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Drug-resistant tuberculosis in Europe

Report¹

Committee on Social Affairs, Health and Sustainable Development

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Summary

In recent years, tuberculosis has risen high on the political agenda in view of the increasing threat of antimicrobial resistance which has a negative impact on the treatment of the disease. This is a particular concern in the World Health Organization European Region, which has the highest rates of multidrug-resistant tuberculosis worldwide. This report – which is designed as the Parliamentary Assembly's contribution to the upcoming United Nations high-level meeting on tuberculosis (September 2018) – identifies the underlying factors for the epidemic in Europe, and singles out a number of region-specific challenges and best practices. It also underlines the root causes of the lack of investment in research and development for new tuberculosis medicines, diagnostic tools and vaccines.

Among the key proposed solutions to address these issues are: early detection and preventive treatment oriented towards socially vulnerable groups who face a higher risk of exposure and infection; offering incentives and rewards for innovation; appropriate treatment and complementary support services, including in particular psycho-social support for patients, with a view to reducing the disease's burden and increasing treatment adherence. In addition, all Heads of States of the Council of Europe member States are strongly encouraged to attend the United Nations high-level meeting.

1. Reference to committee: [Doc. 14164](#) Reference 4250 of 25 November 2016.



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A. Draft resolution²

1. In 2016, tuberculosis caused 1.7 million deaths worldwide, making it the world's leading infectious killer. The World Health Organization European Region, where the disease was thought to be a thing of the past, has the highest rates of multidrug-resistant tuberculosis in the world. These are strains that are particularly difficult and expensive to treat.
2. Tuberculosis is a "social" disease which disproportionately affects socially and economically disadvantaged groups, such as homeless people and people using drugs. It often has a devastating impact on the lives of the patients, as they face months, and sometimes years, of often difficult treatment with multiple side effects, and many end up suffering from long-term physical and psychological consequences of the disease.
3. The high rates of multidrug-resistant tuberculosis in the European Region are due to a number of factors which can differ from country to country, including out-dated health policies, weak and under-financed health-care infrastructures, and a large number of undiagnosed patients, all of which also contribute to the disease's transmission. The stigma associated with tuberculosis and the resulting social isolation often lead to treatment non-adherence, one of the main drivers of drug resistance. People living with HIV, prisoners, refugees and migrants are particularly vulnerable groups in the region, with higher risks of tuberculosis morbidity and mortality.
4. There is a significant lack of investment in research and development for new tuberculosis medicines, diagnostic tools and vaccines. The current pharmaceutical innovation model does not offer enough incentives for investing in a disease like tuberculosis: it is risky and costly because ideally it requires investment in new combination therapies rather than a single new product, and unprofitable because the greatest burden of the disease falls on the poorest parts of the world.
5. The Parliamentary Assembly welcomes the fact that tuberculosis will receive unprecedented attention at a United Nations General Assembly high-level meeting to be held in September 2018. This is a historic opportunity to tackle this preventable and (most often) curable, yet still neglected disease, and to save millions of lives, as well as a significant cost to the global economy. Therefore, every effort should be made to maximise the impact of the upcoming high-level meeting.
6. In the light of these considerations, the Assembly calls on the Council of Europe member States to:
 - 6.1. ensure that every tuberculosis patient is effectively diagnosed (including for different strains of the disease) and has access to appropriate treatment and care, as well as complementary support services, and in particular psycho-social support, with a view to reducing the disease's burden on their lives and increasing treatment adherence;
 - 6.2. provide integrated and people-centred health services, in particular by:
 - 6.2.1. ensuring effective collaboration between all stakeholders involved in the tuberculosis response, including government agencies, local authorities and civil society organisations;
 - 6.2.2. providing tuberculosis care mainly in the ambulatory and community settings, together with appropriate infection-control measures;
 - 6.2.3. involving civil society organisations in patient follow-up and treatment support;
 - 6.3. improve early detection mechanisms for tuberculosis by investing in active tuberculosis case finding among socially vulnerable groups, who face a higher risk of exposure and infection, including prisoners, people with HIV, refugees and migrants, and orient preventive treatment towards these groups to prevent latent tuberculosis from activating;
 - 6.4. invest in research and development for new drugs, diagnostics and vaccines for tuberculosis, including by offering incentives and rewards for innovation;
 - 6.5. develop, fund and implement a tailored national tuberculosis strategy;
 - 6.6. fight the stigma associated with tuberculosis by debunking the myths and raising awareness of the realities of the disease;
 - 6.7. continue to highlight the impact of antimicrobial resistance on tuberculosis and support international efforts to prevent its advance.

2. Draft resolution unanimously adopted by the committee on 20 March 2018.

7. The Assembly strongly encourages all Heads of States of the Council of Europe member States to attend the United Nations high-level meeting on the fight against tuberculosis in 2018.
8. Finally, stressing that tuberculosis and poverty are inextricably linked, the Assembly calls on Council of Europe member States to step up efforts to reduce global and regional inequalities. In this context, it refers to its [Resolution 1975 \(2014\)](#) “Stepping up action against global inequalities: Europe’s contribution to the Millennium Development Goals (MDGs)”.

B. Explanatory memorandum by Mr Serhii Kiral, rapporteur

1. Introduction

“When you have cancer, everyone will feel sorry for you. But when you have tuberculosis, people are afraid, people look down on you.”

Olga Klymenko, former tuberculosis patient

1.1. Procedure

1. On 11 October 2016, the Committee on Social Affairs, Health and Sustainable Development tabled a motion for a resolution on “Inquiry into growing antimicrobial resistance in Europe”. The motion was referred to the committee for report, and, as its initiator, I was appointed rapporteur on 26 January 2017.

2. Antimicrobial resistance (AMR) is the process by which bacteria evolve to become resistant to medicines used to treat the infections they cause, thus rendering these medicines ineffective. In an introductory memorandum presented in April 2017, I stressed that tuberculosis was at the origin of one third of deaths from AMR worldwide, and that Europe was home to the world’s fastest growing drug-resistant tuberculosis (DR-TB) epidemic. In September 2017, the committee held a hearing with the participation of a former TB patient from Ukraine, Ms Olga Klymenko, experts from the Organisation for Economic Cooperation and Development, and the Global TB Caucus.³ The hearing revealed the true magnitude of the suffering caused by the disease and in particular its social, economic and psychological impact on patients. In December 2017, in view of the increasing political exposure in recent and upcoming years of the fight against TB (see below) and Europe’s particularly high disease burden with regard to multidrug-resistant tuberculosis (MDR-TB), I proposed focusing on drug-resistant TB in the report, which the committee ultimately agreed to.

3. In preparing the report, I carried out fact-finding visits to Azerbaijan and Norway, where I held meetings with a range of stakeholders working in the national TB response, including parliamentarians, government and civil society representatives, and medical experts. These visits allowed me to grasp how these two countries with very different levels of TB incidence are addressing this issue and to identify some best practices. I should like to thank all the parties involved in the discussions for their valuable contributions, and the delegations of both parliaments and their secretariats for the excellent organisation of my visits.

1.2. Tuberculosis on the political agenda

4. In September 2016, world leaders met to discuss the response to AMR at a United Nations high-level meeting, and agreed that the international community must take urgent action to prevent its advance, as it threatens effective treatment for many common infections, including TB. A few months later, noting the impact of AMR, in particular on the treatment of TB, the United Nations General Assembly decided to hold a high-level meeting on the fight against TB in 2018.⁴

5. In November 2017, the World Health Organization (WHO) convened a global ministerial conference on “Ending TB in the Sustainable Development Era”, at which Ministers of Health from across the world met to discuss how to respond to the epidemic. The conference resulted in collective commitment to ramp up action on four fronts: achieving universal health coverage by strengthening health systems and improving access to people-centred TB prevention and care; mobilising sufficient and sustainable financing to close gaps in implementation and research; advancing research and development of new tools to diagnose, treat and prevent TB; and build accountability through a framework to track and review progress on ending TB.

6. The upcoming United Nations high-level meeting on TB is an unprecedented step forward by governments and all partners engaged in the fight against TB. It is a historic opportunity to push for a strong and ambitious political declaration which would give the necessary impetus for concrete action to end TB, thus saving millions of lives. This report is designed as the Parliamentary Assembly’s contribution to this first-ever United Nations high-level meeting on TB.

3. The Global TB Caucus is an international network of over 2 300 members of parliament from 133 countries working collectively and individually to tackle the TB epidemic.

4. Resolution A/71/L.41 adopted on 15 December 2016. TB was also singled out in the AMR agenda of the G7 and G20 (which include, among others, France, Germany, Italy and the United Kingdom, and for the G20, the European Union). See G20 Leaders’ Declaration: “Shaping an interconnected world”, Hamburg, 8 July 2017; “United towards Global Health: common strategies for common challenges”, G7 Milan Health Ministers’ Communiqué, 5-6 November 2017.

2. Tuberculosis – the world's leading infectious killer

"Tuberculosis is a disease that affects all aspects of your life, not just your health."

Stefan Radut, tuberculosis patient

2.1. Facts about tuberculosis⁵

7. TB is an airborne infectious disease, caused by the bacterium *Mycobacterium Tuberculosis*, which is spread by coughing or sneezing and mostly affects the lungs, although TB bacteria can be present and cause illness in any part of the body. Symptoms can include a persistent cough, weight loss, fever, pain and fatigue, although other non-specific symptoms can be present, especially in children. In 2016, TB caused 1.7 million deaths worldwide, amongst which were 250 000 children, making it the world's leading infectious killer.

8. The treatment for standard (or drug-susceptible) TB lasts at least six months, and comprises a combination of antibiotics (a regimen). Multidrug-resistant tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to isoniazid and rifampicin, the two most powerful first-line anti-TB drugs. MDR-TB is treatable and curable by using second-line drugs. However, the treatment is much longer (up to two years of treatment), much more challenging for patients, and far more expensive than the treatment for standard TB. Patients not only face up to 14 000 pills over two years, but also painful intravenous injections, and difficult side-effects, including nausea, digestive issues and weakness, permanent disabilities such as blindness and deafness, and psychological difficulties such as depression, anxiety and even psychosis. Extensively drug-resistant tuberculosis (XDR-TB) is a more serious form of MDR-TB caused by bacteria that do not respond to the most effective second-line anti-TB drugs, often leaving patients without any further treatment options.

9. It is estimated that about one quarter of the world's population has been infected by TB bacteria. However, they are not ill (this is known as latent TB) and cannot transmit the disease, as the TB bacteria can only be transmitted by people with active TB. Only a small proportion of those with latent TB (roughly 10%) will develop the disease during their lifetime, the likelihood of developing an active TB being higher for those with compromised immune systems. Thus, people living with HIV⁶ and other chronic illnesses that impact the immune system, such as diabetes, are the groups with a higher risk of falling ill. Moreover, while anyone can contract the disease, people living in poverty, homeless people, people who use drugs, prisoners and detainees, refugees and mobile populations in general, face higher risks of exposure and infection compared to the general population, mainly as a result of their living conditions.

10. A vaccine against TB (the *Bacillus Calmette-Guérin* vaccine – BCG) is available, but it is only partially effective at protecting infants and young children, and poorly protective against pulmonary TB in adolescents and adults. There are also relatively efficient preventive treatments for managing latent TB, which can prevent the disease from activating, with an efficacy ranging between 60% to 90%.

2.2. What went wrong?

11. Why does a disease that is preventable and curable still remain humanity's deadliest infectious killer, despite having been declared a global health emergency by the WHO more than twenty years ago?⁷ Something must have gone terribly wrong.

12. While it is true that TB bacteria can hide in the body for years, undetected, without developing into active TB; that it can be mistaken for other illnesses that affect the lungs and respiratory system, such as the flu or a cold, and that this leads to considerable rates of misdiagnosis and delayed diagnosis; and that it is the only major airborne drug-resistant infection – which makes it difficult to control its spread –, these peculiarities cannot explain the world's collective failure in addressing TB.

13. In fact, national health-care systems' failure to deliver good quality TB treatment is one of the main reasons why the disease continues to take so many lives. Inadequate and erratic treatment made it possible for the disease to mutate into drug-resistant forms, while large gaps in detecting TB,⁸ out-dated health policies

5. For factual information on TB provided in this report, see the WHO and WHO/Europe websites.

6. HIV and TB form a lethal combination, each speeding the other's progress. In 2016, about 40% of deaths among HIV-positive people worldwide were due to TB.

7. WHO declared TB a public health emergency in 1993.

8. In 2016, 49% of those affected by TB were not officially diagnosed, Global TB Report, 2017, WHO.

and weak health-care infrastructures contributed to its transmission. Inextricably linked with poverty, TB has continued to thrive disproportionately in certain parts of the world, as regional and global inequalities have increased. The constant lack of investment in research and development for new drugs, vaccines and diagnostic tools, despite a pressing need as the disease evolved into drug-resistant forms, has exacerbated the problem. Today, the world is still far from achieving target 3.3 of the Sustainable Development Goals – “end the TB epidemic by 2030”. At current rates of progress, it will be 180 years before this target is achieved.

3. Europe: home to the world’s highest rates of multidrug-resistant tuberculosis

14. TB was thought to be a disease of the past in Europe.⁹ Yet, the reality is different, as the region sees around 900 new cases of TB each day. The TB burden is, however, unequally distributed across the region, new cases being highly concentrated in eastern and central European countries. Europe also has the highest rates of MDR-TB in the world, with an estimated one in five cases of MDR-TB worldwide in 2015. Indeed, of the 30 countries identified by WHO as the highest priority for tackling MDR-TB, nine are within the European Region.¹⁰ Of newly registered TB cases, 45% are among people between the ages of 25 and 44, which has an impact on national economies, as this demographic are the most economically productive.

15. Europe is also seeing the highest rates of MDR-TB in those who have contracted TB for the first time, meaning that people are contracting drug-resistant strains of the disease.¹¹ This is a trend which should be cause for urgent concern, as the development of new tools to treat MDR-TB significantly lags behind the rate at which it is developing and spreading.

3.1. Underlying factors

16. There are a range of factors contributing to the high rates of MDR-TB in Europe, amongst them the continued out-dated practice of excessive hospitalisation¹² and a lack of a people-centred approach to care – a model of care which takes into account not only medication, but everything a patient may need to complete their treatment, such as social, psychological and financial support. TB patients are often kept in hospital for an unnecessarily long time, despite most of them ceasing to be infectious within two weeks of starting treatment. Many hospitals have poor airborne infection-control measures, thus increasing the likelihood of cross-infection between patients with different strains of TB (including drug-resistant strains). Isolation in hospitals disrupts patients’ social relations, in particular with their families,¹³ negatively impacting their psycho-social well-being which is critically important for their recovery. Long-term hospitalisation is often incompatible with work life, eventually leading to loss of income and disastrous financial consequences.

17. Stigma associated with the disease and the resulting social isolation also contribute to the high rates of MDR-TB in Europe, as they seriously impact effective TB detection and treatment. In fact, people with TB are often marginalised or rejected by their community, employer, family or friends. Without any psycho-social support to counter the effects of such stigma, people may be unwilling to be diagnosed, or once diagnosed, can interrupt or stop their treatment due to social difficulties and an inability to cope. The latter is particularly problematic as non-adherence to treatment is one of the main drivers of drug resistance, the reason being that unfinished courses of medication have not destroyed the TB bacteria in the body, meaning that the infection remains, or returns, and the bacteria is then likely to have evolved to be resistant to the medication used to treat it. Furthermore, as MDR-TB can only be detected by laboratory tests, which remain underused, especially in the eastern part of the region, it is estimated that there is a substantial number of missing cases, which may also contribute to the transmission of MDR-TB.

9. All references to “Europe” should be understood as the WHO European Region, which comprises the Council of Europe’s 47 member States, as well as Belarus, Israel, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan.

10. These are Azerbaijan, Belarus, the Republic of Moldova, Kazakhstan, Kyrgyzstan, the Russian Federation, Tajikistan, Ukraine and Uzbekistan.

11. An estimated 19% of new cases of TB were multi-drug resistant in 2016 in the European Region. See footnote 8.

12. Traditionally, TB patients in many eastern European and central Asian countries are treated in hospital on an in-patient basis for long periods. “Moving To People-Centred Care: Achieving better TB outcomes”, TB Europe Coalition.

13. During her testimony before the committee, Ms Klymenko explained that she was separated from her daughter for six months and that this had long-lasting effects on their lives.

3.2. Region-specific challenges

3.2.1. Access to anti-TB drugs

18. In some eastern and central European countries, patients encounter difficulties in accessing the few existing new and promising second-line anti-TB drugs that are available on the market, such as Bedaquiline® and Delamanid®, which have been seen to be effective in treating DR-TB, and could help reduce the use of painful and toxic drugs.¹⁴ This is due to a number of legal and bureaucratic obstacles, as well as out-dated procurement policies which mean that States cannot procure these drugs, which therefore cannot be used in treatment regimens.¹⁵

19. Some difficulties also result from the geopolitical context. For example, just a small number of TB patients in Ukraine can currently access the above-mentioned two drugs because the regional distributor authorised to request their registration and supply is a Russian-owned company. The sanctions put in place since the Russian aggression prohibit the procurement of goods and services from Russia paid for by public funds, including for foreign goods supplied through Russian companies. Despite efforts by the Ukrainian authorities, who have approached the relevant pharmaceutical companies requesting them to change their distributor, the problem has not yet been solved, leading to an unacceptable delay for TB patients in Ukraine.

3.2.2. Conflict areas

20. Another specific challenge for the European Region is the likely increase of TB incidence and spread in conflict areas.¹⁶ For obvious reasons, there are delays in diagnosing and treating TB patients in these areas, where health infrastructure is often severely weakened. This may lead to the emergence of MDR-TB and complicate the management of the disease. Experience shows that in conflict areas, if TB is neglected it may quickly result in increased morbidity and mortality.¹⁷

3.2.3. Vulnerable groups

21. Throughout Europe, in particular people living with HIV, prisoners, refugees and migrants have a higher probability than the general population of getting infected with TB, developing the active disease and dying from it. As far as HIV/AIDS is concerned, more than 160 000 people were newly diagnosed with the disease in Europe in 2016, the highest number of people ever newly diagnosed in one year since HIV case reporting began in the 1980s.¹⁸ Against the background of a sharp increase in the HIV/TB co-infection rate in the European Region (from 5.5% to 9% between 2011 and 2015), efforts to tackle these two epidemics are critical, and in this context, further integration of TB and HIV services should be explored. As resistance to anti-TB drugs increases, the likelihood that those TB patients who are also HIV positive will succumb to their illness will increase as well.

22. As for migrants, those with latent TB are more likely to develop the active disease in the country of destination due to a number of factors, including their legal and employment situation, and problems with access to health care. In some cases, migrants move across borders after being diagnosed with active TB in their country of origin.

23. For refugees and migrants with active and latent TB, it is crucial to be diagnosed and receive the appropriate TB treatment in the country of destination. It is also crucial for the country of destination to detect those TB cases early enough so as to avoid transmission amongst the population. To this end, a consensus paper describing the minimum package of cross-border TB control and care was prepared with input from the national TB control programme managers of the WHO European Region and the Wolfheze 2011 Conference.¹⁹ The package addresses the shortcomings in this area and intends to improve the situation by

14. "Introduction of Bedaquiline for the treatment of multidrug-resistant tuberculosis at country level implementation plan", WHO, 2015.

15. "The Crisis of Anti-TB Medicines in Romania: Alert Report", Romanian Health Observatory and the Stop TB Partnership Romania, October 2017.

16. For example, the spread of TB infection is a serious problem in Transnistria. See Assembly [Resolution 1955 \(2013\)](#) on the honouring of obligations and commitments by the Republic of Moldova.

17. "Tuberculosis in complex emergencies", Rudi Coninx, Bulletin of the WHO, Volume 85, No. 8, August 2007, pp. 569-648.

18. Continuing a trend that has persisted for the last decade, the majority (nearly 80%) of people newly diagnosed were from the eastern part of the Region, 17% from the western part and 4% from the central part.

covering several aspects: political commitment (including the implementation of a legal framework for TB cross-border collaboration), financial mechanisms and adequate health-service delivery (prevention, infection control, contact management, diagnosis and treatment and psycho-social support).

3.2.4. Health-care funding

24. As countries in eastern Europe and central Asia become wealthier, they become ineligible for development assistance and are expected to fully fund their health-care system, including the national TB response. However, transitioning from donor funding for health care is a complex process, and a number of countries in the region do not have properly developed, funded and implemented national TB strategies. Coupled with the problem of already weak health-care infrastructures, it is very likely that once external donors withdraw, valuable programmes to address TB will cease to exist, perpetuating the chain of transmission, and undoing any progress already made.²⁰

3.3. Examples of best practice

3.3.1. Azerbaijan

25. TB is a major health problem in many of the world's prisons, where infection rates can be more than 10 times higher than in the general population. Europe is no exception. During my visit to Azerbaijan, I had the opportunity to meet representatives of the Ministry of Justice and the Ministry of Health. Working in close collaboration, the two ministries have put in place a successful TB programme in prisons. The programme includes, amongst others, a routine screening of prisoners/detainees for TB, raising awareness amongst prisoners/detainees and the prison staff about the disease, and a specialised TB hospital for confirmed cases (including a special laboratory) with separate wards for regular and resistant forms of the disease to prevent transmission of resistant TB to those people with drug-susceptible TB.

26. One of the most important objectives of the programme is to ensure that the TB treatment is completed. When the treatment cannot be completed within the penitentiary system (because of the release of the prisoner/detainee), it is continued through a three-party agreement between the Ministry of Justice, the Ministry of Health and a local non-governmental organisation (NGO). The latter provides different services, including follow-up of newly released TB patients, to ensure that they complete their treatment, psychological support, and sample collection for TB tests. Azerbaijan has achieved solid TB cure rates through this prison programme, which has been internationally recognised, including by an award from the International Corrections and Prisons Association in 2013.

3.3.2. Norway

27. Norway has very few TB cases every year (about 350-400) and an overwhelming majority of TB patients are foreign-born. Against this background, the country has put in place a strong and humane TB control programme, by introducing, amongst others, an obligatory TB screening for all asylum seekers, as well as all other migrants coming from countries where TB incidence is high. TB treatment is free of charge for everyone, including all migrants, independent of their legal status.²¹

28. Norway has adopted an integrated approach whereby there is effective collaboration between all stakeholders involved in the fight against TB, including local authorities, civil society organisations and health-care personnel. This collaboration between different TB actors facilitated by "TB co-ordinators" is essential for a co-ordinated and effective TB response. TB co-ordinators also follow patients all the way through their treatment, provide them with emotional support, and organise and facilitate the treatment plan meeting, which is considered to be the cornerstone of treatment success. In fact, all TB patients have an individual treatment plan setting out the rules on where and when they will meet a health worker to take their medicines.²² The plan is established so as to make it as convenient as possible for the patient to get through the treatment period.

19. The Wolfheze Workshops is an important meeting of TB policy makers and researchers from Europe, organised every two years by the KNCV Tuberculosis Foundation in collaboration with WHO/Europe and the European Centre for Disease Control.

20. "Transitioning from donor support, HIV and TB programmes in Eastern Europe and Central Asia: Challenges and Effective solutions", TB Europe Coalition, 25 April 2016.

21. There were concerns that introducing a free-of-charge TB treatment would lead to health tourism. These fears have proven to be wrong, as there was no substantial increase in TB patients in Norway after the introduction of this system.

29. Norway is an excellent example demonstrating that TB can be efficiently fought through the development and maintenance of a strong, humane, integrated and people-centred TB control programme, in particular for other high-income countries in Europe where TB incidence is low.

4. Research and development for new medicines, diagnostic tools and vaccines

30. There is a significant lack of investment in research and development (R&D) for new TB medicines, diagnostic tools and vaccines. The TB drug development field suffers from a prolonged period of disinvestment by the pharmaceutical industry, other than a few exceptions, leaving a thin pipeline of products under development.²³

31. In fact, the current system of R&D does not work well for a disease like TB, where there is little commercial incentive for the production of new tools, because the greatest burden of the disease falls on the poorest parts of the world. Even in low- and middle-income countries, the groups most at risk of contracting the disease tend to be the most marginalised and the poorest section of society. In addition, TB treatments must be delivered as combination therapies, usually using three or more antibiotics together. The complex interaction of medicines means that the individual drugs making up these regimens should ideally be developed as combinations from early on during clinical testing, rather than once they are finished and licensed single products. This poses technical and commercial challenges.²⁴ Hence, pharmaceutical producers are reluctant to invest the significant R&D costs in order to bring new TB drugs onto the market.

32. While it is a global problem, Europe has a specific role in changing this overall market failure for TB drugs, diagnostic tools and vaccines, to avoid not only a significant number of unnecessary deaths, but also a huge cost to national economies due to the expense of treating MDR-TB and XDR-TB. Moreover, it should not be forgotten that solutions that increase R&D for TB could also benefit the problem of wider AMR, due to the need to develop multiple drugs in order to treat TB, which could likely also be used to treat a range of other illnesses.²⁵

33. European governments should invest more in R&D, by offering incentives for innovation through sustained funding of early clinical work, as well as through the so-called pull incentives that rewards products for achieving market entry or important milestones along the drug development pipeline.²⁶

34. Governments should also strengthen existing, and create new, public-private partnerships for encouraging R&D. A major achievement of the European Union in this context is the New Drugs for Bad Bugs programme, the world's biggest public-partnership in the field of AMR. The programme, which was launched under the innovative medicines initiative in 2012, has contributed to increasing the number of large European pharmaceutical companies active in the AMR research area from 4 to 11 in the past five years. Through calls-for-research specifically targeted at small and medium-sized enterprises (SMEs), the European Commission has also strengthened European SMEs involved in AMR-related research. In the past decade, the number of SMEs working on AMR in the biopharmaceutical companies from Europe innovating in AMR (BEAM Alliance) increased from just a few to around 50.²⁷

35. In addition to new drugs, diagnostic tools and vaccines, there is also a need to invest in new technologies that can simplify TB treatment for patients, with a view to increasing treatment adherence and success, considering that incomplete and erratic treatment is one of the main drivers of drug resistance. An encouraging example of such technology was presented to the participants of the 48th World Conference on Lung Health held in Guadalajara (Mexico), in October 2017. The so-called [Wireless Observed Therapy](#) (WOT) is a digital, ingestible alternative to DOT, which is the current gold standard for ensuring treatment adherence. Under WOT, patients swallow an ingestible sensor made of minerals found in food which breaks down in the body, releasing a sensor the size of a grain of sand that sends data to a patch worn on the patient's chest. The patch stores the data (it provides a date and time-stamped recording of medication ingestions) until it

22. Once the patient leaves the hospital, he/she continues the treatment through the DOT (Directly Observed Treatment) method. This method requires health workers to be present and support TB patients when they take their medicines.

23. "Tackling drug-resistant infections globally: final report and recommendations, The review on antimicrobial resistance", May 2016. According to WHO, there are currently 17 TB drugs in Phase I, II or III trials and 12 vaccine candidates in clinical trials.

24. Ibid.

25. "Tuberculosis – The cornerstone of the AMR Threat", TB Europe Coalition.

26. Doctors without borders in collaboration with other public health organisations have developed a proposal referred to as the "3Ps", for "Push, Pull and Pool". It uses a combination of milestone payments, R&D push funding and pooling of intellectual property to overcome the key challenges of TB regimen development. See footnote 23.

27. "Increased momentum in antimicrobial resistance research", *The Lancet*, Vol. 388, 27 August 2016.

comes into contact with a mobile device – a tablet or any mobile phone with Bluetooth capacity. The mobile device encrypts the data and sends it via wireless internet to the patients' health-care provider, facilitating remote monitoring and greatly relieving the burden of treatment on the patient.²⁸

5. The way forward for Europe and the world

36. 2018 is a critically important year for addressing the TB response at the global level, with increased political momentum building as a result of governments coming together in realisation of the growing threat to global public health posed by TB. As the international community steps up efforts to tackle the threat of TB, the European Region has a critical role to play in addressing its own epidemic and showing global leadership in efforts by the international community.

37. As far as the MDR-TB epidemic is concerned, experience shows that a well-crafted public health response can improve things rapidly. In fact, *The Lancet* reports that, following a rise in TB and MDR-TB in New York City in the 1980s, swift public health action caused MDR-TB incidence to drop precipitously and more rapidly than drug-susceptible TB. "Such an effective response to MDR-TB cannot focus on treating DR-TB alone but include strong surveillance systems, drugs susceptibility testing for all patients with TB, rapid linkage to effective treatment and patient-centred care throughout the treatment course".²⁹

38. Diagnosing TB quickly and accurately, so that people receive appropriate treatment, is an imperative first step. Therefore, countries should invest in actively looking for TB cases among high-risk populations, such as people living with HIV.³⁰ Preventive therapy to stop people with latent TB infection from developing active TB disease should also be oriented towards these key populations.

39. Once diagnosed, it is crucial to ensure that patients are adequately treated and monitored so that they finish their course of medication. Completing treatment is crucial with a view to ensuring recovery and preventing the development of resistant bacteria. As the Azerbaijani example clearly shows, the involvement of civil society in patient follow-up, treatment adherence and psycho-social support can contribute to increasing TB cure rates. An effective TB response should therefore involve civil society actors who can provide TB education, treatment support and counselling to patients. In order to combat the social isolation and stigma attached to TB, in addition to providing psycho-social support, countries should raise awareness about the disease amongst the general public and work to debunk myths about the disease.

40. Moreover, countries should replace out-dated TB policies with an efficient and people-centred model of TB care that is in line with international guidelines from WHO. To this end, there should be a shift in TB management from a centralised hospital-dominated model to one embedded within communities and led by the primary-care system. TB care should be provided mainly in the ambulatory and community settings, together with appropriate infection control measures to avoid cross-infection, and treatment support to facilitate adherence to treatment.³¹ Limiting hospitalisation and prioritising treatment in ambulatory settings will reduce the social and economic impact of the disease on patients, be less costly for the State, and improve treatment outcomes.

41. In the coming years, the fragility of national health systems in some countries in the region may be worsened by an overall reduction in external donor funding for TB. Governments concerned should maintain sustained action against TB, ensure sufficient and sustainable financing for TB care in their national budget plans and focus their resources on cost-effective and evidence-based solutions, in order not to undo progress made in this area. International donors should be involved in the planning and implementation of the transition, by providing political and technical assistance and guidance to governments.³²

42. In order to effectively address the TB epidemic, the response at the national level should involve all stakeholders, including patients themselves (or those who have been affected by the disease), health workers, caregivers and different service providers (e.g. civil society organisations), and provide opportunities to work with national decision-makers, such as government representatives and members of national

28. "Ingestible sensor to transform TB treatment adherence methods", see the conference updates on the website of the Conference 48th Union World Conference on Lung Health.

29. "Multidrug-resistant tuberculosis in India: looking back, thinking ahead", *The Lancet public health*, Vol. 2, January 2017.

30. For example, by providing TB testing to all HIV patients.

31. A people-centred model of tuberculosis care: A blueprint for eastern European and central Asian countries, first edition, WHO regional office for Europe, 2017.

32. See footnote 20.

parliaments. This would allow accountability and efficacy in the TB response, as the involvement of those who have first-hand experience of the disease will help identify areas where change is needed, as well as the appropriate action to be taken in response to it.

43. All European countries should develop, fund and implement a tailored national TB strategy, as is recommended by WHO. *The Lancet* reports that the sustained progress in declining TB incidence in the United Kingdom (30% decline between 2011 and 2015) follows a combination of local, national, and global action, as well as changes in migration patterns. A collaborative national TB strategy was developed by Public Health England and NHS (National Health Service) England between 2013 and 2015, while concurrently implementing local and national TB control initiatives, such as active case finding. The strategy involved ten areas of action including two particular priorities: latent TB testing and treatment of new entrants to the United Kingdom and targeted case finding supported by management for vulnerable groups such as people who are homeless, drug and alcohol users, and those in contact with the criminal justice system.³³

44. If the ambitious vision articulated in Sustainable Development Goal 3.3 is to be achieved, with many unnecessary deaths and huge costs to the regional and global economy averted, European States must work together, with low TB incidence countries showing greater solidarity with high TB incidence countries. Low TB incidence countries should also maintain awareness and commitment to TB control, with a view to ensuring the further elimination of TB. We cannot afford to be complacent when it comes to TB control. If we fail to sustain action, re-emergence of TB is one of the few certainties.³⁴

45. The United Nations high-level meeting on TB will provide a platform for these commitments to be made. This is the first time TB has been prioritised for the attention of Heads of State from across the world, and every effort should therefore be made to maximise the impact of this meeting. Therefore, every Head of State from the Council of Europe member States should attend the United Nations high-level meeting on TB in New York in September 2018, and support the agreement of an independent, multi-sectoral accountability framework to ensure that all governments and stakeholders deliver on the commitments made.

33. "Sustaining tuberculosis decline in the United Kingdom", *The Lancet*, Vol. 389, 25 March 2017.

34. Ibid.