in [the UK medical journal] *The Lancet* a few years ago,⁵ TB is not a main priority among any of the main UN agencies; it does not have a special UN programme, is not in UNICEF's portfolio and is not a special presidential initiative in the US. It does not have strong support from the pharmaceutical industry."

This includes significantly lower investment in new drug research, according to Dr Kimerling, who cites a recent report from the Treatment Action Group, an independent AIDS policy and research think-tank, on the drug pipeline that showed some US\$2.6bn in drug research on HIV in 2011,⁶ compared with just US\$674m on TB as recently as 2014.⁷

⁴ WHO and the Global Fund, *Tuberculosis Financing and Funding Gaps*. Available at: http://www.who.int/tb/WHO_GF_TB_financing_factsheet.pdf.

⁵ BJ Marais, MC Raviglione, PR Donald *et al*, "Scale-up of services and research priorities for diagnosis, management, and control of tuberculosis: a call to action", *The Lancet*, 2010; 375:2179-91. Available at: [http://thelancet.com/journals/lancet/article/PIIS0140-6736\(10\)60554-5/fulltext](http://thelancet.com/journals/lancet/article/PIIS0140-6736(10)60554-5/fulltext)

⁶ M Smelyanskaya, *Funding Scientific Innovation: Global Investments in HIV Treatment Research and Development in 2010 and 2011*, Treatment Action Group, March 2013. Available at: http://www.treatmentactiongroup.org/sites/g/files/g450272/ft/201303/TAG_2013_HIV_Report_FINAL.pdf

⁷ M Frick, *2015 Report on Tuberculosis Research Funding Trends, 2005-2014: A Decade of Data*, Treatment Action Group, November 2015. Available at: http://www.treatmentactiongroup.org/sites/default/files/201511/TB_FUNDING_2015_WEB.pdfM

"There is comparatively little funding for basic science and research into TB compared with basic research into cancer, HIV or heart disease."

Fears in the past couple of years about growing resistance to first-line drugs in a number of disease areas have helped to raise the profile of MDR TB, but this has failed to turn the spotlight on the disease more generally. "MDR TB is a very nice rallying cry, but it is insufficient to solve the problem," admits Dr Kimerling. "At the end of the day, if we get more and more classes of new drugs, that will hopefully allow a very new approach to treating TB."

The disease also suffers from a lack of political involvement on the part of patients. "It's hard to find TB patients who want to or can become advocates," Dr Kimerling says. "Stigma remains a barrier in TB control; it's often a hidden disease." Better media coverage about the high cure rate for TB could help to improve public opinion.

One TB patient noted that although she had not faced any stigma as a result of her condition, she was aware of a number of misconceptions surrounding TB—for example, that it is inevitably a disease of the poor.

"I can tell you that TB does not choose, and I am the living proof of that," the patient says. "I was coming from an educated and well-off family, so anyone can get TB, as TB does not discriminate." She adds that she has participated in a few meetings with policymakers as part of an advocacy tour within the European Parliament in an effort to help disseminate accurate information about the disease and put an end to misconceptions.

A March 2015 meeting of the Eastern Partnership Ministerial Conference on Tuberculosis and its Multi-Drug Resistance in Riga, Latvia, committed to working to end the TB epidemic by 2050. By giving political attention to the issue of antimicrobial resistance, the Riga Declaration could provide new opportunities for developing cross border co-operation, as well as helping to expand knowledge about the impact of TB.

"But why should we wait until 2050 to make substantive progress for a curable disease?" Dr Kimerling asks. "Why are communities not screaming for justice and access to quality care?"

Varying progress in national TB control plans

Although most of the hardest-hit countries have a national plan for combating TB, these strategies vary considerably in their detail.

South Africa has taken one of the most proactive approaches. Under the leadership of its health minister, Aaron Motsoaledi—who is also the co-chair of the Global TB Caucus, an international network of parliamentarians and other politicians working to end the TB epidemic—the country has developed a co-operation plan with other members of the BRICS group of countries (Brazil, Russia, India and China) to promote universal access to

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first-line TB medicines for all patients suffering from the disease; collaboration on research and development (R&D); and a common approach to new diagnostics and treatment.⁸

In addition, South Africa is currently developing a new integrated National Strategic Plan for HIV, STI (sexually transmitted infections) and TB for 2017-21.⁹ It will build on its 2012-16 plan, which, as well as incorporating ambitious reduction goals, addresses social and structural barriers to HIV, STI and TB prevention, care and impact; the prevention of new infections; the promotion of health and wellness; and increased protection of human rights and access to justice.¹⁰ Benefiting from its relative wealth in the region, South Africa set a budget of US\$250m to finance TB control in 2015-16, around 84% of which is provided by the national government, with 8% coming from international donors, according to Dr Raviglione.

The countries of Eastern Europe and Central Asia bear one-quarter of the global burden of MDR TB.¹¹ The European Neighbourhood Instrument (ENI), a €15.4bn (US\$17.3bn) programme that governs the EU's relations with 16 of its closest eastern and southern neighbours, is supporting a range of public-health projects, including those related to HIV and TB. In addition, the €1.3bn European Instrument for Democracy and Human Rights (EIDHR), which provides support for the promotion of democracy and human rights in non-EU countries, can allocate grants for health-related and other projects to organisations working to protect the rights of vulnerable groups, such as prisoners and minorities, who are often most at risk of illnesses such as TB.

Moreover, 34 European civil society organisations have called on EU political leaders to develop an EU policy framework for 2016-20 to fight HIV, TB and Hepatitis C, which addresses the particular nature of the diseases in the EU and the Eastern Partnership countries (the six post-Soviet states of Armenia, Azerbaijan, Belarus, Georgia, Moldova and Ukraine), underlining the extent to which efforts to combat all three epidemics are moving up the political agenda in Europe.¹²

By contrast, the Indian government's Revised National TB Control Programme (RNTCP) started in 1997 and was only rolled out across the country in March 2006, with goals including services addressing TB/HIV and MDR TB and the extension of the programme to the private sector.¹³ In 2014 the government set out official standards for TB testing, diagnosis and treatment, which the RNTCP is expected to provide in all parts of India. For the first time, the guidelines acknowledge that patients will be treated by private providers in some cases, rather than requiring patients to be referred to the public sector, suggesting a realisation on the part of the government that it will need to co-operate with private providers to improve diagnosis and treatment rates.

At the same time, a 2014 review by the Joint TB Monitoring Mission (JMM) highlighted a number of problems with the RNTCP, including the fact that projected increases in case of detection had not occurred, that the programme's budget remained in deficit, and that procurement and supply-chain management remained problematic in some parts of the country.¹⁴

⁸ Stop TB Partnership, "BRICS Health Ministers Make Historic Commitments in the Fight against TB", December 5th 2014. Available at: http://www.stoptb.org/news/stories/2014/ns14_081.asp

⁹ WHO Regional Office for Africa, *South Africa - Tuberculosis (TB)*. Available at: <http://www.afro.who.int/en/south-africa/country-programmes/4247-tuberculosis-tb.html>

¹⁰ South African Government, *National Strategic Plan on HIV, STIs and TB 2012-2016*. Available at: http://www.gov.za/sites/www.gov.za/files/national%20strategic%20plan%20on%20hiv%20stis%20and%20tb_0.pdf

¹¹ TB European Coalition, *How to Leverage European Union Funding for Health in Eastern Europe & Central Asia?* Civil Society Guide to EU Funding for Health in ECA, March 2016. Available at: http://www.tbcoalition.eu/wp-content/uploads/2015/03/ThematicReport2016_EC-Research_ENG_WEB.pdf

¹² Global Health Advocates, *European Civil Society Organisations Call For EU Leadership On HIV/AIDS, TB and Hepatitis C*. Available at: <http://www.ghadvocates.eu/en/european-civil-society-organisations-call-for-eu-leadership-on-hiv-aids-tb-and-hepatitis-c/>

¹³ TBFACTS.org, "RNCTP – Government of India TB Treatment & Care". Available at: <http://www.tbfacts.org/rntcp/>

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The situation is not much better elsewhere. Nigeria, which has the third-highest global TB burden, launched its National Strategic Plan for Tuberculosis Control 2015-20 alongside the country's first national TB prevalence survey report. The report noted that, based on the survey results, Nigeria diagnosed and reported just 16% of estimated TB cases in 2013 and that the country accounted for 15% of the 3.3m TB cases globally that were either not diagnosed or diagnosed but not notified in 2013.¹⁵ Part of the problem is a lack of awareness, argues Lovett Lawson, chairman of the board of the Nigeria Stop TB Partnership, the national affiliate of the global Stop TB Partnership, which includes international, technical and non-governmental organisations, civil society, community groups and the private sector. "The centres are there, and the drugs are now available. But people have to know what the symptoms of TB are, and they have to know where to go."

In addition to addressing the political and socioeconomic dimensions of TB, developing new tools for the prevention, diagnosis and treatment of the disease are part of the solution. These are addressed in the next chapter.

¹⁴ *Ibid.*

¹⁵ Association for Reproductive and Family Health, "Nigerian government launches national strategic plan on tuberculosis control for 2015-2020", January 30th 2015. Available at: <http://arfh-ng.org/nigerian-government-launches-national-strategic-plan-tuberculosis-control-2015-2020/>

CHAPTER 2: POLICY AND PROGRESS ON PREVENTION, DIAGNOSIS AND TREATMENT

Meeting the WHO goal of reducing TB by 90% by 2030 will require new tools that are currently lacking, the experts interviewed for this report say, including better prophylaxis, the development of vaccines and new treatment regimens, especially for MDR TB.

In the case of prospective vaccines, TB researchers continue to be stymied by the complex reaction of the TB bacteria within the human body, Dr Raviglione notes. "It requires a certain immune response that allows the bacillus to be contained. It's a very complex immune response that isn't fully understood."

As a result, no vaccine candidates have entered clinical testing since the failure of the MVA85A vaccine in 2013.¹⁶ Two new TB vaccine consortia funded through the Horizon 2020 EU Framework Programme for Research and Innovation—the Tuberculosis Vaccine Initiative Consortium (TBVI) and the Eliciting Mucosal Immunity in Tuberculosis (EMI-TB) Consortium led by the Institute for Infection and Immunity at St George's, University of London—have been awarded grants of €24.6m and €8m, respectively, to develop candidates for clinical testing.¹⁷ A Global Tuberculosis Vaccine Partnership, composed of large financial and non-profit donors, is also in the process of being established.¹⁸ The partnership aims to develop a more effective way of financing a portfolio of TB vaccines on a risk-sharing basis between the public and the private sector.

Promise of improved diagnostics and prevention

As far as diagnosis is concerned, reliably identifying vulnerable populations that are most likely to go on to develop TB would allow for a more rapid management of the disease and avoid exposing those at lower risk to treatment regimes that involve significant side effects, Dr Raviglione says. He adds that current tests only show whether a person has been exposed, but not whether they are likely to develop full-blown TB. Around one-third of the world's population has latent TB—where they have been infected with mycobacterium tuberculosis but have not developed the active disease—according to the WHO.¹⁹

"If I had a predictive test, I would from among the one-third of humanity that has latent TB infection take only those at real risk of developing the active disease and propose preventive therapy. The others would not require any treatment, and I would be able to tell them they don't need anything; we would not expose them to medicines that are unnecessary," Dr Raviglione says. "With what we have today, we cannot make a distinction between the two, and if we treated everyone, we would have to treat a couple of billion people. It's expensive and an ethical issue, because some people

¹⁶ M Schito, GB Migliori *et al*, "Perspectives on Advances in Tuberculosis Diagnostics, Drugs, and Vaccines," *Clinical Infectious Diseases*, 2015:61, p. S102.

¹⁷ *Ibid*, p. S115.

¹⁸ *Ibid*, p. S115.

¹⁹ WHO, Tuberculosis, Fact sheet N°104. Available at: <http://www.who.int/mediacentre/factsheets/fs104/en/>

would die due to drug side effects." Since the early 2000s health systems generally use testing only in populations at particularly high risk, including patients living with HIV/AIDS. Now we are promoting a much more intense programme that reaches other vulnerable populations, like those who have had contact with infectious patients, according to Dr Raviglione.

One key area of progress has been in the expansion of rapid molecular diagnostics, most notably TrueNAT and GeneXpert, the latter of which detect the presence of TB bacteria while at the same time testing for resistance to rifampicin, a key antibiotic that provides the backbone of treatment prescribed for TB.²⁰ The tests can give a result within two hours. "It's becoming routine policy to recommend testing all new cases using rapid molecular diagnosis to detect TB resistance, a policy shift that has occurred in the last two years," Dr Kimerling says. "Instead of using your best test for the worst cases, it's using your best test as the initial test in all cases, with obvious implications for budgeting and laboratory network development."

In addition, two other types of diagnostic tests already in the pipeline promise to increase diagnostic sensitivity, allowing healthcare workers to know within hours whether a patient has MDR TB or standard TB, according to Dr Raviglione. Xpert Omni, one of the new tests due to be rolled out in 2017, is a wireless, battery-operated device, allowing it to be used in the field via a cartridge that downloads data to central laboratories. Other promising rapid diagnostic approaches include imaging and breath analysis of volatile organic compounds.²¹

According to WHO estimates, some 480,000 people developed MDR TB in 2014.²² There has been progress in the number of tests done, and the detection rate is higher than it was five or six years ago, when only 10% of all cases of MDR TB were caught. However, there has been little improvement in the past two years, according to Dr Raviglione, and a lack of resources adds a further challenge. Of the 123,000 cases detected and notified worldwide in 2014, just 111,000 received treatment, he says, with the rest forced to remain on waiting lists.²³ "What's missing is a lot of investment in developing new diagnostics and drugs to test and treat dormant TB." Despite the availability of modern molecular technology, in many settings TB diagnostic procedures continue to rely on sputum microscopy, a test that due to the "mucoid and viscous nature of the sample" is unpleasant to handle and imprecise in detecting cases with small amounts of bacilli around.²⁴

A key advance, says Dr Kimerling, would be a diagnostic based on blood or urine rather than sputum. One promising candidate was recommended by the WHO in late 2015: a dipstick test to detect the LAM antigen (lipoarabinomannan) in urine samples in order to test for TB in HIV patients with CD4 counts (a lab test that measures the number of CD4 cells in a sample of blood) below a certain level. However, the test's low sensitivity level requires further follow-up testing. Nevertheless, the most recent pipeline report from the Treatment Action Group notes that the LAM test is the first ever TB diagnostic to demonstrate a mortality benefit in a randomised controlled clinical trial, and it

²⁰ Schito *et al*, pp. S103, S107.

²¹ Treatment Action Group, *The Tuberculosis Diagnostics Pipeline*, July 15th 2016. Available at: <http://pipelinereport.org/2016/tb-diagnostics>

²² WHO, *Multidrug-resistant tuberculosis (MDR-TB)*, 2015 update. Available at: http://www.who.int/tb/challenges/mdr/mdr_tb_factsheet.pdf

²³ *Ibid.*

²⁴ Schito *et al*, p. S103.

recommends the widespread use of the test in countries with large burdens of TB and HIV.²⁵

Finding missing TB cases and improving treatment regimens

Better diagnostics would also go some way towards narrowing the gap between estimated and officially identified cases, experts say. In 2014 the WHO reported 9.6m estimated cases of TB, of which only 6m were officially reported to national health systems.²⁶ The 3m+ "missing" cases continue to be based on modelling, those interviewed say.

In countries such as India, Pakistan and some parts of Africa, where many patients pay for care outside the national health system, the majority of these are likely to be treated in the private sector, with little oversight or mandatory reporting. Others occur in rural villages in Africa, where many people die at home of HIV/AIDs and related conditions.

"The big countries, where the majority of TB cases are missing, are India, Indonesia and Pakistan, where there is a rampant private sector that competes with the public sector rather than collaborating," Dr Raviglione explains. "You will solve it when you have a good national programme that links to the private sector." Successfully implementing these links, however, requires better engagement among the private sector, professional laboratory networks and municipal initiatives.

A second challenge is the failure in some countries to link TB and HIV responses. For instance, it would be necessary to systematically apply HIV testing for all those diagnosed with TB, Dr Raviglione says. Moreover, all patients coming in to refill antiretroviral medications at HIV clinics should be screened for TB symptoms and given preventive therapy, he adds. "This is happening more and more, but only 1m people received preventive therapy in the last year, when there should be 16m." Understanding the interaction between both diseases is particularly important as drug resistance is beginning to complicate the fight against TB. According to the WHO, antimicrobial resistance in general is a major issue in 2016, and many diseases are now caused by bacteria and viruses that are becoming more and more resistant to medication.²⁷

Developing better regimens would help many of those who have been exposed to TB but are not yet sick with it to avoid the existing longer treatment regimens, which can be difficult for patients to tolerate. "The best we have now is a once-a-week treatment of two drugs for three months, instead of the six-to-nine month regimen," Dr Raviglione says. However, even this shorter course is "not ideal"; he adds that researchers were hoping to develop a regimen that would involve monthly doses of medication for several months.

Dr Raviglione notes that for patients with MDR TB two new drugs, combined with existing ones, are still being evaluated and could help to reduce TB rates among this population. The International Union against Tuberculosis and Lung Disease, a non-profit, non-governmental organisation headquartered in Paris, is currently studying two new

²⁵ E Lessem, "The tuberculosis diagnostics pipeline", *HIV Treatment Bulletin*, July 14th 2016. Available at: <http://i-base.info/htb/30177>

²⁶ WHO, *Global Tuberculosis Report 2015*. Available at: http://www.who.int/tb/publications/global_report/gtbr15_main_text.pdf

²⁷ WHO, *Antimicrobial resistance, Fact sheet*, updated September 2016. Available at: <http://www.who.int/mediacentre/factsheets/fs194/en/>

treatment regimens for MDR TB patients: a six-month regimen and an all-oral nine-month regimen, both of which could replace the current 24-month standard treatment for MDR TB, which requires frequent injections that have in some cases been associated with serious hearing loss.²⁸

Shorter treatment regimens combining new and older drugs could produce fewer side effects overall. Kseniya Shchenina, co-ordinator of the Ukraine-based patient community Tuberculosis: Support and Answers and a member of TB People, a network for people with experience of TB in Eastern Europe and Central Asia, which was set up earlier this year, notes that although anecdotal evidence from her network suggests that patients with access to the new drug regimens have experienced decreased side effects and better outcomes, a lack of information is still having an effect on uptake. In some parts of Eastern Europe, media reports about harmful consequences of the new regimens have had an impact on the uptake of the new regimens.

Some health advocates are also concerned about the lack of knowledge, so far, about the interaction of new drugs with existing treatments. "These [new] treatments have been developed in silo, so they haven't been tested with current medicines," says Fanny Voitzwinkler, head of the office of Global Health Advocates, a non-governmental organisation, at the EU in Brussels.

Meanwhile, the New York-based TB Alliance is currently testing two repurposed drugs and one new drug on patients in South Africa with extensively drug-resistant (XDR) TB. In addition, three trials are testing the combination of the traditional drug regimen for XDR TB and fluoroquinolones (a class of antibiotics) to cut the duration of the regimen from six to four months.²⁹ If the three-drug trial succeeds, it could be used for both XDR TB and the drug-susceptible variety, Dr Raviglione says.

Because health workers are getting to grips with the newest drugs and use them more routinely in practice, they are learning to select patients more carefully, notes Dr Kimerling. "Now we are at a point when we can actually start triaging patients. We are getting smarter about who our patients are and what they need."

Progress and setbacks in policymaking

While some of the newer approaches to tackling TB are promising, the current policy framework remains a work in progress. It is true that the Riga Declaration and the Global TB Caucus suggest a growing willingness among countries to work in partnership to combat TB—including fighting the stigma and social isolation that patients often face—compared with several years ago.

But there is also an absence of strategic focus even in wealthier parts of the world. For example, the EU has an action plan for HIV but no similar policy framework for TB, although both diseases continue to pose major health threats. A recent report from the TB Europe Coalition (TBEC), a civil society advocacy network, noted that the EU has

²⁸ International Union Against Tuberculosis and Lung Disease, "Clinical Trials". Available at: <http://www.theunion.org/what-we-do/research/clinical-trials>

²⁹ Schito *et al*, p. S107.

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some of the lowest MDR TB treatment success rates in the world and that Eastern Europe and Central Asia have the highest rates of MDR TB among new TB cases globally.³⁰

In 2011 the Global Fund, an organisation which aims to accelerate the end of AIDS, TB and malaria as epidemics, announced the eligibility conditions needed for its support. Countries which are classified as high-income or upper-middle-income countries (UMICs) and which have a low disease burden are not entitled to financial support from the Global Fund. However, UMIC countries with a high, severe or extreme disease burden may be financed.³¹

³⁰ TB Europe Coalition, "EU Political Leadership Needed to End HIV, TB and Hepatitis C in Europe", November 2015. Available at: http://www.tbcoalition.eu/wp-content/uploads/2015/11/1511_PP_A4_Health-matters_WEB.pdf

³¹ The Global Fund, *Sustainability Review of Global Fund Supported HIV, Tuberculosis and Malaria Programmes*. Final Report Commissioned by the Technical Evaluation Reference Group, April 2013. Available at: <http://www.theglobalfund.org/en/search/?q=sustainability+review>

CONCLUSION

Two years on from our original report there is evidence of some progress on the global response to TB, including, for example, efforts to shorten treatment regimens. At the same time, however, public-health experts observe that TB retains a relatively low disease profile in terms of R&D, both compared with diseases such as HIV/AIDS and in proportion to the impact of the disease. Major political and socioeconomic challenges remain, notably the lack of universal access to health coverage in many endemic countries, insufficient political will and deficient national TB control plans.

However, even incremental progress is positive. "I think TB progress is always measured, and you have to be patient, because it is an organism that has co-evolved with man," says Dr Kimerling. Nevertheless, he adds, TB suffers from "underinvestment in basic research and a failure of science to serve the needs of a public-health threat. It doesn't have the public-health profile to garner all the research required." Hence, finding new sources of investment remains a key part of making progress towards the WHO goal of reducing the incidence of TB by 90% by 2030.

Ultimately, progress will depend on the political will to underpin greater investment in research and the willingness of more countries to commit to both national policy frameworks and cross border partnerships.

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