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REGIONAL OFFICE FOR **Europe**

ROADMAP TO IMPLEMENT THE TUBERCULOSIS ACTION PLAN FOR THE WHO EUROPEAN REGION 2016–2020

Towards ending tuberculosis and multidrug-resistant tuberculosis

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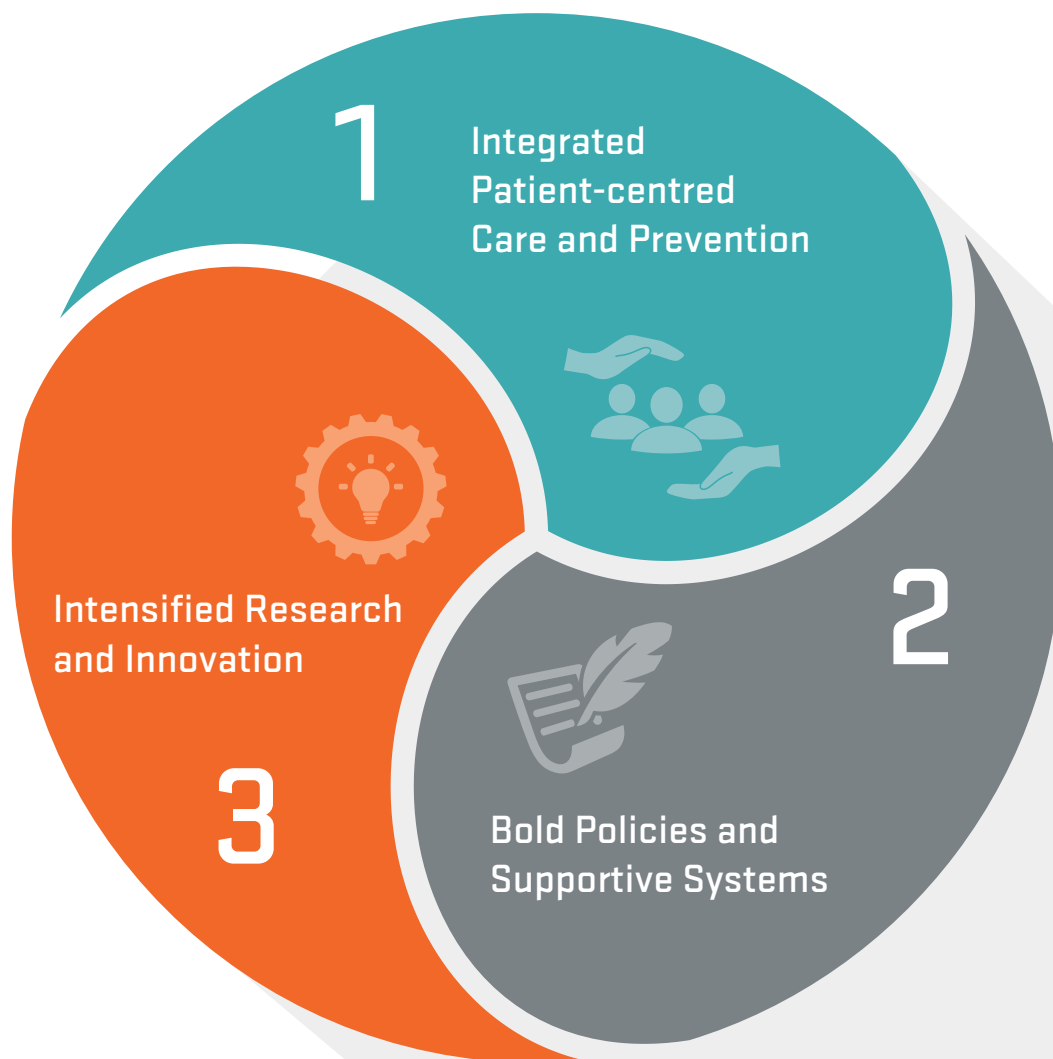# Roadmap to implement the tuberculosis action plan for the WHO European Region 2016–2020

Towards ending tuberculosis and multidrug-resistant tuberculosis

1 Integrated Patient-centred Care and Prevention

2 Bold Policies and Supportive Systems

3 Intensified Research and Innovation

ABSTRACT

WHO Regional Committee for Europe resolution EUR/RC65/17 Rev. 1 on a tuberculosis action plan for the WHO European Region 2016–2020 was developed through a Region-wide participatory process to operationalize the global End TB Strategy in the regional context for its subsequent adaptation at national level according to country specificities. The action plan, which is in line with Health 2020 and other key regional health strategies and policies, sets a regional goal and targets for the care and control of tuberculosis (TB) and drug-resistant TB from 2016 to 2020 by defining strategic directions and describes activities to be carried out by stakeholders. The action plan is based on lessons learnt in the implementation of Regional Committee resolution EUR/RC61/15 on a consolidated action plan to prevent and combat multidrug- and extensively drug-resistant tuberculosis in the WHO European Region 2011–2015. It is applicable to all Member States of the WHO European Region, including high-priority countries and those with a low incidence of TB. Implementation of the new TB action plan would mean an estimated 3.1 million lives would be saved, 1.4 million TB patients would be cured, and 1.7 million new cases of all forms of TB would be prevented. The cost of implementing the plan is estimated at US$ 15 billion. Based on the economic analysis of lives saved and avoidable suffering prevented, as illustrated by an improvement in disability-adjusted life-years, the plan should prove highly cost–effective, resulting in savings of US$ 48 billion.

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Contents

Target audience

This publication is primarily for those responsible for tuberculosis prevention and care in Member States of the WHO European Region, including ministries of health and other government bodies responsible for health in penitentiary services, health financing, health education and social services. It urges and supports intensified involvement of civil society and communities affected by the disease, professional societies, partners and donors, national and international technical agencies and all stakeholders engaged in tuberculosis prevention and care in the Region.

Acronyms and abbreviations

BCG	bacillus Calmette-Guérin
DST	drug-susceptibility testing
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
M/XDR-TB	multidrug- and extensively drug-resistant tuberculosis
MDR-TB	multidrug-resistant tuberculosis
NTP	national tuberculosis programme
PLHIV	people living with HIV
RCC-TB	Regional Collaborating Committee on Tuberculosis Control and Care
rGLC	regional Green Light Committee (for Europe)
TB	tuberculosis
XDR-TB	extensively drug-resistant tuberculosis

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Foreword

The implementation of the consolidated action plan to prevent and combat drug-resistant tuberculosis (TB) 2011–2015 has led to a number of important achievements. Thanks to the strong commitment of Member States of the WHO European Region and our joint intensified efforts with national and international partners, including civil society organizations and communities, the incidence of TB in our Region has been falling at about 5% per year. This is the fastest decrease across the six WHO regions. Today, all patients with multidrug-resistant TB (MDR-TB) are put on treatment, compared to 63% back in 2011. With better treatment and the introduction of new models of care, the proportion of cases of MDR-TB among previously treated patients has stabilized over the past four years. These efforts and achievements have saved many lives.

Despite these great achievements, we still face human suffering and death caused by TB, MDR-TB and TB/HIV coinfection. Our Region has the highest rates of drug-resistant TB globally and only half of patients with MDR-TB are successfully cured (similar to outcomes at global level). Ours is the only Region that has seen an increase in HIV/AIDS, producing yet another challenge to TB and MDR-TB prevention and control.

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To build on the achievements and address the challenges, and in line with the global End TB Strategy and the Health 2020 European policy framework, the TB action plan for the WHO European Region 2016–2020 was developed. The plan was prepared in a Region-wide participatory process and endorsed at the 65th session of the WHO Regional Committee for Europe in September 2015, along with Regional Committee resolution EUR/RC65/17. The current roadmap aims to support full implementation, monitoring and evaluation of the TB action plan 2016–2020.

Framed by the overarching Sustainable Development Goals, underpinned by the principle of equity, and inspired by the idea of leaving no one behind, our vision and goal is to end TB. For this, we need to spark interest among all stakeholders. We need to face the challenge, show good will and engagement, and work in strong partnership for full implementation so that TB truly becomes a disease of the past.

Dr Zsuzsanna Jakab
WHO Regional Director for Europe
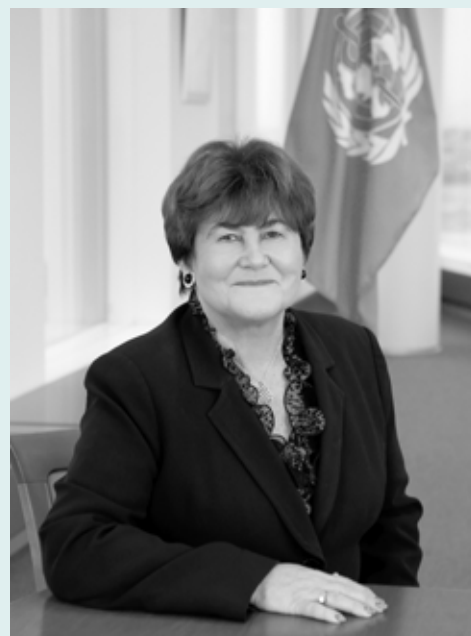
Preface

This roadmap has been developed to guide Member States of the WHO European Region and partners, including funding and bilateral agencies and civil society organizations, on how to contribute to sound implementation of the tuberculosis (TB) action plan for the WHO European Region 2016–2020 (which was endorsed by the WHO Regional Committee for Europe with its accompanying resolution EUR/RC65/17 in September 2015). It presents epidemiological analysis, an overview of the achievements and challenges of the consolidated action plan to prevent and combat multidrug- and extensively drug-resistant TB 2011–2015, a regional analysis of strengths, weakness, opportunities and threats in relation to the TB action plan, an overview of the cost and economic benefits, and a description of the monitoring framework.

The TB action plan for the Region sets out activities and milestones agreed with Member States and partners along with the three pillars of the global End TB Strategy: integrated patient-centred care and prevention; bold policies and supportive systems; and intensified research and innovation. The plan includes multidisciplinary interventions to address social determinants and prevent and manage TB/HIV coinfection and other comorbidities through disease-specific, as well as health system and public health, approaches.

Finding solutions to the gaps and formidable challenges we face calls for a paradigm shift in resource availability, scaling-up of research and innovation, and service reform where necessary. The WHO Regional Office for Europe will continue to provide guidance, strengthen Member States' capacities and build evidence for efficient and effective interventions so that we can move closer to ending TB in our Region and achieve our ultimate goal of eliminating TB altogether.

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Executive summary

WHO Regional Committee for Europe resolution EUR/RC65/17 Rev. 1 on a tuberculosis action plan for the WHO European Region 2016–2020 was developed to strengthen and intensify efforts to address the alarming problem of tuberculosis (TB) in the Region. It involved a Region-wide participatory process with representatives of Member States to operationalize the global End TB Strategy in the regional context for its subsequent adaptation at national level according to country specificities.

The action plan is in line with Health 2020 *(1)*, the strategy for eliminating TB in the European Union *(2)* and other key regional health strategies and policies. It is based on lessons learnt in the implementation of Regional Committee resolution EUR/RC61/15 on a consolidated action plan to prevent and combat multidrug- and extensively drug-resistant tuberculosis in the WHO European Region 2011–2015. The action plan is applicable to all Member States of the Region, including high-priority countries and those with a low incidence of TB.

The WHO Regional Office for Europe has worked with an advisory committee comprising representatives from WHO headquarters, seven Member States, technical and funding agencies, civil society organizations and a former multidrug-resistant TB patient to develop the draft action plan, which was reviewed at a consultation meeting with representatives of 53 Member States and partners and through a public consultation with stakeholders, civil society organizations and communities. The TB action plan for the Region for 2016–2020 with its supporting resolution was endorsed by the 65th session of the Regional Committee in Vilnius, Lithuania on 25 September 2015.

The long-term vision of the TB action plan for the Region is to bring an end to the TB epidemic, with zero affected families facing catastrophic costs due to TB. It sets a regional goal and targets for the prevention, care and control of TB and drug-resistant TB from 2016 to 2020 through strategic directions and describes activities to be carried out by stakeholders.

The action plan has six strategic directions and nine areas of intervention. The strategic directions are crosscutting and are designed to safeguard the values of Health 2020 and highlight the corporate priorities of the European Region.

Task forces led by the Regional Office have developed a comprehensive monitoring and evaluation framework to document progress in the implementation of the plan and enable financial analysis of the costs and benefits of implementation.

The action plan is highly cost–effective according to conventional benchmarks. With a total number of lives saved of 1 089 308, the cost per death averted is US$ 13 805 and cost per disability-adjusted life-years saved is US$ 657. Based on the economic analysis of lives saved and disability-adjusted life-years, the plan should prove to be highly cost–effective, resulting in savings of US$ 48 billion.

References

1. Health 2020: a European policy framework supporting action across government and society for health and well-being. Copenhagen: WHO Regional Office for Europe; 2012 (EUR/RC62/9; http://www.euro.who.int/en/health-topics/health-policy/health-2020-the-european-policy-for-health-and-well-being, accessed 10 May 2016).
2. Framework action plan to fight tuberculosis in the European Union. Stockholm: European Centre for Disease Prevention and Control; 2008 (http://ecdc.europa.eu/en/publications/Publications/0803_SPR_TB_Action_plan.pdf, accessed 10 May 2016).

Introduction and background

Although *Mycobacterium tuberculosis*, the organism that causes tuberculosis (TB) disease, was discovered over a century ago (in 1882), the global burden of TB today remains enormous. There was an estimated 9.6 million cases of TB and 480 000 new cases of multidrug- and extensively drug-resistant TB (M/XDR-TB) worldwide in 2014 *(1)*. Around 340 000 incident TB cases occurred in the WHO European Region in 2014, equivalent to an average of 37 cases per 100 000 population, with an estimated 33 000 TB deaths (equivalent to 3.7 deaths per 100 000 population) *(1)*. TB also negatively affects household and national economies due to loss of income through inability to work of the most economically productive age group, those aged 25–44 years, who represent 45% of new TB cases registered in the Region. TB among children under 15 years represented approximately 4% of the total TB patients reported in the Region in 2013.

TB is mainly caused by *M. tuberculosis* and multidrug-resistant TB (MDR-TB) by the strain that is resistant to at least isoniazid and rifampicin, the two most potent TB drugs. Extensively drug-resistant TB (XDR-TB) is a type of MDR-TB resistant to isoniazid and rifampicin plus any fluoroquinolone and at least one injectable second-line drug.

The rising incidence of M/XDR-TB since 2009 represents a global public health crisis. The European Region has been particularly affected, with nine of the world's 30 high M/XDR-TB burden countries *(2)* and the highest proportion of new and retreated cases with MDR-TB (Fig. 1) *(3,4)*. In 2014, there was an estimated 73 000 MDR-TB cases in the European Region. WHO revised the list of high MDR-TB burden countries in 2015 *(2)*, but in the Region, the list of 18 high TB priority countries remains unchanged. These countries have 85% of the TB burden and 99% of the MDR-TB burden (based on the absolute number and rates) *(3)* (Fig. 1).

Drug-resistant TB can occur either due to suboptimal treatment of susceptible strains *(5)* or transmission of already resistant strains of *M. tuberculosis (6)*. The duration of treatment is much longer for MDR-TB (up to two years) compared to drug-susceptible TB (between six and nine months), with a significantly higher risk for adverse drug

Fig. 1. Percentage of new TB cases with MDR-TB

Percentage of cases
- 0–2.9
- 3–5.9
- 6–11.9
- 12–17.9
- ≥18
- No data
- Subnational data only
- Not applicable
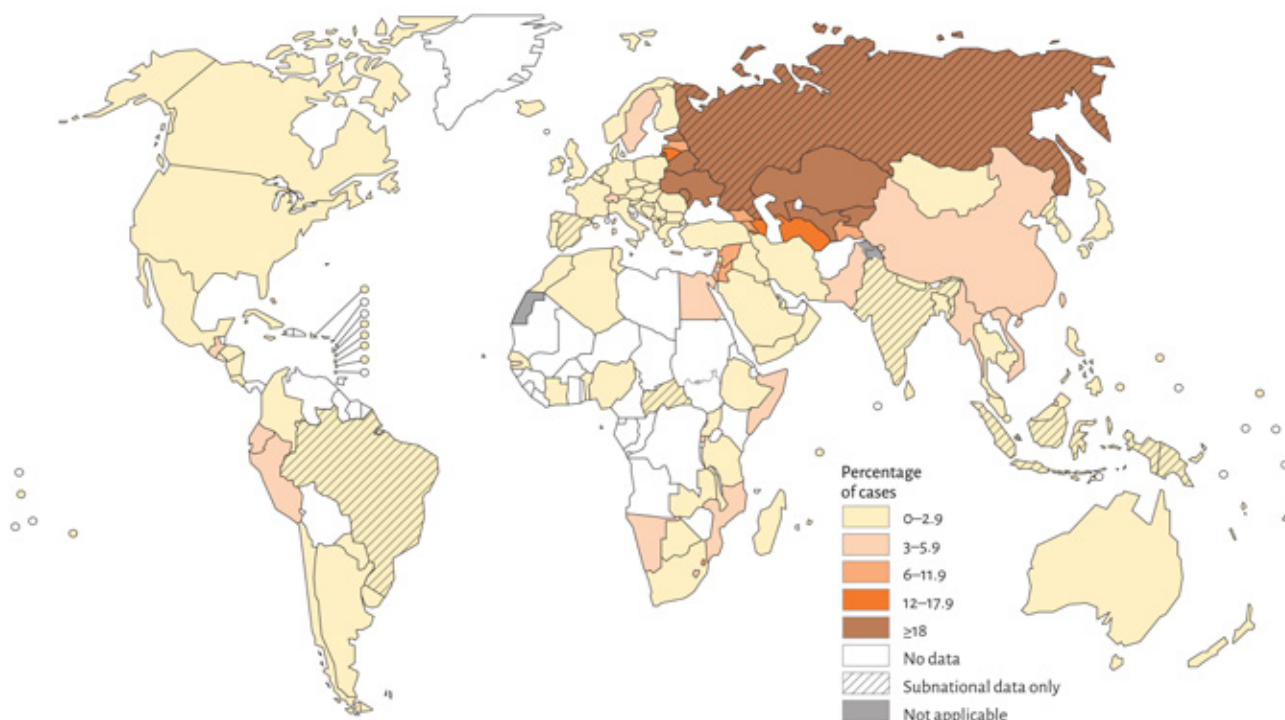
Source: WHO *(1)*.

reactions *(7,8)* and unsuccessful treatment outcomes, particularly death *(9–12)*. The risks are even higher for XDR-TB *(13,14)*.

While only approximately 4% of the global burden of TB in 2014 was found in the European Region, the Region nevertheless has 25% of the world's burden of MDR-TB, indicating the relative importance of MDR-TB in Europe *(1)*. All high-burden MDR-TB countries in the Region are in the east, with 99% of MDR-TB cases *(3)*. The estimated annual incidence of TB and MDR-TB and proportion of MDR-TB among new and previously treated TB cases in high-burden MDR-TB countries are shown in Table 1.

TB in the Region is difficult to treat due to drug resistance. Despite a slight increase in the 2012 cohort, treatment success among MDR-TB patients remains low and is similar to the global level (fewer than 50% of cases treated successfully). TB is one of the leading causes of death among people living with HIV (PLHIV) and this deadly combination

is increasing in the Region (Fig. 2): HIV prevalence among TB patients increased from 3.2% in 2008 to 8.0% in 2014.

XDR-TB accounts for approximately 18% of drug-resistant cases, with most occurring in the 15 high-burden countries *(3)*. The added burden of second-line drug resistance may be much higher, however. A recent study utilizing regional data found that of MDR-TB patients who had second-line drug-susceptibility testing (DST), 41.1% (95% confidence interval (CI): 32.3–50.0) had resistance to either a fluoroquinolone or a second-line injectable agent, or both *(15)*. Only 49% of people diagnosed with MDR-TB in the 2012 cohort had a successful treatment outcome, which is well below the 75% target *(3,4)*.

The consolidated action plan to prevent and combat M/XDR-TB in the WHO European Region 2011–2015

All Member States committed themselves in 2007 to respond urgently to the re-emergence of TB in the European Region and properly address M/XDR-TB through endorsement of

Table 1. Estimated annual incidence of TB and MDR-TB and estimated proportion of new and previously treated TB cases with MDR-TB among all notified TB cases in the 18 high TB priority countries, WHO European Region, 2014

Countries	Estimated number of incident TB cases	Percentage of overall regional TB burden	Estimated annual incidence of MDR-TB	Estimated percentage of TB cases with MDR-TB out of the total notified	
			Cases (95% CI[a])	Newly treated (95% CI)	Previously treated (95% CI)
Armenia	1 400	0.4	160 (160–180)	9.4 (7–12)	43 (38–49)
Azerbaijan	7 400	2.2	1 300 (1 100–1 500)	13 (10–16)	28 (22–34)
Belarus	5 500	1.6	1 700 (1 600–1 800)	34 (32–36)	69 (66–72)
Bulgaria	1 900	0.6	72 (53–91)	2.3 (1.3–3.8)	23 (17–31)
Estonia	270	0.1	62 (48–75)	19 (14–27)	62 (42–79)
Georgia	4 300	1.3	640 (590–700)	12 (10–13)	39 (35–44)
Kazakhstan	17 000	5.0	4 900 (4 800–5 000)	26 (25–27)	58 (57–59)
Kyrgyzstan	8 300	2.4	2 000 (1 800–2 100)	26 (23–31)	55 (52–58)
Latvia	980	0.3	84 (66–100)	8.2 (5.8–11)	30 (21–40)
Lithuania	1 800	0.5	300 (270–340)	14 (12–16)	49 (43–55)
Republic of Moldova	6 200	1.8	1 500 (1 400–1 600)	24 (21–26)	62 (59–65)
Romania	16 000	4.7	650 (490–810)	2.8 (1.8–4.2)	11 (8.0–15)
Russian Federation	120 000	35.3	39 000 (33 000–45 000)	23 (21–25)	49 (40–59)
Tajikistan	7 600	2.2	880 (810–950)	8.1 (6.9–9.4)	52 (47–57)
Turkey	14 000	4.1	360 (320–410)	2.5 (2.1–3.0)	18 (15–21)
Turkmenistan	3 400	1.0	450 (390–520)	14 (11–17)	38 (30–45)
Ukraine	43 000	12.6	13 000 (12 000–14 000)	22 (20–24)	56 (50–61)
Uzbekistan	24 000	7.1	7 000 (6 100–7 900)	23 (18–29)	62 (52–71)

[a] CI = confidence interval.

Fig. 2. Percentage of TB/HIV coinfection among all TB cases, WHO European Region, 2008–2014
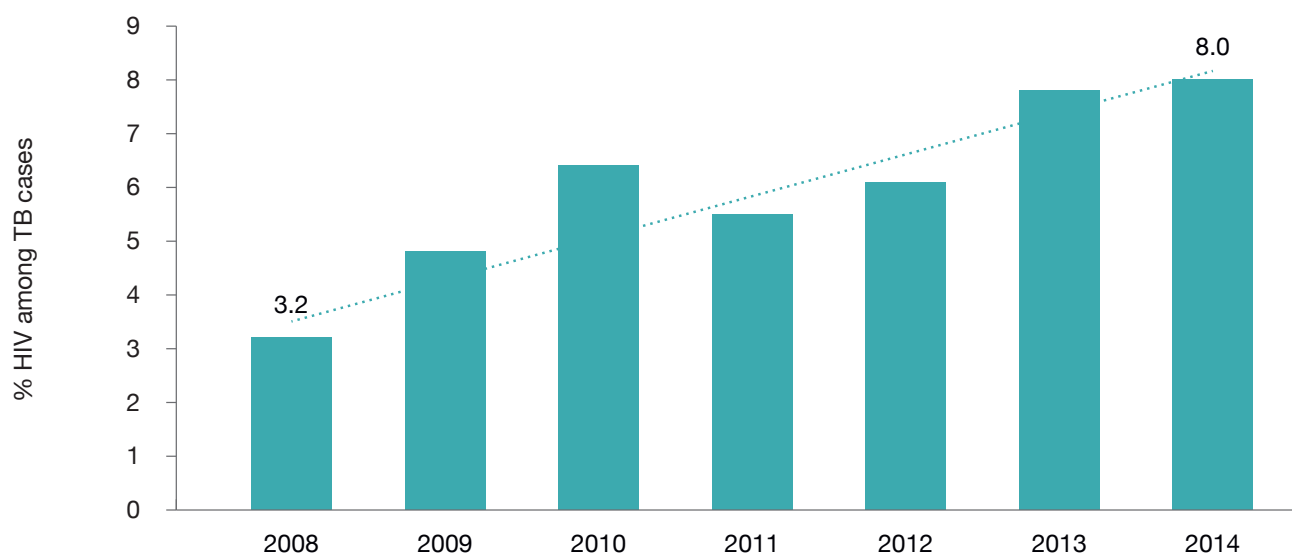
Source: European Centre for Disease Prevention and Control/WHO Regional Office for Europe *(3)*.

the Berlin Declaration on Tuberculosis *(16)*. Subsequently, ministers from the 27 countries of the world with a high M/XDR-TB burden met in Beijing, China on 1–3 April 2009 to address the alarming threat of M/XDR-TB. This was reflected in a call for action to help strengthen health agendas and ensure that urgent and necessary commitments to action and funding were made to prevent the impending M/XDR-TB epidemic *(17)*. The Sixty-second World Health Assembly in May 2009 urged all Member States through resolution WHA62.15 to achieve universal access to diagnosis and treatment of M/XDR-TB as part of the transition to universal health coverage, thereby saving lives and protecting communities.

Building on these commitments and to address the M/XDR-TB situation in the European Region, an action plan was developed in 2010 for all 53 Member States *(4)*. The plan was developed in extensive consultation with national TB programme (NTP) managers, key partners and civil society organizations. Following this consultation, the consolidated action plan to prevent and combat M/XDR-TB in the Region for 2011–2015 and Regional Committee resolution EUR/R61/R7 were endorsed at the 61st session of the WHO Regional Committee for Europe in Baku, Azerbaijan in September 2011. The plan's goal was to contain the spread of drug-resistant TB by achieving universal access to prevention, diagnosis and treatment of M/XDR-TB in all Member States by 2015 *(4)*. Its six strategic directions and seven areas of intervention were aligned with the *Global plan to stop TB 2011–2015 (18)* through the following specific targets: decrease by 20% the proportion of MDR-TB among re-treatment patients; diagnose at least 85% of all estimated MDR-TB patients; and successfully treat at least 75% of all

patients notified as having MDR-TB. Implementation of the plan began in 2011.

Since then, much progress has been made in the prevention and control of TB and M/XDR-TB in the Region and Millennium Development Goal 6 on reversing the incidence of TB has been achieved. TB incidence in the Region has been falling at an average of 5.5% per year since implementation of the consolidated action plan, which is the fastest decline in TB rates in any WHO region (Fig. 3). Diagnosis of MDR-TB cases has increased from less than one third of the estimated number in 2011 to 61% in 2014 (the most recent reporting year) and treatment coverage of notified cases from 63% in 2011 to universal coverage in 2014. Prevalence of MDR-TB among previously treated patients slightly decreased to 46% in 2014 (Fig. 4) *(3)*, following implementation of the consolidated action plan.

All high MDR-TB-burden countries in the Region have developed national M/XDR-TB response plans in consultation with WHO. The plans are based on country TB drug-resistance surveys, HIV burden and other national contexts *(19)*. Technical advisory mechanisms have also been established to achieve the comprehensive goals of the action plan and national M/XDR-TB response plans, including: the regional Green Light Committee for Europe (rGLC Europe), which is the WHO technical advisory body developed to support countries with state-of-the-art clinical advice and scale-up programmatic management of M/XDR-TB *(20)*; the European Respiratory Society and WHO TB consilium (a multidisciplinary team of specialists organized to give expert clinical consultation on M/XDR-TB and other difficult-to-treat TB cases, such as TB/HIV and paediatric
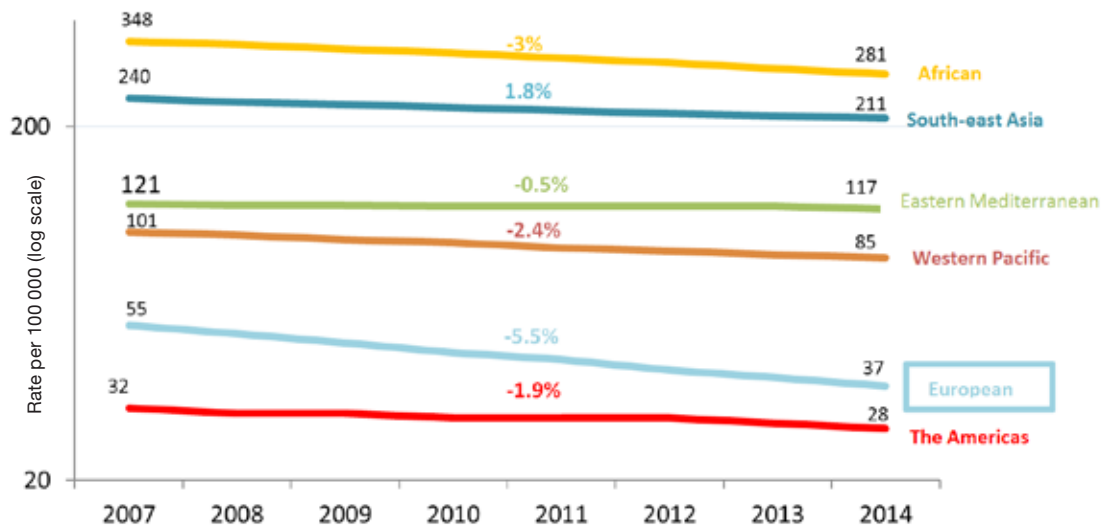
Source: WHO *(1).*

Fig. 4. Percentages of MDR among notified previously treated TB cases, WHO European Region, 2007–2014
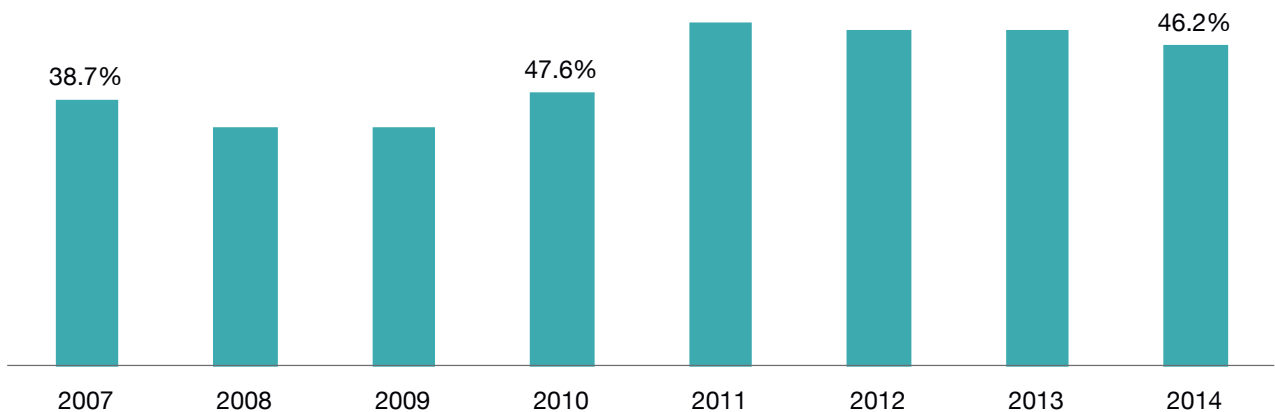
Source: European Centre for Disease Prevention and Control/WHO Regional Office for Europe *(3).*

cases) *(21)*; the European Tuberculosis Laboratory Initiative, which aims to improve and expand quality-assured diagnosis with particular attention to DST and rapid molecular tests *(22)*; and the Regional Collaborating Committee on TB Control and Care (RCC-TB), which works to improve partnerships and strengthen coordination among partners *(23)*. Representative data on levels of MDR-TB in Azerbaijan, Belarus and Turkmenistan have been available through nationwide drug resistance surveys since 2010 *(5,15,24)*.

Global End TB Strategy

With the Global Plan to Stop TB 2006–2015 coming to an end, WHO developed an ambitious global End TB Strategy *(25)* that was endorsed by the World Health Assembly in 2014 through resolution WHA67.1 *(26)*. The strategy aims to end the TB epidemic and comprises four principles, three main pillars, 10 components, milestones for 2020, 2025 and 2030, and targets for 2035. The resolution urges all Member States to adapt their use of the strategy to their national context and invites WHO and regional partners to support implementation. The strategy is summarized in Annex 1. The shift from the Millennium Development Goals to Sustainable Development Goals further emphasizes the importance of linking TB prevention and care to other development issues.

Rationale and process of development of the TB action plan for the WHO European Region, 2016–2020

The consolidated action plan to prevent and combat M/XDR-TB in the Region also ended in 2015. To continue to move forward and address the challenges in TB and M/XDR-TB prevention and care, the WHO Regional Office for Europe developed a TB action plan for the Region for 2016–2020. The action plan is based on lessons learnt in implementing the consolidated action plan and is applicable to all Member States, including high-priority countries[1] and those with a low incidence of TB. Its intention is to implement the global End TB Strategy in the regional context for subsequent adaptation at national level according to country specificities.

The action plan is aligned with the WHO European policy for health and well-being, Health 2020 *(27)*, the European Centre for Disease Prevention and Control framework action plan to fight TB in the European Union *(28)* and the action framework for eliminating TB in low-incidence countries *(29)*. It also addresses the Eastern Partnership Ministerial Conference on Tuberculosis and Multidrug-resistant Tuberculosis, in which Member States committed to end TB in the European Region through the Joint Riga Declaration on Tuberculosis and its Multidrug-resistance in 2015.

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1   The 18 high-priority countries in the WHO European Region are: Armenia, Azerbaijan, Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, the Republic of Moldova, Romania, the Russian Federation, Tajikistan, Turkey, Turkmenistan, Ukraine and Uzbekistan.

The long-term vision is to bring an end to the TB epidemic, with zero affected families facing catastrophic costs due to TB. The action plan sets a regional goal and targets for the prevention and care of TB and drug-resistant TB from 2016 to 2020 through six strategic directions and five areas of intervention to be carried out by Member States, the Regional Office and partners. It serves as a framework for immediate actions and long-term solutions for health-systems strengthening, directing adequate TB care to vulnerable populations and addressing social determinants of, and risk factors for, TB.

The Regional Office has worked with an advisory committee comprising representatives of WHO headquarters, seven Member States (Armenia, Austria, Belarus, Germany, Kazakhstan, the Netherlands and the United Kingdom), technical and funding agencies, civil society organizations and a former MDR-TB patient (see acknowledgements section). The advisory committee met twice, on 3 October 2014 and 4 March 2015, to review the draft action plan.

The draft action plan was also reviewed at a consultation meeting with representatives of 53 Member States and partners on 27 November 2014 in Copenhagen, Denmark, and through an Internet-based public consultation in March–May 2015. It was finalized during the meeting of NTP managers on 27 May 2015 in The Hague, the Netherlands. Contributions and suggestions were incorporated into the draft at each stage of review.

The TB action plan for the WHO European Region for 2016–2020 with its supporting resolution (Annex 2) was endorsed at the 65th session of the Regional Committee in Vilnius, Lithuania on 17 September 2015. A summary of the development process is shown in Fig. 5.

Areas of intervention under the new action plan are described within the current context and major activities of the plan in Annex 3. Task forces led by the Regional Office have developed a comprehensive monitoring and evaluation framework to document progress in implementation (Annex 4) and financial analysis of the costs and benefits of implementation (Annex 5).

Opportunities to continue the work initiated between 2011 and 2015

The action plan presents an opportunity to continue the work initiated under the consolidated action plan 2011–2015 and address the challenges of ending TB in the Region.

High levels of MDR-TB cases with additional resistance to either a fluoroquinolone, a second-line injectable agent, or both (XDR-TB), is of great concern *(15)*. Despite widespread

coverage of second-line drugs, there is still inadequate treatment and insufficient patient support mechanisms in some countries in eastern Europe, including some members of the European Union *(19)*. Evidence of this is seen in projects that were not supported internationally by technical agencies such as WHO or rGLC Europe in which treatment success among MDR-TB patients is extremely low (28% in some settings) *(30)*, mainly due to incomplete treatment regimens and a lack of full access to all necessary second-line drugs. Adverse drug events leading to poor treatment adherence during the long course of M/XDR-TB therapy also severely compromised treatment success *(31)*. Despite bedaquline and delamanid being approved conditionally by international drug regulatory authorities, their full-scale use has not been achieved due to the need for Member States to meet certain safeguarding conditions, including the establishment of strong pharmacovigilance systems.

The practice in some countries of hospitalizing patients unnecessarily while awaiting DST results or during the intensive phase of drug-susceptible TB treatment contributes to the spread of drug-resistant forms of TB *(32–37)*. Ambulatory services and other models of care, including home-based treatment, are not fully functional in these countries *(19)*. In the absence of adequate airborne infection control, hospitalization can lead to nosocomial transmission and superinfection with M/XDR-TB strains among patients and health care workers. A recent meta-analysis found no difference in treatment outcomes between patients treated in ambulatory and hospital settings *(38)*. WHO currently recommends minimizing unnecessary hospitalization and using ambulatory rather than hospital-based models of care for MDR-TB treatment *(11)*, an option that is likely to be much more acceptable to patients over the longer term.

New rapid molecular tests for MDR-TB such as GeneXpert MTB/RIF (a cartridge-based, automated diagnostic test that can identify *M. tuberculosis* and resistance to rifampicin) play a vital role in the rapid identification and control of drug-resistant TB *(39)*. In theory, the quicker the detection of drug-resistant strains, the quicker patients can be initiated on appropriate treatment regimens, thereby minimizing the window of transmission (although this also depends on good links with, and referral systems to, care services). Rapid diagnostic technologies, however, are not yet universally available *(4,31,40)*. Decreases in funding as a result of the financial crisis in some countries have also exacerbated difficulties in scaling-up diagnostic capacities, including the use of molecular tests and improving biosafety.

Fig. 5. Process of development of the TB action plan for the WHO European Region, 2016–2020

Review lessons learnt from implementation of consolidated action plan 2011–2015	
Drafting outline of TB action plan	**August–September 2014**
First meeting of the TB action plan advisory committee	**3 October 2014**
Technical advisory group and first regional consultation, WHO Regional Office for Europe, Copenhagen	**25–27 November 2014**
Second meeting of the TB action plan advisory committee	**4 March 2015**
Draft TB action plan public consultation	**March–May 2015**
Draft TB action plan reviewed by the Standing Committee of the Regional Committee	**16 May 2015**
Final review of TB action plan at NTP managers' meeting/Wolfheze workshops	**27 May 2015**
Endorsement of TB action plan by Regional Committee along with MDR-TB action plan final report	**September 2015**

Azerbaijan *(41)*, Kyrgyzstan, Tajikistan, Turkmenistan *(42)*, Ukraine and Uzbekistan *(43)* conducted their first nationwide drug-resistance surveys between 2010 and 2014 to better understand the burden of MDR-TB and guide the planning of diagnostic, treatment and care services. The most effective approach to monitoring trends in drug resistance, however, is continuous surveillance based on routine DST of TB patients and systematic collection and analysis of data. Only a limited number of countries in the Region have established such high-quality continuous surveillance systems.

Data on testing for second-line drug susceptibility is still limited and electronic data management is lacking in many countries of eastern Europe, which adds to difficulties in analysing programme performance. Some eastern European countries collect second-line anti-TB drug-resistance data only during subnational surveys that are not repeated, and others have limited or no data *(15)*. Rapid second-line DST testing is essential in enabling treatment to be adapted to resistance patterns in a timely manner, but several high MDR-TB priority countries still do not have universal or near-universal coverage of second-line DST *(3)*.

Another serious challenge to M/XDR-TB control is reaching vulnerable populations, such as children, migrants, prisoners and PLHIV, who are at greater risk of contracting and developing M/XDR-TB *(44)*. Considerable efforts have been made on this front since 2011, with the development of a minimum package for cross-border TB control and care in 2012 *(45)* and an official statement of 12 action points to improve TB prevention and control in prisons issued in 2013 by the International Union Against Tuberculosis and Lung Disease (The Union), WHO and other international stakeholders *(46)*. In addition, awareness of ethical and human-rights dimensions of M/XDR-TB treatment has been enhanced through specific analysis and assistance in selected countries *(47)*, although many countries in eastern Europe have yet to implement the recommendations.

Risk factors for TB, such as diabetes mellitus, use of alcohol and smoking tobacco, are identified as having an impact on the TB epidemic but are still not being addressed properly. A demonstration project in Estonia taken forward with WHO support, for instance, was not developed adequately *(48)*.

Children are vulnerable to M/XDR-TB, but their needs are often neglected due to the low number of sputum bacilli *(49)*, which makes TB and M/XDR-TB more difficult to diagnose with sputum-smear microscopy, culture and molecular tests *(50)*. WHO guidelines on childhood TB, including paediatric diagnostics and drug formulations, have recently been updated but need to be adopted in national strategic TB plans and practices.

Migrants often face myriad challenges, including discrimination, economic adversity, language barriers, stigma and fear of deportation *(51)*. These challenges, combined with the migratory nature of the population, pose enormous barriers and difficulties in accessing diagnosis and continuous TB treatment services *(51)*. Internal and cross-border migration are enhancing factors for TB transmission. Many migrants also live in close proximity with family members or others, as in the case of refugees or seasonal migratory workers residing in temporary housing. All of these factors further the risk of developing, contracting and transmitting drug-resistant forms of TB. Complicating the situation, some countries in eastern and western Europe deport migrants with TB without considering the public health and human rights issues involved or without taking adequate infection control measures, consequently increasing the risk of cross-border transmission *(45,52)*. Levels of migration vary substantially across eastern Europe, as do reported rates of TB among migrants *(53,54)*

Similar to migrants, prisoners have a much higher risk of developing or contracting drug-resistant TB compared to the general population. Prisons in eastern Europe are often poorly ventilated and crowded, with prisoners spending long periods of time in these environments *(55)*. Other determinants include high rates of HIV infection, injecting drug use and poor nutritional status *(46)*. Human and financial resources for TB and MDR-TB prevention and control in prisons are often scarce in eastern Europe and gaps in coordination between civilian and penitentiary TB services persist *(19)*. Good-practice examples of TB and M/XDR-TB control in the Azerbaijan prison sector and effective continuity of TB care for released prisoners in Azerbaijan and the Republic of Moldova *(56)* have recently emerged, however, and these should be scaled-up in the Region.

PLHIV are highly susceptible to TB *(57)*. Eastern Europe has one of the fastest growing HIV epidemics in the world *(58,59)*, but most countries lack a functioning TB/HIV coordinating mechanism to facilitate the delivery of integrated TB and HIV services, including those related to narcology services for people with drug or alcohol dependency *(19)*.

Lack of sustainable human resources and sound health financing mechanisms represent important challenges that affect all levels of M/XDR-TB prevention, control and care. Specialized human resources to manage cases of drug-resistant TB in children and adults, deliver adequate services for case-detection and scale-up diagnostic and laboratory capacity are particularly required *(19,60)*.

Outline of the TB action plan

Vision

The vision is of an end to the TB epidemic, with zero affected families facing catastrophic costs due to TB.

Goal

The goal is to end the spread of drug-susceptible and drug-resistant TB by achieving universal access (meaning evidence-based practices and quality services that are available, accessible, affordable and acceptable to people irrespective of their age, sex, sexual orientation, religion, origin, nationality, socioeconomic status or geographic background) to prevention, diagnosis and treatment in all Member States of the Region, thereby contributing to the End TB Strategy goal of ending the TB epidemic.

Targets (to be achieved by 2020)

The targets for 2020 are to achieve:

- 35% reduction in TB deaths;
- 25% reduction in TB incidence rate; and
- 75% treatment success rate among the MDR-TB patient cohort.

Strategic directions

The six strategic directions are to:

- work towards TB elimination by strengthening health systems' responses to TB and drug-resistant TB prevention, control and care;
- facilitate intersectoral collaboration to address the social determinants – the conditions in which people are born, grow, work, live and age, and the wider set of forces and systems shaping the conditions of daily life, including economic policies and systems, development agendas, social norms, social policies and political systems – and underlying risk factors of TB;
- work in national, regional and international multistakeholder partnerships, including with civil society and communities;
- foster collaboration for the development and use of new diagnostic tools, medicines, vaccines and other treatment and preventive approaches;
- promote the rational use of existing resources, identify gaps and mobilize additional resources to ensure sustainability; and
- ensure that the promotion of sound TB ethics, human rights and equity is embedded in all areas of the strategic interventions listed above.

Areas of intervention

Areas of intervention are shown in Table 2.

Table 2. Areas of intervention	
Areas	**Interventions**
1. Integrated patient-centred care and prevention	A. Systematic screening of contacts and high-risk groups B. Early diagnosis of all forms of TB and universal access to drug-susceptibility testing, including the use of rapid tests C. Equitable access to quality treatment and continuity of care for all TB patients, including drug-resistant TB, and patient support to facilitate treatment adherence D. Collaborative TB/HIV activities and management of comorbidities E. Management of latent TB infection and preventive treatment of people at high risk, and vaccination against TB
2. Bold policies and supportive systems	A. Political commitment with adequate resources, including universal health coverage policies B. Health-systems strengthening in all of its functions, including well aligned financing mechanisms for TB and human resources C. Regulatory frameworks for case-based surveillance, strengthening vital registration, quality and rational use of medicines, and pharmacovigilance D. Airborne infection control, including regulated administrative, engineering and personal protection measures in all relevant health care facilities and congregate settings; E. Community systems and civil society engagement F. Social protection, poverty alleviation and actions on other determinants of TB, such as migration and prisons
3. Intensified research and innovation	A. Discovery, development and rapid uptake of new tools, interventions and strategies B. Research to optimize implementation and impact, and promote innovations

Costs and economic benefits of implementing the plan

Analyses of the cost–effectiveness and total finance required for implementation of the action plan were carried out. These followed the principles of, and updated, the 2011–2015 analysis by taking a bottom-up approach to estimate unit costs and resource use. Analysis of costs and impacts of treating drug-sensitive TB was also included.

The total budget for the five-year implementation period (2016–2020) is US$ 15 billion for the screening and treatment of drug-sensitive and M/XDR-TB in the Region, increasing annually from US$ 2.5 billion in 2016 to US$ 3.7 billion in 2020. Most of the costs (74%) are incurred in high-priority countries and consist mainly of hospital, outpatient and pharmaceutical costs.

The action plan is highly cost–effective, according to conventional benchmarks. With a total number of lives saved of 1 089 308, the cost per death averted is US$ 13 805 and cost per disability-adjusted life-years (DALY) saved is US$ 657. The cost per DALY saved is a fraction of the Region's average per capita gross domestic product (GDP), making the action plan very cost–effective. Annex 5 presents an overview of the costs, economic benefits and methodology of the TB action plan.

Expected achievements

Epidemiological modelling developed by the Regional Office indicates that implementation of the action plan in the Region between 2016 and 2020 will result in:

- 3.1 million lives saved
- 1.4 million TB patients cured
- 1.7 million new cases of all forms of TB prevented
- US$ 48 billion saved.
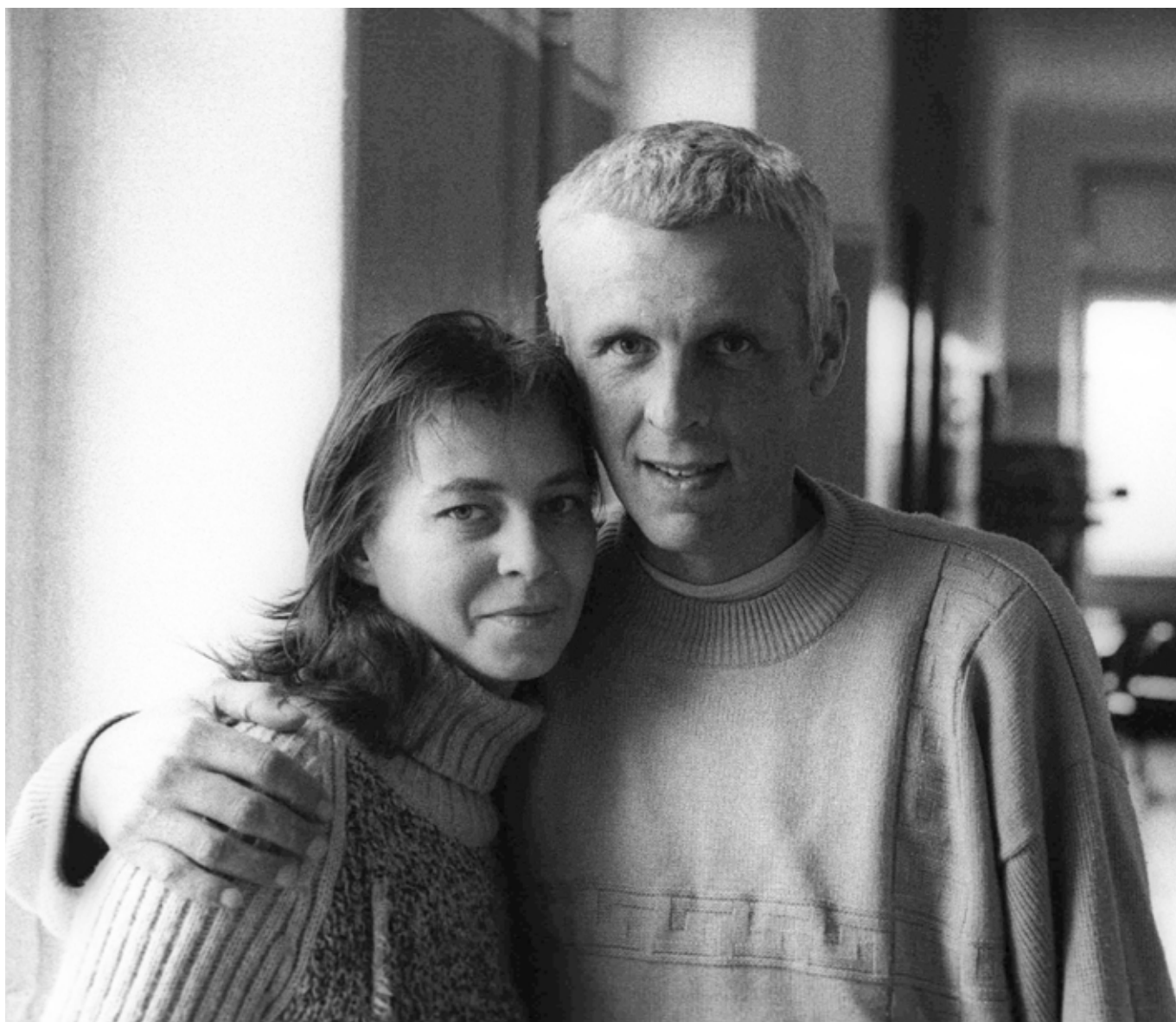
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Activities related to areas of intervention

1. Integrated patient-centred care and prevention

1A Systematic screening of contacts and high-risk groups

1A.1 Member States, with support from the Regional Office, will develop or revise strategies for systematic screening, including active case-finding and/or contact investigation (and potentially source-case investigation), including among high-risk and vulnerable populations[2] with limited or no access to health services (by the end of 2017).

1A.2 Member States will ensure that TB and M/XDR-TB screening is available in relevant congregate settings, including penitentiary services, across the Region (by 2016).

1A.3 Member States will ensure systematic engagement of communities and civil society organizations to support screening of contacts and high-risk groups (ongoing activity).

1B Early diagnosis of all forms of TB and universal access to DST, including the use of rapid tests

1B.1 The Regional Office, in collaboration with partners, will prepare a guide and diagnostic algorithms for expanded and accelerated quality-assured new diagnostic technologies (taking into account paediatric TB and extrapulmonary TB diagnostics) (by 2016).

1B.2 The Regional Office and partners will strengthen national TB laboratory services and networks for diagnosis of all forms of TB to ensure effective treatment with first- and second-line drugs, as appropriate (by 2017).

1B.3 The Regional Office and partners will help NTPs to develop strategies to maximize the benefits of rapid diagnostic tools for hard-to-reach and vulnerable populations (by 2017).

1B.4 The Regional Office will facilitate the provision of technical assistance to national TB laboratory networks, including reference laboratories, to ensure the uptake of quality-assured WHO diagnostic technologies (ongoing activity).

1B.5 The Regional Office will support NTPs of high-priority countries in finding ways to increase efficiency in sample transportation and subsequent communication of results (by 2018).

1B.6 All Member States will ensure the availability of rapid tests endorsed by WHO, using national resources and donor funding. The Regional Office will liaise with donors and countries to facilitate sustainable arrangements for funding (ongoing activity).

1B.7 Member States will ensure that quality management systems are in place within the laboratory network, covering all tests (by 2017).

1B.8 The Regional Office and key partners will support NTPs of high-priority countries in developing sustainable strategies for laboratory maintenance (by 2018).

1C Equitable access to quality treatment and continuity of care for all people with TB, including drug-resistant TB, and patient support to facilitate treatment adherence

1C.1 Member States will ensure their TB and drug-resistant TB treatment guidelines, including childhood TB guidelines, are regularly updated and implemented to comply with the latest available evidence and WHO recommendations (ongoing activity).

1C.2 Member States will develop a plan for achieving universal access to treatment, including the treatment of vulnerable populations and children, and uninterrupted drug supply (ongoing activity).

1C.3 Member States will ensure the rational, safe and effective introduction of new TB medicines, including for children, in compliance with the most recent WHO policy guidance (as soon as possible and not later than 2016) (see section 2C).

1C.4 Member States will sustain countrywide use of first-line fixed-dose combination drugs (for adults and children) and paediatric drug formulations in the treatment of drug-susceptible TB, where possible (by the end of 2016).

1C.5 Member States will ensure that surgery is available for eligible M/XDR-TB patients where indicated (by 2017) *(61)*.

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2   These include, but are not limited to: (undocumented) migrants, refugees, stateless populations, homeless people and those suffering from alcohol and drug misuse, people with mental health disorders, prisoners and those with a history of imprisonment.

1C.6 All high-priority countries will specify strategies and mechanisms for ensuring people-centred TB services and expanding and maintaining the provision of ambulatory treatment integrated into different levels and settings of service delivery (by 2016).

1C.7 All Member States will specify strategies and mechanisms for patient-centred support to TB patients and their families to enable effective treatment adherence and completion (by 2016).

1C.8 The Regional Office and partners will continue to provide technical assistance to Member States on measures to strengthen integrated delivery of TB services, including primary care and community-based TB prevention and care, with increasing use of modern information and communication technologies (ongoing activity).

1C.9 Member States will improve access to TB prevention and care and appropriate support for hard-to-reach and vulnerable populations (by 2018).

1C.10 The Regional Office and Member States will implement a mechanism for cross-border TB prevention and care that enables continuity of treatment for migrants (by 2016).

1C.11 The Regional Office will assist Member States in adopting evidence-based policies and practice for cost-effective screening of TB among receiving migrants (by the end of 2016).

1C.12 The Regional Office will promote the minimum package for cross-border TB control and care, including for migrant populations, and support Member States in its implementation through health authorities and main stakeholders (ongoing activity).

1C.13 The Regional Office will facilitate a policy-dialogue meeting for Member States and key stakeholders on cross-border TB control and care (by 2016).

1C.14 The Regional Office, in collaboration with partners, will assist Member States in further developing cooperation between penitentiary and civilian services to ensure continuity of care for patients transferred between penitentiary and civilian institutions (ongoing activity).

1C.15 Member States will ensure that palliative care services are available for all TB patients with the aim of relieving suffering from the disease and its treatment, with priority given to patients with poor chances of a cure due to limited treatment options. Specific protocols for M/XDR-TB patients who fail to respond to treatment that assess the patient's clinical condition and determine whether treatment using new or repurposed drugs is appropriate or whether the patient should be referred for end-of-life care should be established (by the end of 2016).

1C.16 The Regional Office, in collaboration with partners, will provide technical support in designing and implementing appropriate hospice/end-of-life care for M/XDR-TB patients who fail to respond to treatment and for whom all other curative treatment options, including surgery and new and repurposed drugs, are exhausted (by the end of 2016).

1D Collaborative TB/HIV activities and management of comorbidities

1D.1 The Regional Office, in collaboration with partners, will assist Member States in establishing effective coordination mechanisms at national and regional levels to facilitate the delivery of integrated TB and HIV services (by 2018).

1D.2 Member States will ensure that all TB patients have access to HIV counselling and testing supported by national HIV and TB guidelines (as soon as possible and not later than 2016).

1D.3 Member States will ensure that people living with HIV are screened and treated for latent and active TB without exposing them to possible TB infection and will provide preventive treatment where indicated (as soon as possible and not later than 2020).

1D.4 Member States will ensure that all TB/HIV patients have access to early and monitored (complying with the most recent WHO recommendations) antiretroviral therapy and co-trimoxazole preventive therapy (as soon as possible and not later than 2016).

1D.5 Member States will ensure implementation of collaborative frameworks and mechanisms for integrated management of the most frequently occurring conditions associated with TB, such as diabetes mellitus, alcohol and drug use disorders, conditions related to smoking tobacco, lung diseases and immunocompromising disorders (by 2018).

1D.6 The Regional Office, in collaboration with partners, will provide assistance for the development of collaborative frameworks and mechanisms for integrated management of TB and its most common comorbidities (by 2018).

1E Management of latent TB infection and preventive treatment of people at high risk, and vaccination against TB

1E.1 Member States will adopt and adapt their national policies to align with the most up-to-date WHO recommendations on diagnosis and treatment of latent TB infection for high-risk populations (by the end of 2017).

1E.2 Member States will ensure that WHO policy recommendations on bacillus Calmette-Guérin (BCG) vaccination for infants are implemented and BCG revaccination is discontinued (immediately).

1E.3 Member States will ensure that people accessing harm-reduction services for drug misuse will be provided the option of TB preventive therapy (by 2016).

2. Bold policies and supportive systems

2A   Political commitment with adequate resources, including universal health coverage policy

2A.1 Member States will improve leadership and participatory governance for TB control, including implementation of whole-of-government and whole-of-society approaches in line with Health 2020 *(27)*. At the same time, the Regional Office will provide technical assistance to Member States to ensure improved, accountable and effective central coordination of TB control and implementation of results-based management approaches to improve performance (by 2020).

2A.2 Member States, with the assistance of the Regional Office and partners, will ensure the rational use of existing financial and other resources, identification of gaps and mobilization of additional resources to ensure sustainable and effective prevention and control of TB (by 2018).

2A.3 Member States will ensure universal coverage of TB services through the provision of a full range of high-quality TB prevention, diagnosis, treatment and care, free of charge and with equitable access to all in need, especially the most vulnerable populations (by 2020).

2A.4 The Regional Office and partners will assist Member States in updating their national TB plans in line with the TB action plan, including updated guidance on new tools and interventions (including e-health). The plans will include organograms endorsed by health systems and NTPs, with explicit roles and responsibilities (executive decrees and administrative orders), lines of authority and operational plans up to provider level. They will take into account health systems and financial reforms undertaken during 2011–2015, social determinants of TB and ethical and human rights concerns, and will also ensure that the role of primary health care, prison services, TB hospitals and general hospitals, nongovernmental organizations and private services are included, with the aim of improving public–private partnerships (by the end of 2016).

2A.5 Member States will ensure that external reviews of their national TB programmes/interventions are undertaken every 3–5 years by the Regional Office and other partners, with the involvement of civil society organizations and communities (ongoing activity).

2B   Health-systems strengthening in all functions, including well aligned financing mechanisms for TB and human resources

2B.1 The Regional Office, in collaboration with partners, will assist Member States in identifying and addressing gaps and will provide technical assistance to improve institutional capacity for all functions of TB programmes in the health system (stewardship/governance, financing, service delivery and resource generation) towards universal health coverage and rational use of hospital care (as soon as possible).

2B.2 Member States will ensure that national TB programmes have the institutional capacity to develop, implement, analyse and adapt the TB policy, and will manage and allocate resources towards ensuring effective universal access to treatment. Health authorities will also engage the TB provider network and/or programme in health systems reform initiatives (by 2020).

2B.3 The Regional Office and partners, in collaboration with Member States, will conduct an in-depth health financing review for more effective TB prevention and control. This relates to analysis of current resources available for TB prevention and control interventions at regional level, including the organization of funding flows, to identify: sources of fragmentation; potentially misaligned provider payment incentives associated with different types of TB intervention; formal or informal out-of-pocket payments (catastrophic costs) that hinder access to care; and other financial (such as levels of insurance) and non-financial barriers to access, as well as the role of private and public providers and financial incentives in place for each. Recommendations for measures to improve health-financing reform in line with defined service-delivery strategies will be made (by the end of 2016).

2B.4 The Regional Office will provide technical assistance to Member States to develop sustainability plans to increase domestic funding and shared responsibility schemes for TB control and care in countries that have received donor funding (immediately).

2B.5 The Regional Office will support the development of performance assessment frameworks for national TB control programmes, including evaluation of cost–efficiency and effectiveness (by 2017).

2B.6 Member States will revise and implement strategic plans for development of the human resources required to adapt and subsequently implement the TB action plan at national level. These plans will include human resources policies, finance, education, leadership, job descriptions and workload assessment, and will determine staff needs, supervision and monitoring, performance-based

assessment and remuneration (both monetary and non-monetary) of staff, in line with plans for national health systems (by the end of 2017).

2B.7 The Regional Office, in collaboration with the European Tuberculosis Laboratory Initiative and the Global Laboratory Initiative, will support the Tuberculosis Supranational Reference Laboratories Network and Member States in building sustainable human resources capacity. This will be done through regular country visits to monitor the performance of laboratory networks and through the provision of technical assistance (on, for example, exchange of data, information and samples) both in-country and through internships of 1–2 months in their supranational reference laboratories (by 2018).

2B.8 Member States will continue to ensure supervised and continuous training (including on infection control), increased application of e-learning methods, and coaching and support for health care staff in case-detection and scaling-up treatment of TB, M/XDR-TB and TB/HIV patients (by 2016).

2B.9 The Regional Office and partners (such as WHO collaborating centres and NTPs) will support the building of human resources capacity. Human resources capacity-building will be carried out through: (i) regular country visits to monitor the performance of national and subnational health authorities and primary health care providers involved in TB prevention, control and treatment; and (ii) the provision of in-country technical assistance (through, for example programme management, the efficient use of resources, operational research and the application of new diagnostic and programme tools) (ongoing activity).

2B.10 In coordination with the WHO Collaborating Centre on Prevention and Control of Tuberculosis in Prisons in Baku, Azerbaijan, the Regional Office will assist Member States in improving TB control in penitentiary services by supporting training activities facilitated by the collaborating centre (immediately).

2C Regulatory frameworks for case-based surveillance, strengthening vital registration, quality and rational use of medicines, and pharmacovigilance

2C.1 The Regional Office, with WHO headquarters, partners and Member States, will develop a minimum set of social determinant variables to be included in routine surveillance at country level. This will enable the monitoring of upstream and downstream risk factors for TB disease and treatment outcomes (by 2016).

2C.2 The Regional Office will provide technical assistance

for subregional workshops on surveillance standards and benchmarks, and the development of country plans for implementation at national level (immediately).

2C.3 All Member States will implement the new standards and benchmarks for the TB surveillance system (immediately).

2C.4 Member States will implement the WHO-recommended TB case definitions and reporting framework to ensure the categorization of TB cases to facilitate appropriate treatment and cohort reporting (as soon as possible and not later than 2016).

2C.5 Member States, with the support of the Regional Office, will facilitate the establishment of laboratory information management systems (by 2017).

2C.6 Member States will establish interoperable links between different sources of data useful for TB surveillance, including demographic and vital statistics, clinical management, geopositioning, and laboratory and drug management systems (by 2020).

2C.7 The Regional Office will support Member States and other partners with data collection to assist in the reliable estimation of drug needs (immediately).

2C.8 The Regional Office, partners and Member States, in their respective roles, will ensure the use of quality-assured (WHO-prequalified and stringent drug regulatory authority-approved) drugs and will request fast-track registration of such drugs (by 2017).

2C.9 The Regional Office and partners will conduct a gap analysis of pharmaceutical legislation and regulations (as a follow up to that conducted under the consolidated action plan) and facilitate their update, revision and improvement (by 2019).

2C.10 The Regional Office will assist Member States in developing procedures for the procurement of medical supplies (with an emphasis on quality assurance through strengthened regulatory authorities) including, but not limited to, paediatric TB diagnostics and treatment (drug formulations), and limiting the availability of new drugs on the free market (over the counter) without a TB-indicated prescription sale (by 2017).

2C.11 The Regional Office and partners will engage countries in the WHO Good Governance for Medicines programme and pharmacovigilance (immediately).

2C.12 Member States will ensure continued capacity-building in planning, procurement and supply management of anti-TB medicines at all levels of the health care system in compliance with WHO recommendations (immediately).

2C.13 The Regional Office will deliver guidance to Member States on a continuous basis to develop their legal frameworks at national and subnational levels for compassionate use of medicines under development (ongoing activity).

2C.14 Member States will strengthen or establish the country-level mechanism to routinely collect data on adverse drug events for patients on new and novel regimens (by the end of 2016).

2C.15 The Regional Office, in collaboration with other partners and Member States, will establish a sufficiently resourced data repository on drug-related adverse events (by the end of 2016).

2D Airborne infection control, including regulated administrative, engineering and personal protection measures in all relevant health care facilities and congregate settings

2D.1 Member States will ensure that all health care facilities delivering services to TB or suspected TB patients implement sound infection control standard operating procedures, including individual respiratory protection programmes (by the end of 2016).

2D.2 Governments in high-priority countries will ensure that environmental (engineering) preventive measures are available in high-risk facilities and congregate settings (by 2016).

2E Community systems and civil society engagement

2E.1 Member States and WHO will systematically include representatives of affected communities and civil society in national and regional TB programme reviews, design, planning, implementation and monitoring, and assessments of quality of services (immediately).

2E.2 To achieve systematic involvement and engagement of civil society and people affected by TB, Member States will regularly assist and coordinate with local civil society organizations and community representatives in devising and implementing effective plans in line with NTP policies and priorities. This may include subcontracting activities when civil society and community organizations have a comparative advantage, such as in case-finding and social support (ongoing activity).

2E.3 High-priority countries will review their advocacy, communication and social mobilization strategy with civil society and communities and develop community systems-strengthening plans to increase knowledge of, and access to, improved health service delivery. This includes increasing the capacity of community organizations, strengthening infrastructures and systems, building partnerships and developing sustainable financing solutions. These plans should be implemented and fully funded by 2016.

2E.4 Member States, recognizing the special value, contribution and support that patient groups can provide, will assist and support the creation, development and involvement of such groups wherever feasible (as soon as possible and not later than 2020).

2E.5 Member States will continue to develop innovative communication strategies with affected communities, religious and community leaders and civil society, making use of the Internet and other media (TV, radio, press, social media) to reduce TB-related stigma (ongoing activity).

2E.6 The Regional Office will strengthen involvement of, and foster collaboration among, national and international partners and private providers to raise awareness about TB, advocate resource mobilization and catalyse an exchange of best practices regarding TB and M/XDR-TB prevention and care through the RCC-TB (ongoing activity).

2F Social protection, poverty alleviation and actions on other determinants of TB, such as migration and prisons

2F.1 Member States will measure the occurrence of catastrophic costs to patients and their households due to TB, in compliance with WHO guidelines (by 2019).

2F.2 Member States will develop TB-specific mechanisms of social protection, with the allocation of relevant funds (by 2017).

2F.3 The Regional Office, in collaboration with partners, will provide technical assistance for developing effective social protection mechanisms for TB patients and their families (by 2017).

2F.4 Member States will ensure effective mechanisms for the promotion and protection of human rights and ethical principles as part of social protection measures, including capacity-building, legal support and accountability mechanisms (ongoing activity).

2F.5 The Regional Office and partners will work with Member States in an interdepartmental and intersectoral approach to explore a legal mechanism for cross-border TB control and care (by 2017) (see also 1C.9).

2F.6 Member States, in collaboration with civil society organizations, will assist with cross-border TB care for migrant communities to help increase awareness of TB and knowledge of local health services so that symptomatic individuals refer and enrol themselves appropriately for treatment in the host country (ongoing activity).

3. Intensified research and innovation

3A   Discovery, development and rapid uptake of new tools, interventions and strategies

3A.1   The Regional Office, in close consultation with WHO headquarters, will coordinate the development/ establishment of the European Tuberculosis Research Initiative (by 2017), under which the Regional Office and key partners will work with Member States to:

- identify needs, capacities and gaps (financial support for basic research, operational research, language/translation support and so on);
- develop research agendas at regional and national levels;
- develop a platform for sharing new research and study results (on, for example, equity, indicators and costs of non-action) and create research networks;
- map collaboration among major research institutes and identify new areas for cooperation;
- motivate funding agencies to link with civil society organizations for research advocacy; and
- serve to provide the evidence base for policy and practice for TB prevention, control and care.

3A.2   Member States will identify key partners, such as nongovernmental organizations and institutions, to carry out respective research agendas on the basis of sound methodologies and ethical principles (by 2017).

3A.3   The Regional Office will work with all Member States and regional partners to promote and secure funding for national research priority areas and agendas (ongoing activity).

3A.4   The Regional Office will assist Member States in assessing and ensuring that adequate research ethics mechanisms are in place in key institutions and partner organizations that carry out national research agendas (ongoing activity).

3A.5   The Regional Office, working with Member States, will facilitate research to support the development of new tools, including those for TB treatment regimens, and will help Member States to hold sound clinical trials on a continuous basis and report on progress through the European Tuberculosis Research Initiative (ongoing activity).

3A.6   The Regional Office and partners will advocate the continuous involvement of European research institutes in the development of new diagnostic tools, medicines and other treatment modalities, vaccines, research on basic mechanisms of drug resistance and so on (ongoing activity).

3A.7   The Regional Office and partners will advocate for the mobilization of regional resources from, for example, the European Union, and national resources, including planning and budgeting tools aimed at developing new technologies (ongoing activity).

3B   Research to optimize implementation and impact, and promote innovations

3B.1   The Regional Office will provide guidance and technical assistance to Member States to develop operational research priorities within national research platforms and corresponding social science research on health-seeking behaviour, adherence to treatment, and stigma and discrimination to inform policies and practices (ongoing activity).

3B.2   Member States and key working partners will develop operational research plans that cover quantitative and qualitative research reflecting priority areas and coordinate with existing research plans for consideration by national and international funding sources, including the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). Research generated under these plans should serve as the basis for improving programme performance (by 2016).

3B.3   The Regional Office and key partners will assist Member States in building capacity for research training and translating research into action (ongoing activity).

3B.4   Member States will ensure the results of operational research and other studies are included in the development of TB control policies (ongoing activity).

3B.5   The Regional Office, in collaboration with partners, will continuously document best practices in the implementation of models of care and patient support (including inpatient, outpatient, home/ community-based models of care, financing/ avoidance of catastrophic costs, and prevention) in different settings and will share these practices with Member States (ongoing activity).

Regional analysis of strengths, weaknesses, opportunities and threats in relation to the TB action plan for the WHO European Region 2016–2020

Strengths

Strategy

- The TB action plan 2016–2020 is based on lessons learnt from the consolidated action plan to prevent and combat M/XDR-TB in the WHO European Region 2011–2015.
- The action plan is aligned with the global End TB Strategy *(25)*, Health 2020 *(27)*, the framework action plan to fight TB in the European Union *(28)* and the framework towards TB elimination in low-incidence countries *(29)*.
- The RCC-TB has been established as an interactive platform for exchange of information on activities and joint action with regard to M/XDR-TB responses.
- Strategic directions are crosscutting and are designed to safeguard the values of Health 2020.
- The strategic directions aim to strengthen the health systems environment, support a multisectoral approach involving all possible stakeholders (including civil society and community organizations), promote ambitious resource mobilization, foster innovative tools and interventions, and safeguard human rights.
- Documented best practices are used to support the strategic directions.

Targets

- The target of 25% reduction in TB incidence is more ambitious than the global target.
- The target of 75% success rate in treatment of MDR-TB is ambitious, but realistic.
- Systematic screening of contacts and high-risk groups has explicitly been included in the interventions.

Case-finding and diagnosis

- MDR-TB detection numbers, especially in central Asia, have increased significantly (from 28 000 cases in 2009 to 45 000 in 2014).
- Ninety-one per cent of TB/HIV patients were detected in 2014.
- Eleven high-priority countries have achieved 90% DST coverage.

- The use of Xpert MTB/RIF was reported in 17 of 18 high-priority countries in 2014.
- All countries have established at least one central reference laboratory that is quality assured by a supranational reference laboratory.
- Laboratory networks in many countries (such as Uzbekistan) have been strengthened.
- The European Tuberculosis Laboratory Initiative has been established.

Treatment

- Treatment enrolment of MDR-TB has increased from 60% before the MDR-TB action plan to 113% after.
- Treatment default rates are falling (although inconsistently).
- Antiretroviral therapy and co-trimoxazole coverage for TB/HIV coinfected patients increased, reaching 51% and 57% respectively in 2014.

Drug management

- Reported stock-out decreased from eight countries in 2011 to five in 2014.
- There is increased emphasis on pharmacovigilance (which allows the study of adverse treatment events), especially in drug-resistant patients, to achieve better clinical management of adverse events.

Information systems

- Almost all countries have introduced case-based surveillance.
- Forty-one of the 53 Member States maintain an electronic case-based data-management system for MDR-TB at national level.

Equitable access to quality treatment and continuity of care

- Universal access to diagnosis, treatment and uninterrupted drug supply, including for vulnerable and hard-to-reach populations and children, is being planned.
- There is growing acceptance of ambulatory care from day one.

- Disruption to care continuity for cross-border migrants has been recognized and will be addressed.
- Interventions are being considered for patients who fail treatment and for whom all treatment options are exhausted.
- Civil society is included in many interventions.

Political commitment and health financing
- A number of high-priority and low-incidence countries have asked for an independent review of their national programmes to improve performance.
- Civilian and prison sectors are being linked.
- Greater emphasis on ambulatory care from day one contributes to cost savings (as has been seen in countries such as Armenia).

Infection control
- Fourteen of the 18 high-priority countries had endorsed a TB infection control plan by 2014.

Research
- There is now greater emphasis on research and innovation.
- Prioritization of key interventions and target groups should be based on epidemiological and health systems assessment in each setting, guided by data analysis and operational research.

Weaknesses

Strategy
- The suggested decline of 19% annually may be overoptimistic.
- Integrated TB and HIV services with central coordination have not yet been achieved in all countries.

Targets
- The long-term vision is dualistic: an end to the TB epidemic is the final target, and zero affected families facing catastrophic costs due to TB is a target on the road towards ending the TB epidemic that will be difficult to measure. If it cannot be measured, it should not be used as a target.

Case-finding and diagnosis
- The overall decline in the TB epidemic is only 5% annually.
- Although paying attention to screening for latent infections in risk groups is a good intervention, the impact of screening on transmission and incidence and its cost–effectiveness, especially when screening is not well targeted, is not clearly understood.
- There is still a considerable gap in second-line drugs DST coverage in most high-priority countries, with only 64% of MDR-TB patients having had DST for second-line drugs in 2014.

- HIV coinfection among TB patients increased from 3.4% in 2008 to 8.0% in 2014.
- Some laboratories have still not been quality assured by a national reference laboratory.
- Some countries still lack algorithms for the use of rapid diagnostic tools, especially for hard-to-reach populations.
- Laboratory maintenance remains an overlooked aspect of TB plans in several countries.

Treatment
- Despite significant progress in MDR-TB detection, treatment challenges compromise gains: the average treatment success rate in the 2012 MDR-TB cohort was only 49%.

Drug management
- Only two countries in the Region take part in the WHO Good Governance for Medicines programme.
- A sufficiently resourced data repository of drug-related adverse events does not yet exist.

Information systems
- Surveillance standards and benchmarks still have to be developed.
- Vital registration is weak in many countries.

Equitable access to quality treatment and continuum of care
- Only a limited scale-up of access for vulnerable groups has been achieved in most high-priority countries.
- Not all patients can receive prequalified TB medicines due to legislation prohibiting access.
- Growing inequity with insufficient social protection will lead to an increase in the TB burden.
- The lack of an adequate mechanism means that cross-border migration leads to interruption of treatment.

Infection control
- Although considerable progress in infection control implementation has been achieved, the risk for airborne TB transmission in congregate settings (such as HIV facilities and prisons) still needs to be addressed in some countries.

Health financing
- Overreliance on donor funds in a number of high-priority countries continues to lead to insufficient (and even decreasing) domestic funding.

Research
- Not all countries have a research agenda.
- Implementation of recommendations resulting from (operational) studies in many countries is slow or does not take place at all.

Opportunities

Case-finding and diagnosis
- The involvement of civil society and communities may promote a better public health response.
- Guidelines and algorithms for the use of new diagnostic tools are being developed with help from WHO and partners.
- New promising diagnostic tools are in the pipeline.

Treatment
- Shorter treatment regimens may be advised in the near future, improving adherence.
- A mechanism for cross-border migration may improve continuity of care and monitoring of migrant cases.

Information systems
- Modern information technology allows for linkage of different sources of data useful for TB surveillance, including demographic and vital statistics, clinical management, geopositioning, and laboratory and drug management systems.

Political commitment and health financing
- The new GFATM funding model helps governments to develop sustainable plans to increase domestic funding.
- Financial reforms (in countries such as Armenia) have led to a more rational infrastructure, improved TB control, greater satisfaction for patients and providers, and money being saved – this may stimulate political commitment.
- If domestic resources remain insufficient through the GFATM funding model, countries will be encouraged to search for alternative sources of funding.

Human resources
- Capacity-building with competent staff would benefit from new technologies such as e-learning.

Community strengthening
- Patient groups can provide good feedback on TB programme performance. The creation of such groups will increase knowledge and access to improved health service delivery.

Research
- The European Tuberculosis Research Initiative has been established.
- The Regional Office has prepared a list of research priorities.
- National research plans are being linked to national TB and health research plans.
- Progress has been made globally in the development of pre- and post-exposure vaccines.

Threats

Strategy
- Baseline data from 1990 (before the introduction of directly observed treatment, short-course) are not documented in several countries.
- In low-incidence countries and/or in a declining epidemic, the TB problem becomes less visible, meaning political commitment may be difficult to maintain. This can lead to insufficient financing, an inadequate public health response, diminishing public awareness and, eventually, dismantling of TB programmes.

Case-finding and diagnosis
- The TB burden in the European Region is unequally distributed among countries: 85% of TB cases are found in 18 high-priority countries. Low visibility in low-incidence countries may lead to diminishing political commitment, with all its sequelae.
- MDR-TB is a major challenge. Prevalence is rising, with an increase from 10% to 18% among new TB cases and from 38% to 46% among re-treatment cases in the last seven years.
- A quarter of MDR-TB patients globally are located in the European Region.
- Low-incidence countries are experiencing delays in case-detection.
- TB is the leading cause of death among PLHIV, while rates of TB/HIV confection are increasing.
- Comorbidity with noncommunicable diseases (such as diabetes) is a risk factor for an increase in the TB burden.

Drug management
- Funding of medicines is inadequate.
- Regulatory frameworks may prohibit the importation of prequalified non-registered drugs, which endangers continuity of care and increases the chance of the use of drugs of uncertain quality that may contribute to further development of drug-resistant TB.

Infection control
- Transmission in institutions that lack adequate infection control due to insufficient knowledge continues in low-incidence countries.

Health financing
- A declining epidemic, especially in low-burden countries, may lead to inadequate funding.
- Continuation of the bed-based financing scheme may prove to be too costly and absorb funds that could be used in a better way.
- Unexpected financial crises pose risks to ongoing financing.

References

1. Global tuberculosis report 2015. Geneva: World Health Organization; 2015 (http://www.who.int/tb/publications/global_report/en/, accessed 10 May 2016).

2. Use of high burden country lists for TB by WHO in the post-2015 era. Geneva: World Health Organization; 2015 (http://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020.pdf, accessed 23 May 2016).

3. European Centre for Disease Prevention and Control, WHO Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2016. Stockholm: European Centre for Disease Prevention and Control; 2016 (http://www.euro.who.int/__data/assets/pdf_file/0012/304104/ecdc-tuberculosis-surveillance-monitoring-Europe-2016.pdf, accessed 23 May 2016).

4. Roadmap to prevent and combat drug-resistant tuberculosis. Copenhagen: WHO Regional Office for Europe; 2011 (http://www.euro.who.int/__data/assets/pdf_file/0014/152015/e95786.pdf, accessed 10 May 2016).

5. Multidrug and extensively drug-resistant TB (M/XDR-TB). 2010 global report on surveillance and response. Geneva: World Health Organization; 2010 (http://whqlibdoc.who.int/publications/2010/9789241599191_eng.pdf, accessed 10 May 2016).

6. Zalutskaya A, Wijkander M, Jureen P. Multidrug-resistant *Myobacterium tuberculosis* caused by the Beijing genotype and a specific T1 genotype clone (SIT No. 266) is widely transmitted in Minsk. Intl J Mycobacteriol. 2013;2(4):194–8. doi:10.1016/j.ijmyco.2013.08.001.

7. Nathanson E, Gupta R, Huamani P, Leimane V, Pasechnikov AD, Tupasi TE et al. Adverse events in the treatment of multidrug-resistant tuberculosis: results from the DOTS-Plus initiative. Int J Tuberc Lung Dis. 2004;8(11):1382–4.

8. Yee D, Valiquette C, Pelletier M, Parisien I, Rocher I, Menzies D. Incidence of serious side effects from first-line antituberculosis drugs among patients treated for active tuberculosis. Am J Respir Crit Care Med. 2003;167(11):1472–7.

9. Coninx R, Mathieu C, Debacker M, Mirzoev F, Ismaelov A, de Haller R et al. First-line tuberculosis therapy and drug-resistant *Mycobacterium tuberculosis* in prisons. Lancet 1999;353(9157):969–73.

10. Mitnick C, Bayona J, Palacios E, Shin S, Furin J, Alcántara F et al. Community-based therapy for multidrug-resistant tuberculosis in Lima, Peru. N Engl J Med. 2003;348(2):119–28.

11. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bitstream/10665/130918/1/9789241548809_eng.pdf?ua=1&ua=1, accessed 24 May 2016).

12. Falzon D, Jaramillo E, Wares F, Zignol M, Floyd K, Raviglione MC et al. Universal access to care for multidrug-resistant tuberculosis: an analysis of surveillance data. Lancet Infect Dis. 2013;3(8):690–7.

13. Shean K, Streicher E, Pieterson E, Symons G, van Zyl Smit R, Theron G et al. Drug-associated adverse events and their relationship with outcomes in patients receiving treatment for extensively drug-resistant tuberculosis in South Africa. PLoS One 2013;8(5):e63057. doi:10.1371/journal.pone.0063057.

14. Pietersen E, Ignatius E, Streicher EM, Mastrapa B, Padanilam X, Pooran A et al. Long-term outcomes of patients with extensively drug-resistant tuberculosis in South Africa: a cohort study. Lancet 2014;383(9924):1230–9.

15. Zignol M, Dara M, Dean AS, Falzon D, Dadu A, Kremer K et al. Drug-resistant tuberculosis in the WHO European Region: an analysis of surveillance data. Drug Resist Updat. 2014;16(6):108–15.

16. The Berlin Declaration on Tuberculosis. Copenhagen: WHO Regional Office for Europe; 2007 (http://www.euro.who.int/__data/assets/pdf_file/0008/68183/E90833.pdf, accessed 10 May 2016).

17. Global tuberculosis control and patient care. A ministerial meeting of high M/XDR-TB burden countries, Beijing, China, 1–3 April 2009. Geneva:

World Health Organization; 2009 (http://www.who.int/tb_beijingmeeting/en/, accessed 10 May 2016).

18. Global Plan to stop TB 2011–2015. Geneva: World Health Organization; 2010 (http://apps.who.int/iris/bitstream/10665/44437/1/9789241500340_eng.pdf, accessed 10 May 2016).

19. Regional Committee for Europe: progress report, 65th session. Copenhagen: WHO Regional Office for Europe; 2015 (http://www.euro.who.int/__data/assets/pdf_file/0007/283372/65wd12e_ProgressReports_150501.pdf, accessed 23 May 2016).

20. Green Light Committee initiative. Scaling up the global fight against MDR-TB. Annual report 2009. Geneva: World Health Organization; 2010 (http://whqlibdoc.who.int/hq/2010/WHO_HTM_TB_2010.14_eng.pdf, accessed 10 May 2016).

21. Blasi F, Dara M, van der Werf MJ, Migliori GB. Supporting TB clinicians managing difficult cases: the ERS/WHO Consilium. Eur Respir J. 2013;41(3):491–4.

22. European tuberculosis laboratory initiative [website]. Copenhagen: WHO Regional Office for Europe; 2016 (http://www.euro.who.int/en/what-we-do/health-topics/communicable-diseases/tuberculosis/activities/european-tuberculosis-laboratory-initiative, accessed 10 May 2016).

23. Terms of reference for RCC-TB [website]. Copenhagen: WHO Regional Office for Europe; 2016 (http://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/activities/regional-collaborating-committee-on-tuberculosis-control-and-care-rcc-tb/terms-of-reference-for-rcc-tb, accessed 10 May 2016).

24. Skrahina A, Hurevich H, Zalutskaya A, Sahalchyk E, Astrauko A, Hoffner S et al. Multidrug-resistant tuberculosis in Belarus: the size of the problem and associated risk factors. Bull World Health Organ. 2013;91(1):36–45 (http://www.who.int/bulletin/volumes/91/1/12-104588.pdf, accessed 23 May 2016).

25. The end TB strategy. Global strategy and targets for tuberculosis prevention, care and control after 2015. Geneva: World Health Organization; 2014 (http://www.who.int/tb/strategy/End_TB_Strategy.pdf?ua=1, accessed 23 May 2016).

26. Sixty-seventh World Health Assembly. Resolutions and decisions. Geneva: World Health Organization; 2014 (http://apps.who.int/gb/ebwha/pdf_files/WHA67-REC1/A67_2014_REC1-en.pdf#page=1, accessed 23 May 2016).

27. Health 2020: a European policy framework supporting action across government and society for health and well-being. Copenhagen: WHO Regional Office for Europe; 2012 (EUR/RC62/9; http://www.euro.who.int/en/health-topics/health-policy/health-2020-the-european-policy-for-health-and-well-being, accessed 10 May 2016).

28. Framework action plan to fight tuberculosis in the European Union. Stockholm: European Centre for Disease Prevention and Control; 2008 (http://ecdc.europa.eu/en/publications/Publications/0803_SPR_TB_Action_plan.pdf, accessed 10 May 2016).

29. Framework towards tuberculosis elimination in low-incidence countries. Geneva: World Health Organization; 2014 (http://www.who.int/tb/publications/elimination_framework/en/, accessed 10 May 2016).

30. Cegielski JP, Dalton T, Yagui M, Wattanaamornkiet W, Volchenkov GV, Via LE et al. Extensive drug resistance acquired during treatment of multidrug-resistant tuberculosis. Clin Infect Dis. 2014;59(8):1049–63. doi:10.1093/cid/ciu572.

31. Lange C, Abubakar I, Alffenaar JW, Bothamley G, Caminero JA, Carvalho AC et al. Management of patients with multidrug-resistant/extensively drug-resistant tuberculosis in Europe: a TBNET consensus statement. Eur Respir J. 2014;44(1):23–63.

32. Dara M, Mkrtchyan Z, Ghukasyan G, editors. Extensive review of TB prevention, care and control services in Armenia. Copenhagen: WHO Regional Office for Europe; 2012 (http://www.euro.who.int/__data/assets/pdf_file/0007/160864/e96506.pdf, accessed 10 May 2016).

33. Dara M, Gozalov O, Javadli O, Turusbekova N, editors. Review of tuberculosis prevention, control and care in Azerbaijan. Copenhagen: WHO Regional Office for Europe; 2012 (http://www.euro.who.int/__data/assets/pdf_file/0005/193703/NTP-AZE_review_report_ENG_final-4.pdf?ua=1, accessed 10 May 2016).

34. de Colombani P, editor. Review of the national tuberculosis programme in Belarus. Copenhagen: WHO Regional Office for Europe; 2012 (http://www.euro.who.int/__data/assets/pdf_file/0003/170337/Review-of-the-National-Tuberculosis-Programme-in-Belarus.pdf, accessed 10 May 2016).

35. de Colombani P, Ahmedov S, Blondal K, Ciobanu S, Dadu A, de Lussigny S et al. Review of the national tuberculosis programme in the Republic of Moldova. Copenhagen: WHO Regional Office for Europe; 2013 (http://www.euro.who.int/en/countries/republic-of-moldova/publications2/review-of-the-national-tuberculosis-programme-in-the-republic-of-moldova, accessed 10 May 2016).

36. de Colombani P, Veen J, editors. Review of the national tuberculosis programme in Ukraine. Copenhagen: WHO Regional Office for Europe; 2011 (http://www.euro.who.int/en/publications/abstracts/review-of-the-national-tuberculosis-programme-in-ukraine-2011, accessed 10 May 2016).

37. Nodieva A, Jansone I, Broka L, Pole I, Skenders G, Baumanis V. Recent nosocomial transmission and genotypes of multidrug-resistant *Mycobacterium tuberculosis*. Int J Tuberc Lung Dis. 2010;14(4):427–33.

38. Bassili A, Fitzpatrick C, Qadeer E, Fatima R, Flod K, Jaramillo E. A systematic review of the effectiveness of hospital- and ambulatory-based management of multidrug-resistant tuberculosis. Am J Trop Med Hyg. 2013;89(2):271–80.

39. Evans CAC. GeneXpert – a game-changer for tuberculosis control? PLoS Med. 2011; 8(7):e1001064–e1001064.

40. Drobniewski FA, Hoffner S, Rusch-Gerdes S, Skenders G, Thomsen V, WHO European Laboratory Strengthening Task Force. Recommended standards for modern tuberculosis laboratory services in Europe. Eur Respir J. 2006;28(5):903–9.

41. Alikhanova N, Akhundova I, Seyfaddinova M, Mammadbayov E, Mirtskulava V, Rüsch-Gerdes S et al. First national survey of anti-tuberculosis drug resistance in Azerbaijan and risk factors analysis. Public Health Action 2014;4(Suppl. 2):S17–S23. doi:10.5588/pha.14.0049.

42. Multidrug-resistant tuberculosis in Turkmenistan: results of nationwide survey, 2012 to 2013. Copenhagen: WHO Regional Office for Europe; 2015 (http://www.euro.who.int/__data/assets/pdf_file/0005/282884/Multidrug-resistant-tuberculosis-Turkmenistan-results-nationwide-survey_REV1.pdf, accessed 10 May 2016).

43. Ulmasova DJ, Uzakova G, Tillyashayhov MN, Turaev L, van Gemert W, Hoffmann H et al. Multidrug-resistant tuberculosis in Uzbekistan: results of a nationwide survey, 2010 to 2011. Euro Surveill. 2013;18(42):pii=20609. doi: http://dx.doi.org/10.2807/1560-7917.ES2013.18.42.20609.

44. Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. Soc Sci Med. 2009;68(12):2240–6.

45. Dara M, de Colombani P, Petrova-Benedict R, Centis R, Zellweger JP, Sandgren A et al. The minimum package for cross-border TB control and care in the WHO European Region: a Wolfheze consensus statement. Eur Respir J. 2012;40(5):1081–90 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3485571/, accessed 23 May 2016).

46. Dara M, Chadha SS, Vinkeles Melchers NV, van den Hombergh J, Gurbanova E, Al-Darraji H et al. Time to act to prevent and control tuberculosis among inmates. Int J Tuberc Lung Dis. 2013;17(1):4–5 (http://www.euro.who.int/__data/assets/pdf_file/0007/185155/Time-to-act-to-prevent-and-control-tuberculosis-among-inmates.pdf, accessed 23 May 2016).

47. Tuberculosis, ethics and human rights. Report of a regional workshop. Copenhagen: WHO Regional Office for Europe; 2014 (http://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/publications/2014/regional-workshop-on-tuberculosis,-ethics-and-human-rights, accessed 10 May 2016).

48. Viiklepp P, de Colombani P, Kurbatova A, Sandgren A, Lonnroth K. Collaborative action on tuberculosis and alcohol abuse in Estonia. First report of a demonstration project. Copenhagen: WHO Regional Office for Europe; 2013 (http://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/publications/2013/collaborative-action-on-tuberculosis-and-alcohol-abuse-in-estonia, accessed 10 May 2016).

49. Acosta CD, Rusovich V, Harries AD, Ahmedov S, van den Boom M, Dara M. A new roadmap for childhood tuberculosis. Lancet Glob Health 2014;2(1):e15–7.

50. Stop TB Partnership Childhood TB Subgroup. Guidance for national tuberculosis programmes on the management of tuberculosis in children. Int J Tuberc Lung Dis. 2006;10(11):1205–11.

51. Bone A. A human rights approach to tuberculosis. Geneva: World Health Organization; 2001 (http://www.who.int/hhr/information/A%20Human%20Rights%20Approach%20to%20Tuberculosis.pdf, accessed 10 May 2016).

52. Heldal E, Kuyvenhoven JV, Wares F, Migliori GB, Ditiu L, Fernandez de la Hoz K et al. Diagnosis and treatment of tuberculosis in undocumented migrants in low- or intermediate-incidence countries. Int J Tuberc Lung Dis. 2008;12(8):878–88.

53. van der Werf MJ, Hollo V, Noori T. Is tuberculosis crossing borders at the eastern boundary of the European Union? Eur J Public Health 2013;23(6):1058–63.

54. Gorbunov AV, Kochetkova EI. [Organization of detection of patients with tuberculosis in Moscow.] Problemy Tuberkuleza i Bolezneĭ Legkikh 2005;(8):18–22 (in Russian).

55. Dara M, Acosta CD. Tuberculosis prevention and control in prisons: do we know enough? Int J Tuberc Lung Dis. 2014;18(7):758–9.

56. Dara M, Acosta CD. Best practices in prevention, control and care for drug-resistant tuberculosis. Copenhagen: WHO Regional Office for Europe; 2013 (http://www.euro.who.int/__data/assets/pdf_file/0020/216650/Best-practices-in-prevention,control-and-care-for-drugresistant-tuberculosis-Eng.pdf?ua=1, accessed 10 May 2016).

57. Corbett EL, Watt CJ, Walker N, Maher D, Williams BG, Raviglione MC et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med. 2003;163(9):1009–21.

58. Global report. UNAIDS report on the global AIDS epidemic 2013. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2013 (http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf, accessed 24 May 2016).

59. HIV/AIDS in Europe and central Asia. Progress report 2011. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2012 (http://www.euro.who.int/__data/assets/pdf_file/0015/240045/Progress-report-2011,-HIV-AIDS-in-Europe-and-central-Asia.pdf?ua=1, accessed 24 May 2016).

60. Atun R, Weil DE, Eang MT, Mwakyusa D. Health-system strengthening and tuberculosis control. Lancet 2010;375(9732):2169–78.

61. The role of surgery in the treatment of pulmonary TB and multidrug- and extensively drug-resistant TB. Copenhagen: WHO Regional Office for Europe; 2014 (http://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/publications/2014/the-role-of-surgery-in-the-treatment-of-pulmonary-tb-and-multidrug-and-extensively-drug-resistant-tb, accessed 10 May 2016).

Annex 1. Global End TB Strategy

Global End TB Strategy				
VISION	**A world free of tuberculosis** – zero deaths, disease and suffering due to tuberculosis			
GOAL	**End the global tuberculosis epidemic**			
INDICATORS	**MILESTONES**		**TARGETS**	
	2020	**2025**	**SDG 2030**[a]	**END TB 2035**
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20% (<85/100 000)	50% (<55/100 000)	80% (<20/100 000)	90% (<10/100 000)
TB-affected families facing catastrophic costs due to TB (%)	Zero	Zero	Zero	Zero

PRINCIPLES

1. *Government stewardship and accountability, with monitoring and evaluation*
2. *Strong coalition with civil society organizations and communities*
3. *Protection and promotion of human rights, ethics and equity*
4. *Adaptation of the strategy and targets at country level, with global collaboration*

PILLARS AND COMPONENTS

1. INTEGRATED PATIENT-CENTRED CARE AND PREVENTION
A. Early diagnosis of tuberculosis including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
B. Treatment of all people with tuberculosis including drug-resistant tuberculosis, and patient support
C. Collaborative tuberculosis/HIV activities, and management of comorbidities
D. Preventive treatment of persons at high risk, and vaccination against tuberculosis

2. BOLD POLICIES AND SUPPORTIVE SYSTEMS
A. Political commitment with adequate resources for tuberculosis care and prevention
B. Engagement of communities, civil society organizations, and public and private care providers
C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
D. Social protection, poverty alleviation and actions on other determinants of tuberculosis

3. INTENSIFIED RESEARCH AND INNOVATION
A. Discovery, development and rapid uptake of new tools, interventions and strategies
B. Research to optimize implementation and impact, and promote innovations

The global strategy and targets for tuberculosis prevention, care and control after 2015, were endorsed by all Member States at the 2014 World Health Assembly.

[a] Targets for 2030 for the United Nations Sustainable Development Goals.
Source: adapted from: The end TB strategy [fact sheet]. Geneva: World Health Organization; 2015 (http://www.who.int/tb/post2015_TBstrategy.pdf?ua=1, accessed 23 May 2016).

Annex 2. Resolution EUR/RC65/R6 of the 65th session of the WHO Regional Committee for Europe

Resolution
Tuberculosis action plan for the WHO European Region 2016–2020

The Regional Committee,

Having considered the Tuberculosis action plan for the WHO European Region 2016–2020 (document EUR/RC65/17 Rev.1);

Recognizing the importance of tackling tuberculosis within the framework of Health 2020, the WHO European policy framework, to improve the health and well-being of populations and to reduce health inequalities;

Noting the commitment of the WHO European Region to respond urgently to the threat tuberculosis poses to public health and among those Member States that participated, through the Berlin Declaration on Tuberculosis, adopted by the WHO European Ministerial Forum – All Against Tuberculosis in 2007, and the Eastern Partnership Ministerial Conference on Tuberculosis and Multidrug-resistant Tuberculosis; and to end tuberculosis in the European Region through the Joint Riga Declaration on Tuberculosis and its Multidrug-resistance in 2015;

Recalling World Health Assembly resolution WHA62.15 on prevention and control of multidrug-resistant and extensively drug-resistant tuberculosis (M/XDR-TB) as part of the transition to universal health coverage, and the 2009 Beijing "Call for Action" on tuberculosis control and patient care;

Recalling resolution EUR/RC61/R7, which adopted the Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis in the WHO European Region, 2011–2015 as a strategic framework for action by Member States in the European Region;

Recalling resolutions EUR/RC61/R6 and WHA68.7 on antibiotic resistance as policies to prevent and mitigate antimicrobial resistance, which also contribute to the prevention and control of M/XDR-TB;

Acknowledging that most of the milestones for Member States, the Secretariat and partners to scale up a comprehensive response to prevent and control tuberculosis and M/XDR-TB under the Consolidated Action Plan have been achieved, including significant increases in case detection and treatment coverage, and that Millennium Development Goal 6 on reversing tuberculosis incidence has been reached;

Concerned that despite this progress, there is continuing primary transmission of MDR-TB and decreasing treatment success rates among M/XDR-TB patients in several Member States;

Concerned over an increasing prevalence of HIV among tuberculosis cases and a growing inequality highlighted by the divergent epidemiological picture of tuberculosis across the Region and within countries, particularly among vulnerable groups, and aware that tuberculosis and MDR-TB are also cross-border health threats due to increased mobility of the population;

Recognizing the need for increased political commitment to ensure efficient and evidence-based tuberculosis prevention and expanded access to new models of care, new drugs and tools, as well as social approaches and strategies for tuberculosis management in the context of health systems strengthening;

Noting that the post-2015 global End TB Strategy for ending the global tuberculosis epidemic by 2035, endorsed by resolution WHA67.1, calls for regional support in the implementation of the Strategy; and acknowledging alignment of the Tuberculosis action plan for the WHO European Region 2016–2020 with the global End TB Strategy;

Understanding that this resolution covers the period from 2016–2020 and thereby succeeds resolution EUR/RC61/R7,

which endorsed the Consolidated Action Plan from 2011–2015;

1. ADOPTS the Tuberculosis action plan for the WHO European Region 2016–2020 and its targets;

2. URGES Member States:[1]

(a) to align, as appropriate, their national health strategies and/or national tuberculosis and M/XDR-TB response with the Tuberculosis action plan for the WHO European Region 2016–2020 and to closely monitor and evaluate implementation as outlined in the action plan;

(b) to facilitate equitable access to early diagnosis and effective treatment until completion for all forms of tuberculosis including rational and adequate use of new drugs;

(c) to identify and address health systems challenges related to the prevention and care of all forms of tuberculosis, particularly to integrate tuberculosis services into the primary health care level and to scale-up patient-centred care initiatives and approaches and improve access to tuberculosis prevention and care for hard-to-reach and vulnerable populations;

(d) to address social determinants of tuberculosis, the

prevention of insurmountable costs to patients and their households due to tuberculosis, and the provision of social support to patients, including multisectoral and civil society collaboration as appropriate;

(e) to adopt sustainable financial mechanisms and strengthen human resources capacity for tuberculosis prevention and care, particularly in countries with decreasing external funding, and to move from external financing to self-financing: working with all relevant actors, including ministries of health and finance, parliaments, intergovernmental and non-State actors, to secure the long-term sustainability of programmes, including services for hard-to-reach and vulnerable populations, from domestic resources;

3. REQUESTS the Regional Director:

(a) to support Member States in the implementation of the Tuberculosis action plan for the WHO European Region 2016–2020 by providing leadership, strategic direction and technical support to Member States, upon request;

(b) to continue working in partnership with international, intergovernmental and non-State actors;

(c) to monitor implementation and report to the Regional Committee at its 68th and 70th sessions in 2018 and 2020, respectively, on implementation of the Tuberculosis action plan for the WHO European Region 2016–2020.

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1   And regional economic integration organizations, where applicable.

Annex 3. Areas of intervention under the tuberculosis (TB) action plan for the WHO European Region

The areas of intervention under the action plan described in Table A3.1 encompass a series of activities for which technical assistance from the WHO Regional Office for Europe and/or partners is necessary.

Table A3.1. Areas of intervention under the action plan			
Problem	**Proposed solutions**	**Major activities**	**Timeline**
1. Integrated patient-centred care and prevention			
A. *Systematic screening of contacts and high-risk groups*			
Vulnerable groups and hard-to-reach populations often have limited or no access to health facilities. Active cases of TB that go undetected among these groups (but also in congregate settings, including penitentiary institutions) contribute to the spread of TB.	Systematic screening in high-risk groups and in congregate settings should be undertaken to contribute to the early detection of TB. Hard-to-reach populations need their own approach. Ensuring universal access and appropriate selection of people to be tested for TB has high priority.	Strategies for systematic screening for TB among vulnerable groups, hard-to-reach populations and in congregate settings (including prisons) should be developed or revised. This screening should be targeted to the groups with the highest risk of TB and measurements of effectiveness should be incorporated.	End 2017
Infected contacts of infectious TB (source) cases may go undetected and develop active disease, thereby contributing to ongoing transmission and possible outbreaks of TB.	Contact investigation (and potentially source-case investigation) should be promoted to contribute to the detection of active and latent cases of TB. The less generalized the epidemic becomes, the more emphasis needs to be put on this activity.	Strategies for contact investigation, including source-case investigation among recently infected cases (young children) and outbreak management, should be developed and/or revised.	End 2017
B. *Ensure early diagnosis of TB and universal drug-susceptibility testing, including the use of rapid tests*			
A number of new technologies have been developed or are in the pipeline. The uptake of new rapid diagnostic technologies is slow and implementation is not always well thought through.	When new technologies are introduced, guidelines on how to use them and algorithms for cases in which they are appropriate and when they should be used should be developed. This should include difficult-to-diagnose paediatric TB and extrapulmonary TB.	A guide and diagnostic algorithms for expanded and accelerated quality-assured new technologies (including paediatric and extrapulmonary TB diagnostics) should be prepared.	By 2016
Hard-to-reach and vulnerable populations often have limited or no access to health facilities. When they do arrive at health facilities, the duration of the diagnostic process over several days may discourage them from returning for results and possible treatment.	Rapid diagnostic tools can produce a point-of-care result in a few hours. Strategies should be developed to have a rapid point-of-care diagnosis for those who have limited or no access to health facilities.	Strategies to maximize the benefits of rapid diagnostic tools for hard-to-reach and vulnerable populations should be developed.	By 2017

Table A3.1. Areas of intervention under the action plan (contd)

Problem	Proposed solutions	Major activities	Timeline
Laboratory capacity for quality-assured drug-resistance testing is inadequate for first- and second-line drugs.	National TB laboratory networks should be strengthened.	The national TB laboratory networks should be strengthened (in areas such as planning, infrastructure, biosafety, validation, maintenance of equipment, sputum collection and transportation, procurement and supply, laboratory information systems and human resources) for diagnosis of all forms of TB to ensure effective treatment with first- and second-line treatment as appropriate.	By 2017
For a variety of reasons (financial, proficiency), uptake of quality-assured WHO diagnostic technologies is often late.	Assistance for the uptake of quality-assured WHO diagnostic technologies should be facilitated.	To ensure the uptake of quality-assured WHO diagnostic technologies, assistance to national TB laboratory networks, including reference laboratories, should be facilitated.	Ongoing
Sample transportation can be delayed in high-priority countries for a variety of reasons, leading to compromised testing results. Reporting on results by traditional methods may lead to long delays to the outcome of the tests becoming known.	Sample transportation should be more efficient and communication on results should be prompt, using modern communication technologies.	The national programmes of high-priority countries should be facilitated in finding ways for more efficient sample transportation and subsequent communication of results.	By 2018
Using rapid tests is costly and often goes beyond national funding capacity.	The availability of rapid tests should be ensured through sustainable arrangements.	Sustainable arrangements for funding, using national resources and donor funding to ensure the availability of rapid tests, should be facilitated.	Ongoing
Laboratory maintenance in high-priority countries is often not budgeted. Poor maintenance may lead to low-quality results and biosafety hazards.	Sustainable strategies for laboratory maintenance in high-priority countries should be developed.	The development of sustainable strategies for laboratory maintenance by national TB programmes of high-priority countries should be supported.	By 2018
C. *Ensure equitable access to quality treatment and continuum of care for all TB patients, including drug-resistant TB, and patient support to facilitate patients' adherence*			
In many countries, primary health care and patients' social networks are insufficiently involved in the recognition of symptoms and treatment support. Vulnerable populations and hard-to-reach risk groups are particularly affected by delay in diagnosis, incomplete treatment and stigmatization.	A patient-centred care and support approach that is sensitive and responsive to patients' needs and founded on ethical principles should be introduced or strengthened. Supportive treatment supervision should be carried out in a context-specific and patient-sensitive manner. This is best done by involving primary health care, encouraging community participation and using modern communication technologies.	Assistance should be provided for strengthening primary health care integration in TB prevention and control, including community-based TB treatment and patient-centred care delivery, with increasing use of modern information and communication technologies.	Ongoing
Patients may migrate during TB treatment (or may migrate to access TB care of perceived higher quality, particularly if they have multidrug- or extensively drug-resistant TB (M/XDR-TB)). This creates challenges for treatment follow up, continuity of care, contact investigation, outbreak management and surveillance.	TB services across borders should coordinate their efforts and exchange information, which should prevent insufficient quality of care, continued transmission and incomplete TB surveillance.	A mechanism for cross-border TB control and care that enables continuity of treatment for internal and external migrants and stateless populations should be implemented.	By 2017

Table A3.1. Areas of intervention under the action plan (contd)

Problem	Proposed solutions	Major activities	Timeline
Prisoners treated for TB often avoid civilian services for continuation of treatment on release from prison. Similarly, TB patients on treatment hide their disease when entering a penitentiary institution. Often there is no information exchange between civilian and penitentiary services.	Collaboration between civilian and prison services with improved information exchange on transfer should contribute to interrupted transmission of TB and better continuity of care.	Further collaboration between prison and civilian services should be developed to ensure continuity of care for patients transferred between penitentiary and civilian institutions.	Ongoing
No treatment options remain for some TB patients. Providers then have to deliver palliative care, but hospices are often inadequate or non-existent.	Appropriate hospice/end-of-life care services should be established and palliative care ensured.	Support should be provided in designing and implementing appropriate hospice/end-of-life care for M/XDR-TB patients who fail treatment and for whom all treatment options, including surgery and new and repurposed drugs, are exhausted.	End 2016
D. *Collaborative TB/HIV activities and management of comorbidities*			
TB is the leading cause of death among people living with HIV and is increasing in the Region. Eighty per cent of HIV patients coinfected with TB were detected in 2013; 54% were offered antiretroviral treatment. HIV among TB cases was 7.8% in 2013. TB and HIV/AIDS services still operate as separate vertical services without adequate information exchange.	Integrated TB and HIV service delivery should be established, with coordination at central and regional levels.	Effective mechanisms for delivering integrated TB and HIV services should be established to ensure coordination is present at central and regional levels.	By 2018
Management of TB and (non-infectious) comorbidities (diabetes, substance abuse, malnutrition) is often inadequate.	Diagnosis and clinical management of comorbidities should be integrated within TB services to mitigate the risk of TB.	Management of TB and comorbidities that increase the risk of TB should be integrated.	By 2018
2. Bold policies and supportive systems			
E. *Political commitment, including universal health coverage policy with adequate resources*			
Some countries lack central coordination for TB control. Governments are insufficiently committed to having a national TB control programme embedded in health and social sector planning.	Central coordination under government stewardship should ensure the development of national strategic plans for TB embedded in national health and social sector plans, and accountability for implementation.	Improved, accountable and effective central coordination of TB control should be ensured and results-based management approaches to improve performance implemented.	By 2020
Although most countries have a strategic plan on TB control and prevention, the response to an increasing multidrug-resistant TB (MDR-TB) problem is often insufficiently defined. The plan may have no or only a limited budget overview, roles and responsibilities are often unclear (primary health care versus specialist care, ambulatory care versus hospital care), and new tools and/or interventions may not be included.	National strategic plans that address TB and MDR-TB should be developed or revised and should include organograms endorsed by health systems, with explicit roles and responsibilities (executive degrees and administrative orders), lines of authority and operational plans up to provider level, a costing overview and guidance on new tools and interventions (including e-health).	National TB plans and MDR-TB response plans in high-priority countries should be updated and implemented, adequately costed and be compliant with updated guidance on new tools and interventions (including e-health).	End 2016

Table A3.1. Areas of intervention under the action plan (contd)			
Problem	**Proposed solutions**	**Major activities**	**Timeline**
Absence of continuous monitoring hinders the measurement of progress and effectiveness of implementation of the national strategy; some weaknesses will not be identified and will therefore not be improved.	Independent external reviews every 3–5 years, with the collaboration of national staff and including partners, civil society and communities, should help to identify existing weaknesses and provide recommendations for improvement.	Leadership should be provided for regular (3–5 year) external reviews of national TB programmes and/or TB interventions.	Ongoing
F. *Strengthened health systems, including well aligned financing mechanisms for TB and human resources*			
TB control is vertically organized and not well aligned with overall health coverage in a number of high-priority countries. There are gaps in institutional capacity for all functions of the TB programme within the health system (stewardship/governance, financing, service delivery and resource generation) and overemphasis on hospital-based care.	All functions of TB programmes in the health system that contribute to universal health coverage and rational use of hospital care should be improved. Gaps in institutional capacity should be identified and addressed.	Gaps should be identified and addressed and institutional capacity improved for all functions of TB programmes in the health system (stewardship/governance, financing, service delivery and resource generation) that contribute to universal health coverage and rational use of hospital care.	Immediately
Current resources available for TB prevention, control and care interventions and the organization of funding flows are fragmented and potentially misaligned. They may hinder access to care (out-of-pocket payments, financial incentives for public and private providers).	An in-depth health financing analysis should be conducted to recommend measures to improve health financing reform in alignment with service delivery strategies.	An in-depth health financing review for more effective TB prevention, control and care should be conducted.	End 2016
In an environment of decreasing donor funding, increases in domestic funding for aspects of TB prevention, control and care programmes are needed.	Plans should be developed to sustainably increase domestic funding and shared responsibility schemes.	Sustainable plans should be developed to increase domestic funding and shared responsibility schemes for TB prevention, control and care in countries previously in receipt of donor funding.	Immediately
Many countries do not know if the funds for TB control (donor/domestic) are spent efficiently or effectively.	Performance-based financial management should provide a platform to demonstrate that financing converts into results. A framework describing the methodology and indicators should be in place.	Performance assessment frameworks of national TB control programmes should be developed, including evaluation of cost–efficiency and effectiveness.	By 2017
The growing need for quality-assured laboratory investigations, including new tools, is being met insufficiently due to shortages of competent staff.	With support from the European Tuberculosis Laboratory Initiative and the Global Laboratory Initiative, sustainable human capacity should be built for the supranational laboratory network and Member States through regular country visits, technical assistance and 1–2 months' internships at supranational reference laboratories.	Sustainable human capacity for the supranational TB reference laboratories network and Member States should be built.	By 2018

Table A3.1. Areas of intervention under the action plan (contd)

Problem	Proposed solutions	Major activities	Timeline
Expansion of the TB control and prevention programme, with involvement of primary health care, other health and social sectors, civil society and communities, poses a challenge for human resources in terms of numbers and competencies.	Human resource capacity should be enhanced through: (i) regular country reviews (to monitor the performance of national and subnational health authorities and primary health care providers involved in TB prevention, control and care); and (ii) technical assistance to TB control management (programme management, efficient use of resources, operational research and application of new tools).	Human resource capacity should be enhanced in all aspects of TB prevention, control and care programmes.	Ongoing
Prison inmates are at greater risk of becoming TB infected and/or developing TB disease than people in the general population due to their close, prolonged indoor confinement and other associated conditions common among inmates. Prison staff, however, often lack competence to deal with TB prevention, control and care.	TB control in prisons should be improved through training activities coordinated with the WHO Collaborating Centre on Prevention and Control of Tuberculosis in Prisons.	Training activities facilitated by the collaborating centre should be supported to improve TB control in penitentiary services.	Immediately
G. *Improved regulatory frameworks for case-based surveillance, strengthening vital registration, quality and rational use of medicines and pharmacovigilance*			
The lack of a minimum set of social determinant variables in routine surveillance at country level hinders the study and monitoring of social risk factors.	A minimum set of social determinant variables for inclusion in routine surveillance should be developed with WHO headquarters, partners and Member States. This will enable monitoring of upstream and downstream risk factors for TB disease and treatment outcomes.	A minimum set of social determinant variables should be developed to be included in routine surveillance at country level.	By 2016
Quality-assured data collection and data analysis are not yet standardized in all countries, and capacity at all levels of the health system for surveillance, programmatic monitoring and evaluation is still weak in many.	Surveillance standards and benchmarks should contribute to improved data quality management; subregional workshops on surveillance standards and benchmarks and plans for implementation at country level should be developed.	Subregional workshops on surveillance standards and benchmarks should be supported and plans for implementation at country level should be developed.	Immediately
Heterogeneity of information systems for laboratory management, both paper-based and electronic, exists. Electronic case-based data collection allows for more rapid reporting on individual results and monitoring of laboratory performance.	Standardized electronic laboratory information management systems should be established.	The establishment of laboratory information management systems should be supported.	By 2017
Reported stock-out decreased from eight countries in 2011 to four in 2013. Stock-outs are caused by incomplete patient data, weak drug management capabilities (including forecasting) and/or no strategy for rational drug use (including fixed-dose combinations).	Quality-assured data collection is needed for the development of reliable estimates of drug needs and trends.	Data collection should be supported to develop reliable estimates of drug needs and trends.	Immediately

Table A3.1. Areas of intervention under the action plan (contd)

Problem	Proposed solutions	Major activities	Timeline
Unqualified TB medicines (especially second-line medicines) are not only much costlier than the WHO-prequalified ones, but also pose a major threat for the development of drug resistance due to their uncertain quality. A number of countries are hesitant to accept WHO-prequalified drugs.	National registration of drugs that have passed the WHO prequalification programme mechanism is often cumbersome, yet these drugs are of assured quality and cheaper. The use of WHO-prequalified drugs should be promoted.	The WHO prequalification programme mechanism should be promoted to ensure speedy registration (such as fast-track mechanisms) of products already prequalified by WHO.	By 2017
Pharmaceutical legislation and regulations often prohibit the importation of prequalified drugs. Not all countries have made progress to deal with this.	A gap analysis should clarify what countries have done to improve the legislation and regulatory framework on the registration of WHO-prequalified drugs.	A gap analysis of pharmaceutical legislation and regulations should be conducted (as follow up to that conducted under the consolidated action plan) and their improvement should be facilitated.	By 2019
Different countries have different procurement procedures, which are often complicated and prolonged for some. Over-the-counter sales of TB drugs without prescription is common in many countries. Now new TB medicines are being introduced, it is imperative that they are used only in an appropriate way to prevent the development of further drug resistance.	Regulatory mechanisms and procedures for the procurement of medical supplies should be developed, with an emphasis on quality assurance through strengthened regulatory authorities with the emphasis including, but not limited to, paediatric TB diagnostics and treatment (drug formulations) and limiting the availability of new drugs on the free market (over-the-counter sales) without prescription.	Procedures for the procurement of medical supplies should be developed.	By 2017
Only two countries have so far adopted the WHO Good Governance for Medicines programme that supports policy-makers and national officials to understand where strengths and weaknesses in national pharmaceutical systems lie and where appropriate interventions can be developed and applied.	The WHO Good Governance for Medicines programme for TB medicines and pharmacovigilance should be adopted by countries.	Countries should be engaged in the WHO Good Governance for Medicines programme and pharmacovigilance.	Immediately
Medicines that are under development but have not undergone final trials may be allowed for compassionate use, but not all countries have the regulatory framework to facilitate this.	Legal frameworks for the compassionate use of drugs under development should be developed at national and subnational levels.	Continual guidance should be delivered to develop legal frameworks at national and subnational levels for compassionate use of medicines under development.	Ongoing
TB patients on treatment take more than one anti-TB medicine simultaneously, and regimens last from many months to two years or more. This increases the likelihood of adverse drug events, some of which are severe. These events may damage public confidence in national treatment programmes and affect patient adherence. Patients who stop taking anti-TB medicines pose a risk to themselves and others. The generation of drug resistance is a very real risk. Frequency of adverse effects of TB treatment is not routinely monitored.	A sufficiently resourced data repository on drug-related adverse events should be established in collaboration with the WHO Collaborating Centre on Pharmacovigilance.	A sufficiently resourced data repository on drug-related adverse events should be established.	End 2016

Problem	Proposed solutions	Major activities	Timeline
Table A3.1. Areas of intervention under the action plan (contd)			
H. *Community systems strengthening and coordination with civil society*			
In many countries, representatives of affected communities are not seen as partners in monitoring the TB programme. Patient groups can provide good feedback on TB programme performance and the creation of such groups will increase knowledge and access to improved health service delivery.	Representatives of affected communities should be included systematically in TB programme reviews, design, planning, implementation and monitoring, as well as in assessing the quality of services.	Representatives of affected communities and civil society should systematically be included in national and regional TB programme reviews, design, planning, implementation and monitoring, and in assessing the quality of services.	Immediately
Awareness of TB among government officials, health professionals and the general public is low in many countries.	Awareness about TB should be raised. The WHO Regional Office for Europe has established the Regional Collaborating Committee on TB Control and Care (RCC-TB). The mission of RCC-TB is to achieve universal access to evidence-based TB and M/XDR-TB prevention, diagnosis, treatment and care across the WHO European Region. Key objectives are to strengthen involvement and foster collaboration between national and international partners. The RCC-TB aims to raise awareness about TB, advocate for resource mobilization and catalyse an exchange of best practices regarding TB and M/XDR-TB prevention, care and control.	To raise awareness about TB, advocacy for resource mobilization and exchange of best practices through the RCC-TB and involvement of national and international partners and private providers should be strengthened and collaboration between them fostered.	Ongoing
I. *Social protection, poverty alleviation and actions on other determinants of TB, such as migration and prisons*			
Medical care can prolong survival and improve prognosis, but more important for the health of the population are the social and economic conditions that make people ill. Universal access to medical care is an important determinant of health, but so far, few of these determinants have been addressed in the Region.	Capacity should be built to address the social determinants of TB and develop effective mechanisms of social protection for TB patients and their families.	Technical assistance should be provided for health systems capacity-building to address the social determinants of TB and develop effective mechanisms of social protection for TB patients and their families.	By 2017
A coordinated public health mechanism to guarantee TB prevention, diagnosis, treatment and care across borders is not in place. Among the problems that need to be addressed are: political commitment, including the implementation of a legal framework for TB cross-border collaboration; financial mechanisms; and adequate health service delivery.	A minimum package for cross-border collaboration between departments and sectors that addresses current shortcomings and aims to improve the situation should be explored, with an emphasis on a legal framework.	Legal mechanisms for cross-border TB control and care should be explored within an interdepartmental and intersectoral approach.	By 2017

Problem	Proposed solutions	Major activities	Timeline
Table A3.1. Areas of intervention under the action plan (contd)			
3. Intensified research and innovation			
J. *Discovery, development and rapid uptake of new tools, interventions and strategies*			
New technologies and service-delivery models are needed to achieve TB elimination. This will require an intensification of research, from fundamental research to drive innovations, to operational and health systems research to improve current programmatic performance. TB research is greatly underfunded, which has resulted in a meagre pipeline of new technologies for diagnosis, treatment and prevention. The research agenda is too wide to be tackled by individual countries.	Broad-based concerted effort is needed to develop research capacity, resource mobilization and advocacy. A European TB research initiative should be established to: - identify needs, capacities and gaps (financial support for basic and operational research, language/translational support, etc.); - develop regional and national research agendas; - develop a platform for sharing new research and study results, and creating networks for research; - map collaboration between major research institutes and identify new areas for cooperation; - activate funding agencies to link with civil society organizations for research advocacy; and - provide the evidence base for policy and practice for TB prevention, control and care.	A European TB research initiative should be established/formulated (in close consultation with WHO headquarters) to develop a research agenda, improve research capacity, and promote resource mobilization and advocacy.	By 2017
Research priorities have not been formulated at country level and funding has not been secured.	A national research agenda should be drafted and funding found.	National research priority areas and agendas should be promoted and funding secured.	By 2017
Research methodologies may not reflect ethical principles, which can lead to infringement of human rights.	Information should be provided on how ethical principles are part of the mechanisms for TB research.	Assistance should be provided to assess and ensure that adequate research ethics mechanisms are in place in the key institutions and partner organizations that carry out national research agendas.	By 2017
The development of new tools, including new treatment regimens, is subject to clinical trials for which not all countries will have the relevant expertise.	Research, the development of new tools and sound clinical trials should be supported by the European TB research initiative.	Research and development of new tools, including TB treatment regimens, should be facilitated. Assistance should be provided by the European TB research initiative to ensure sound clinical trials.	By 2017
There is a plethora of European research institutes, but their TB research agenda is small or non-existent.	European research institutes should be involved in fundamental TB research.	The ongoing involvement of European research institutes in the development of new diagnostic tools, medicines and other treatment modalities, vaccines and research on basic mechanisms of resistance should be advocated.	By 2017
Funding is scarce and countries may not give priority to funding research on new TB technologies.	Advocacy is needed to mobilize regional and national resources for the development of new TB technologies.	The mobilization of regional and national resources, with the use of planning/budgeting tools aiming to develop new technologies, should be advocated.	By 2017

Table A3.1. Areas of intervention under the action plan (contd)

Problem	Proposed solutions	Major activities	Timeline
K. *Research to optimize implementation and impact and promote innovation*			
Operational research priorities, including social science research on health-seeking behaviour, adherence to treatment and stigma, are not always well defined, and results of studies may not be used to adapt policies and practices.	Guidance should be provided to help national research platforms to prioritize what should be studied and assistance should be given on how to use the results to adapt policies.	Guidance and technical assistance should be provided to develop operational research priorities within national research platforms, and the corresponding social science research on health-seeking behaviour, adherence to treatment, stigma and discrimination, to inform policies and practices.	By 2017
Capacity for (operational) research is low in many countries.	Training should be provided to increase capacity for operational research, with an emphasis on translating results into action.	Assistance in capacity-building for operational research training and translating research results into action should be provided.	By 2017
Adapted programme policies based on the results of operational results are often not shared with other countries or within the country of origin.	Best practices in the implementation of models of care and patient support (inpatient, outpatient, home/community-based models of care, financing/avoidance of catastrophic costs, prevention, etc.) in different settings should be continuously documented and shared.	Best practices should be documented and shared.	By 2017
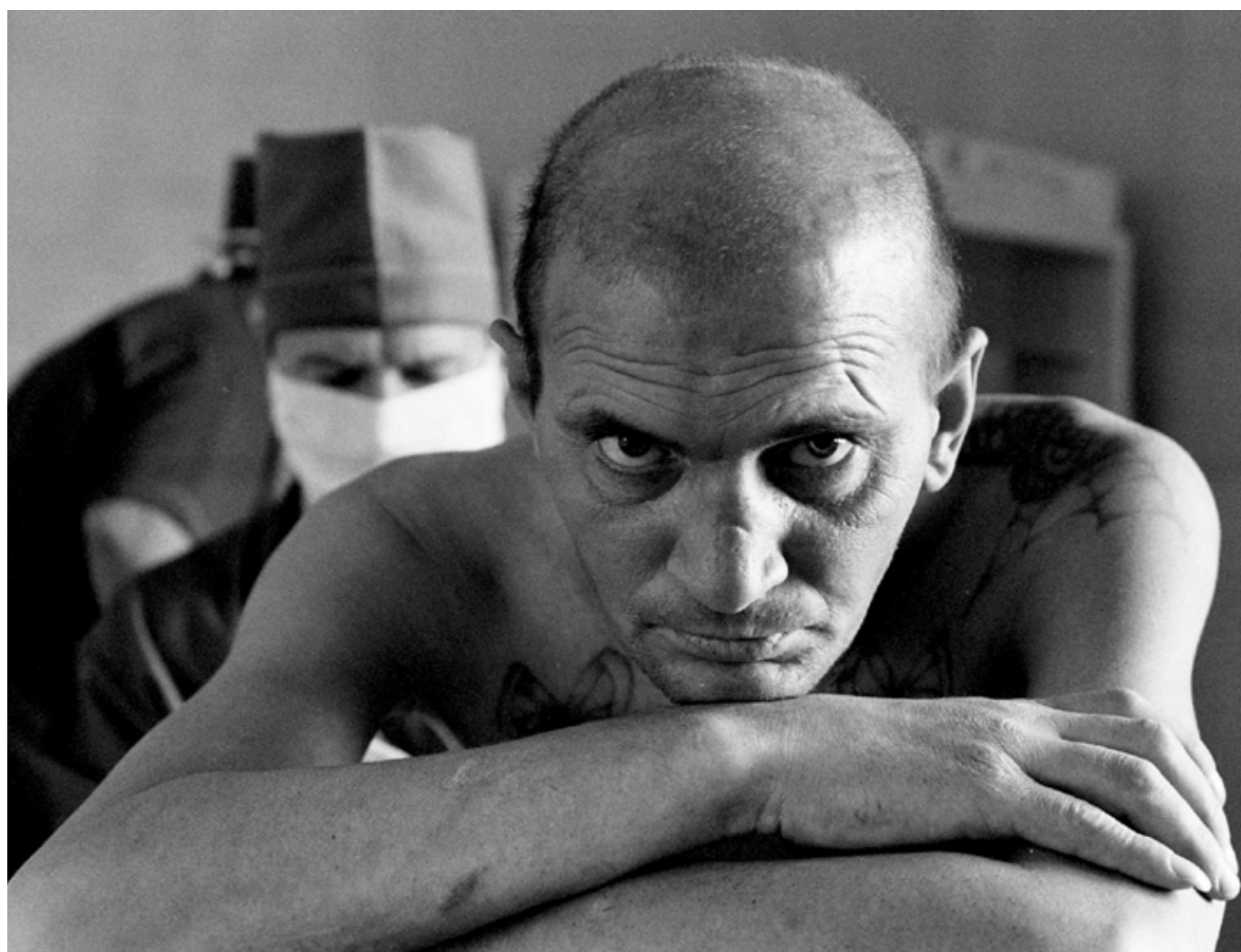
Annex 4. Monitoring and evaluation framework for follow up of the tuberculosis action plan

The tuberculosis (TB) action plan for the WHO European Region 2016–2020 is supported by a monitoring and evaluation (M&E) framework that enables a harmonized approach to monitoring progress towards action plan targets at national and regional levels and actions taken to put the End TB Strategy into practice. Monitoring is not limited to tracking data on TB surveillance and implementation of activities, but also includes evaluating the effectiveness and impact of interventions, consequently providing a foundation for advocacy and policy development.

The current framework is based on a detailed review of the action plan, maintaining the structure and aims of the M&E framework of the consolidated action plan to prevent and combat multidrug- and extensively drug-resistant TB in the WHO European Region 2011–2015, while limiting the total number of indicators and adding details on calculations of each of the indicators used. Limiting the number of indicators is intended to avoid overburdening the framework and stay focused on issues that directly affect decision-making and provide measures of effectiveness.

The framework consists of 26 indicators that allow monitoring of performance of the areas of interventions in the action plan. Nine were selected as core indicators for monitoring and reporting to the WHO Regional Committee for Europe (those highlighted in the list with E (European) (see Table A4.1)). The list of indicators closely follows the structure of the action plan. Each area of intervention is reflected in the framework by one or more indicators, assessed by the task force to represent the most accurate measure of performance of the group of activities.

The monitoring framework includes indicators that allow oversight of progress towards achievement of regional targets:

1. impact indicators that measure progress towards the three End TB Strategy and WHO European Region targets;
2. outcome indicators that monitor broader changes in TB control enhanced as a result of a set of interventions;
3. process indicators that monitor progress of specific interventions; and
4. input indicators that measure policy environment, commitment and capacity among Member States.

Indicator development was guided by principles which defined that the indicators should be:

- broad enough to reflect all aspects of the ambitious action plan;
- sufficiently specific to address critical markers of success; and
- concise, so as not to overburden national programmes.

In addition, selection of indicators was harmonized with the End TB Strategy's recommended top 10 global indicators (highlighted in the list with G (Global) (see Table A4.1)) and focusing on indicators that are collected regularly through the routine recording and reporting system. These indicators, while regional in scope, are designed to serve as a guide to the development or adjustment of comprehensive monitoring plans at country level.

Baseline value, desired target, assessment frequency, monitoring mechanism and data source are defined for each indicator/group of indicators. The framework includes quantitative and qualitative indicators: if quantitative, numerators and denominators are listed; if qualitative, basic criteria of favourable assessment (Yes/No) are listed.

Baseline levels in most cases were defined using information provided by each country through the WHO/European Centre for Disease Prevention and Control (ECDC) annual TB data collection process. This is standardized to the WHO recommended recording and reporting framework, has Region-wide coverage, is undertaken only once (therefore avoiding duplication of effort by countries and partners) and ensures a user-friendly mechanism for data collection (1). The absence of baseline information in a limited number of indicators from the full list might be explained by the unavailability of these data and/or questionable reliability of the information available.

To prioritize the area of intervention, indicators will be measured according to the following layers: 18 high-priority countries to stop TB in the WHO European Region (2);[1] European Union/European Economic Area countries; and regional level. Analysis by country will be performed to assess country-specific benchmarks, performance over time and the eventual achievement of all objectives.

Most indicators will be monitored annually. In addition to the joint WHO/ECDC annual data collection, desk reviews will be performed at the beginning of implementation of the action plan and when full implementation is expected to monitor activities that are not reflected in the WHO/ECDC TB data collection form. In-depth assessment of reports from countries and external technical support will provide additional material to support the measurement of indicators. In the absence of these main sources of information, an interview with the national programme (or equivalent) will be undertaken to assess performance on

interventions implemented as part of the action plan. Only data approved by Member States will be used in monitoring the action plan.

The indicators outlined in the regional M&E framework should be integrated with national TB control programmes' M&E frameworks at country level. In addition to the indicators outlined in the regional framework, countries may also include additional indicators to monitor progress of national strategies, taking into account country-specific priorities.

The full results of assessments of performance on interventions delivered through implementation of the action plan will be presented every second year via a joint WHO/ECDC report on TB surveillance and monitoring in Europe. The report will consist of analysis and interpretation of data based on the indicators and will include recommendations. Progress in action plan implementation will be reported every second year to the Regional Committee and monitoring reports will be presented to the meeting of national TB programme managers/country focal points that is open to stakeholders and civil society organizations involved in TB control in the Region.

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1   The 18 high-priority countries for TB control in the WHO European Region are: Armenia, Azerbaijan, Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, the Republic of Moldova, Romania, the Russian Federation, Tajikistan, Turkey, Turkmenistan, Ukraine and Uzbekistan.

Table A4.1. Monitoring framework for follow up of the TB action plan for the WHO European Region, 2016–2020

Intervention area	Indicator	Baseline EUR[a]	Target	Frequency	Data source	Layers of analysis	Monitoring mechanism	Input–impact level
1. INTEGRATED PATIENT-CENTRED CARE AND PREVENTION								
1A *Systematic screening of contacts and high-risk groups*								
1A.1	Coverage of population at risk with systematic screening for active TB and LTBI[b]	N/A	Full coverage	01–2016 01–2021	NTP[c]	EUR HPC[d] EU/EEA[e]	Desk review	Outcome
1B *Early diagnosis of all forms of TB and universal access to DST,[f] including the use of rapid tests*								
1B.1	Percentage of TB patients diagnosed using WHO-recommended rapid tests (G9)[g]	N/A	30%	Annually	NTP	EUR HPC EU/EEA	Desk review	Outcome
1B.2	First-line DST coverage (%) among all bacteriologically-confirmed TB cases (G1)	91.9%	Close to 100%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Outcome
1B.3	MDR-TB[h] case detection rate (%) (G3)	46.5%	85%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Outcome
1B.4	TB notification rate per 100 000 population (E1)[i]	32.8	24.6	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Impact

Intervention area	Indicator	Baseline EUR[a]	Target	Frequency	Data source	Layers of analysis	Monitoring mechanism	Input–impact level
1B.5	TB case-detection rate (%)	84.1%	Increase	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Impact
1B.6	Percentage of MDR-TB among new TB patients (E2)	16.9%	Decrease	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Impact
1B.7	Percentage of MDR-TB among previously treated TB patients	48.0%	Decrease	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Impact
1C *Equitable access to quality treatment and continuity of care for all people with TB, including drug-resistant TB, and patient support to facilitate treatment adherence*								
1C.1	Percentage of hospitalization of new TB patients (E3)	N/A	Decrease	01–2016 01–2021	NTP	EUR HPC EU/EEA	Desk review	Outcome
1C.2	Percentage of detected MDR-TB enrolled in treatment according to WHO norms (G3)	61.9%	Close to 100%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Output
1C.3	Treatment success rate (%) among all new and relapsed TB patients (G4)	75.2%	85.0%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Outcome
1C.4	Treatment success rate (%) among the MDR-TB treatment cohort (G4) (E4)	49.0%	75.0%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Outcome
1C.5	TB mortality rate (ICD[j] A15–19) per 100 000 population (G5) (E5)	4.1	2.7	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Impact
1D *Collaborative TB/HIV activities and management of comorbidities*								
1D.1	TB/HIV case-detection rate (%)	84.8%	Close to 100%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Outcome
1D.2	HIV testing coverage (%) (G6) (E6)	67.6%	Close to 100%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Process
1D.3	Percentage of HIV among all TB	7.8%	Decrease	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Impact
1D.4	ART[k] coverage (%) among TB/HIV cases	53.8%	Close to 100%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Output
1D.5	LTBI treatment enrolment rate (%) among PLHIV[l] (G7)	4.8%	30%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Output

Table A4.1. Monitoring framework for follow up of the TB action plan for the WHO European Region, 2016–2020 (contd)

Table A4.1. Monitoring framework for follow up of the TB action plan for the WHO European Region, 2016–2020 (contd)

Intervention area	Indicator	Baseline EUR[a]	Target	Frequency	Data source	Layers of analysis	Monitoring mechanism	Input–impact level
1E *Management of LTBI and preventive treatment of people at high risk, and vaccination against TB*								
1E.1	Contact-tracing coverage (%) (G2) (E7)	N/A	90%	01–2016 01–2021	NTP	EUR HPC EU/EEA	Desk review	Output
1E.2	LTBI treatment coverage (%) in childhood TB contact persons aged under 5 years (G7)	N/A	90%	01–2016	01–2016	EUR HPC EU/EEA	Desk review	Output
2. BOLD POLICIES AND SUPPORTIVE SYSTEMS								
2A *Political commitment with adequate resources, including universal health coverage policy*								
2A.1	Number of Members States that have a regular TB control/elimination performance publication every five years (E8)	N/A	53	Cumulative 2016–2020	NTP	EUR HPC EU/EEA	Desk review	Output
2B *Health system strengthening in all functions, including well aligned functioning mechanisms for TB and human resources*								
2B.1	Percentage of TB patients and their households that experience catastrophic financial consequences due to TB (G8) (E9)	N/A	Close to 0	Annually	NTP	EUR HPC EU/EEA	Desk review	Impact
2C *Regulatory frameworks for case-based surveillance, strengthening vital registration, quality and rational use of medicines and pharmacovigilance*								
2C.1	Treatment coverage (%) with new TB drugs	N/A	20%	Cumulative 2016–2020	NTP	EUR HPC EU/EEA	Desk review	Process
2D *Community systems and civil society engagement*								
2D.1	Number of Member States with functioning multistakeholder coalitions advocating for TB care and resources	N/A	53	Cumulative 2016–2020	NTP	EUR HPC EU/EEA	Desk review	Output
2E *Social protection, poverty alleviation and actions on other determinants of TB, such as migration and prisons*								
2E.1	Treatment success rate (%) of new and relapsed TB cases among prisoners	63.2%	85.0%	Annually	WHO global TB database	EUR HPC EU/EEA	Routine reporting	Impact
3. INTENSIFIED RESEARCH AND INNOVATION								
3A *Discovery, development and rapid uptake of new tools, interventions and strategies*								
3A.1	European TB research initiative established by mid-2016		Established	Cumulative 2016–2020	NTP		Desk review	Output

[a] EUR = Europe.
[b] LTBI = latent TB infection.
[c] NTP = national TB programme.
[d] HPC = high-priority country.
[e] EU/EEA = European Union/European Economic Area countries.
[f] DST = drug-susceptibility testing.
[g] G = global (indicator).
[h] MDR-TB = multidrug-resistant TB.
[i] E = European (indicator)
[j] ICD = International Classification of Diseases.
[k] ART = antiretroviral therapy.
[l] PLHIV = people living with HIV.

References

1. Definitions and reporting framework for tuberculosis – 2013 revision. Geneva: World Health Organization; 2013 (http://www.who.int/tb/publications/definitions/en/, accessed 10 May 2016).

2. Plan to stop TB in 18 high-priority countries in the WHO European Region, 2007–2015. Copenhagen: WHO Regional Office for Europe; 2007 (http://www.euro.who.int/__data/assets/pdf_file/0005/68180/E91049.pdf, accessed 10 May 2016).

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Annex 5. Costs and benefits of the tuberculosis action plan

Key findings

The total budget of the action plan for the five-year implementation period 2016–2020 is US$ 15 billion for the screening and treatment of drug-sensitive and multidrug- and extensively drug-resistant tuberculosis (M/XDR-TB) in the WHO European Region, increasing annually from US$ 2.5 billion in 2016 to US$ 3.7 billion in 2020. Most of the costs (74%) are incurred in high-priority countries (HPC) and consist mainly of hospital, outpatient and pharmaceutical costs.

The action plan is highly cost–effective according to conventional benchmarks. With a total number of lives saved of 1 089 308, the cost per death averted is US$ 13 805 and cost per disability-adjusted life-years (DALYs) saved is US$ 657. The cost per DALY saved is a fraction of the average per capita gross domestic product (GDP) of the European Region.

Introduction

M/XDR-TB requires expensive screening and treatment interventions, consisting of molecular and traditional culture screening for first-line drug resistance and a combination of second-line drugs often administered in an inpatient or similar support system for the initial months of treatment. Despite advances in recent years, screening must be scaled-up in the Region, where 61% of estimated multidrug-resistant TB (MDR-TB) patients were notified in 2013, but with country estimates being as low as 33% *(1)*.

Funding for the control of M/XDR-TB has been increasing since 2007, with the bulk of finances in the next five years required for HPCs. For the purposes of this analysis, HPC and non-HPC stratification is identical to the 2011–2015 action plan.[1] The following sections describe methods

and results for the estimation of total finance required for implementation of the 2016–2020 action plan and a cost-effectiveness analysis. The analysis follows the same principles of, and updates, the 2011–2015 analysis, taking a bottom-up approach to estimate unit costs and resource use. In contrast to the 2011–2015 action plan, the present analysis also includes the costs and impacts of treating drug-sensitive TB.

Methods

Perspective of analysis

A health system perspective was adopted. Direct costs incurred by the health system were included, and indirect costs to patients and society were excluded. A lump-sum expenditure covering stewardship, supervision and capacity-building was included.

Costs

Unit costs for the screening and treatment of drug-sensitive and X/MDR-TB were estimated using a bottom-up approach, including the cost of in- and outpatient clinic use, staff, instruments, consumables and pharmaceuticals. Unit costs for instruments, consumables and pharmaceuticals were obtained from the International Drug Price Indicator Guide *(2)*, the Stop TB Partnership Global Drug Facility *(3)*, Foundation for Innovative New Diagnostics (FIND) negotiated prices and the WHO Planning and Budgeting for TB Control Activities tool *(4)*.

Instruments

All HPCs (except Turkey) were eligible for the FIND High-burden Developing Country concession price of the GeneXpert instrument and cartridges *(5)*, while non-HPC unit prices were based on the regular commercial price *(6)*. Most HPCs (11 of 18 countries *(5)*) were not eligible for the concession price of the BACTEC MGIT liquid culture and drug-susceptibility testing (DST) system; consequently, a weighted average HPC/non-HPC price based on the most recent (2013) number of MDR-TB cases reported in individual HPCs and their price eligibility was used *(4)*. The majority (11 of 18) of HPCs were eligible for FIND negotiated prices on line-probe assay (LPA) equipment *(5)*, and a weighted average price was also calculated in this case

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1 HPCs in the WHO European Region are: Armenia, Azerbaijan, Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, the Republic of Moldova, Romania, the Russian Federation, Tajikistan, Turkey, Turkmenistan, Ukraine and Uzbekistan. The non-HPCs are: Albania, Andorra, Austria, Belgium, Bosnia and Herzegovina, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Israel, Italy, Luxembourg, Malta, Monaco, Montenegro, the Netherlands, Norway, Poland, Portugal, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, the former Yugoslav Republic of Macedonia and the United Kingdom.

(4). The commercial price of LPA was assumed to be 200% of the FIND concession price (5). Costs of equipment for microscopy, solid media culture and DST facilities were not differentiated between HPCs and non-HPCs. The total cost of instruments and other necessary laboratory facilities (such as glassware, racks, gas burners, timers and stirrers) for all diagnostic facilities were bundled with the equipment price (4).

Consumables
The cost of consumables for microscopy, solid media culture and DST consumables were not differentiated between HPCs and non-HPCs (4). Following the same procedure as for instrument costs, weighted average prices were based on MDR-TB cases reported across countries when not all HPCs were eligible for discounted prices. As above, this was the case for liquid culture, liquid DST and LPA. For LPA, consumable prices in HPCs are assumed to be 25% of those in non-HPCs (5). Outpatient and inpatient hotel costs (7) and staff costs (8–10) were based on the most recent WHO-CHOICE estimates and inflated to 2016 values at 3% per annum. The average of EURO-B and EURO-C costs were used for HPCs, and EURO-A for non-HPCs.

The total programme budget was based on the costs of screening and treating all patients enrolled in the 2016–2020 programme, excluding costs of continued treatment beyond 2020.

Cost-effectiveness
The cost–effectiveness of the action plan was determined as the cost per death averted and cost per DALY averted as a result of the intervention (11). Implementation was compared to a no-action scenario. The number of deaths averted was estimated using the following identities and formulae.

Patient population
The total estimated population of TB patients is based on extrapolation of the most recent three years of data. Total estimated M/XDR-TB patients is a subset of total TB patients (probability of a patient being M/XDR-TB denoted P[M/XDR]) and consists of detected (P[detected]) and undetected cases. Among the cases detected, a percentage are enrolled (P[enrolled]) in treatment, and of those enrolled, a certain percentage have a successful treatment outcome (P[treatment success]):

$$\text{TB-Patients}_{ESTIMATED} = \{\text{extrapolation over previous years}\}$$

$$\text{M/XDR-TB-Patients}_{ESTIMATED} = \text{TB-Patients}_{ESTIMATED} * P[\text{M/XDR}]$$

$$= \text{M/XDR-TB-Patients}_{ESTIMATED} * (P[\text{detected}] + (1 - P[\text{detected}]))$$

$$= \text{M/XDR-TB-Patients}_{ESTIMATED\&DETECTED} * (P[\text{enrolled}] + (1 - P[\text{enrolled}])) + \text{M/XDR-TB-Patients}_{ESTIMATED\&UNDETECTED}$$

$$= (\text{M/XDR-TB-Patients}_{ESTIMATED\&DETECTED\&ENROLLED} * (P[\text{treatment success}] + (1 - P[\text{treatment success}])) + \text{M/XDR-TB-Patients}_{ESTIMATED\&DETECTED\&NOTENROLLED}) + \text{M/XDR-TB-Patients}_{ESTIMATED\&UNDETECTED}$$

$$= ((\text{M/XDR-TB-Patients}_{ESTIMATED\&DETECTED\&ENROLLED\&SUCCESS} + \text{M/XDR-TB-Patients}_{ESTIMATED\&DETECTED\&ENROLLED\&FAILURE}) + \text{M/XDR-TB-Patients}_{ESTIMATED\&DETECTED\&NOTENROLLED}) + \text{M/XDR-TB-Patients}_{ESTIMATED\&UNDETECTED}$$

Number of lives saved
Among the proportion of patients detected (P[detected]), enrolled in treatment (P[enrolled]) and successfully cured (P[treatment success]), a proportion (P[spontaneous cure]) would have been cured spontaneously without the intervention and are therefore subtracted from the number of lives saved:

$$\text{Lives saved} = \text{M/XDR-TB-Patients}_{DETECTED\&ENROLLED\&SUCCESS} - (\text{M/XDR-TB-Patients}_{DETECTED} * P[\text{spontaneous cure}])$$

Cost per DALY saved
Each life saved is conservatively assumed to result in 21 DALYs saved (11), and consequently the number of DALYs saved is obtained by multiplication:

$$\text{DALYs saved} = \text{number of lives saved} * 21 \text{ DALYs/life saved}$$

Cost-effectiveness ratios
Costs and effects are not discounted in the cost-effectiveness analysis. The cost per life saved is obtained by dividing total programme costs by the number of lives saved through implementation of the programme. Similarly, cost per DALY saved is obtained by dividing total programme costs with the total number of DALYs saved. The latter is benchmarked against the following criteria (11,12):

- highly cost–effective: cost per DALY is less than the GDP per capita;
- cost–effective: cost per DALY is one to three times the GDP per capita; and
- not cost–effective: cost per DALY is more than three times GDP per capita.

Economic gain
The long-term economic gain from implementation of the action plan was estimated by multiplication of DALYs averted with GDP per capita in the Region over the period 2016–2020.

Results

Costs of managing TB cases include the costs of diagnostics and pharmaceuticals plus their associated consumables, staff time and in- and outpatient health facility use. Some inputs are made available at preferential prices to HPCs: for example, the HPC price for the GeneXpert diagnostic consumable cartridge decreased from US$ 17 in 2011 to US$ 9.98 in 2016.

The unit costs of pharmaceuticals and associated disposables (syringes, needles, sterile water) required for the treatment of TB are relatively volatile, with significant increases and decreases observed since 2011 (Table A5.1). In addition, treatment regimens have changed to include the drugs bedaquiline, linezolid, clofazimine, imipenem/cilastatin and pyrazinamide.

Between 2011 and 2016, the impact of price changes on total treatment costs (including pharmaceuticals, diagnostics,

labour and hospital overheads) is between 7.8% and 16.3% depending on the resistance profile of the patient (Table A5.2).

The budget for the action plan over the implementation period in million US$ and the percentage of total budget by activity is detailed in Table A5.3. Most costs (56.9%) are attributable to treatment of drug-sensitive TB, followed by the treatment of MDR-TB (36.4%). Although the treatment of XDR-TB is the costliest per case, it accounts for only 4.5% of the total budget.

By input, the analysis shows that most costs (53.7%) are associated with inpatient care, followed by ambulatory care (31%) and pharmaceuticals (8%), as shown in Table A5.4. The annual expenditure on all inputs increases across the implementation period as screening and treatment are scaled-up.

Table A5.1. Pharmaceutical unit costs per dose, 2011 and 2016, in US$

Dose form	2011	2016	Δ (%)
2-FDC-RH	0.09	0.17	94
3-FDC-B (RHE)	0.18	0.23	27
4-FDC-B (RHEZ)	0.22	0.29	33
Amx/clv	0.07	n/a	n/a
Amx/clv 875/125	n/a	0.18	n/a
Capreomycin	5.24	7.88	50
Clr	0.68	1.12	64
Cycloserine	2.18	1.29	-41
E (E400-B)	0.09	0.13	42
Ethionamide	0.31	0.25	-20
Kanamycin	3.16	1.14	-64
Levofloxacin	0.24	0.32	33
Mfx	0.24	n/a	n/a
Mfx 400	n/a	1.53	n/a
PAS	3.84	3.36	-12
Pto	0.51	0.49	-4
Bedaquiline	n/a	37.33	n/a
Linezolid	n/a	8.75	n/a
Clofazimine	n/a	1.76	n/a
Imi/Cls	n/a	19.17	n/a
Pyrazinamide	n/a	0.16	n/a
S&N	0.06	0.07	28
Streptomycin S1 (100)	0.88	0.81	-8
Water for injection (solvent) BB	0.20	0.12	-40
Z (Z400-B)	0.07	0.13	92

Table A5.2. Impact on price changes between 2011 and 2016 on total treatment costs per patient

	Patients	Total treatment costs (US$/patient)		
		2011	2016	Δ (%)
HPC	New DS[a] TB smear +	5 110	5 879	769 (13.1%)
	New DS TB smear –	4 005	4 597	592 (12.9%)
	Previously treated TB	6 126	7 034	907 (12.9%)
	MDR-TB	25 266	26 180	914 (3.5%)
	XDR-TB	62 636	75 558	12 923 (17.1%)
Non-HPC	New DS TB smear +	13 499	15 478	1 978 (12.8%)
	New DS TB smear –	9 773	11 156	1 383 (12.4%)
	Previously treated TB	26 642	30 690	4 048 (13.2%)
	MDR-TB	55 955	60 702	4 747 (7.8%)
	XDR-TB	143 165	167 511	24 345 (14.5%)

[a]   DS = drug-susceptible.

Table A5.3. Budget for the action plan over the implementation period in million US$ and percentage of total budget by activity

	2016	2017	2018	2019	2020	Total	%
Screening for M/XDR-TB	30	37	45	53	66	231	1.5
HIV screening of M/XDR-TB patients	1	1	2	2	3	9	0.1
Treatment of MDR-TB	750	887	1 037	1 230	1 653	5 557	36.4
Treatment of XDR-TB	32	77	125	179	274	687	4.5
Treatment of DS TB	1 742	1 725	1 729	1 751	1 744	8 691	56.9
Additional costs for HIV treatment	4	5	6	7	10	32	0.2
Stewardship expenditure	15	15	15	15	15	73	0.5
M/XDR-TB total	**2 575**	**2 747**	**2 957**	**3 237**	**3 764**	**15 280**	**100**

Table A5.4. Budget for the action plan over the implementation period in million US$ and percentage of total budget by input

	2016	2017	2018	2019	2020	Total	%
Pharmaceuticals	146	179	215	260	354	1 154	7.6
Diagnostics	131	146	164	187	227	855	5.6
Ambulatory care	826	867	920	992	1 128	4 733	31.0
Inpatient care	1 423	1 499	1 595	1 725	1 961	8 204	53.7
Patient support costs	30	36	43	51	70	229	1.5
Additional costs for HIV treatment	4	5	6	7	10	32	0.2
Stewardship expenditure	15	15	15	15	15	73	0.5
M/XDR-TB total	**2 575**	**2 747**	**2 957**	**3 237**	**3 764**	**15 280**	**100**

The action plan is considered very cost–effective, with a total of 1 089 308 lives saved over the implementation period at a cost of US$ 15 billion, resulting in a cost per life saved of US$ 13 805 and a cost per DALY of US$ 657 (Table A5.5).

The action plan is more cost–effective in HPCs, where the incidence of TB is significantly higher, but in both cases the cost per DALY is well within the range normally considered very cost–effective.

Table A5.5. Cost–effectiveness of action plan over the implementation period

Region	Number of lives saved	Budget of the plan (million US$)	Cost per death averted (US$)	Average of DALYs gained per death averted (years)	Costs per DALY gained (US$)	GDP per capita (US$)	Assessment result
WHO European Region	1 089 308	15 038	13 805	21	657	31 020	Very cost–effective
HPC	906 889	11 195	12 344	21	588	8 997	Very cost–effective
Non-HPC	182 419	3 771	20 671	21	984	41 698	Very cost–effective

The indirect economic gain of the action plan is calculated based on number of DALYs averted and GDP per capita across the Region. As shown in Table A5.6, significant indirect economic gains are realized both in the short term (total of US$ 169 billion) and long term (US$ 710 billion). Direct economic gains result from cost savings relating to TB cases averted and associated reduction in treatment costs. Table A5.7 stratifies these savings by XDR-TB, MDR-TB and drug-sensitive TB patients. In total, direct economic benefits amount to US$ 16.5 billion, with most savings attributable to reduction in drug-sensitive TB treatment costs followed by MDR-TB-related costs.

Table A5.6. Short- and long-term indirect economic gains resulting from the action plan

Region	Number of lives saved	GDP per capita (US$)	Short-term (5 DALYs/life saved)		Long-term (21 DALYs/life saved)	
			Total DALYs averted	Indirect gain (US$ million)	Total DALYs averted	Indirect gain (US$ million)
WHO European Region	1 089 308	31 020	5 446 540	168 952	22 875 468	709 599
HPC	906 889	8 997	4 534 443	40 798	19 044 659	171 353
Non-HPC	182 419	41 698	912 097	38 032	3 830 809	159 736

Table A5.7. Direct economic gains resulting from reduced transmission and treatment costs

Region	Total patients enrolled	Cost per patient	Number of cases averted	Direct economic gain (million US$)
XDR-TB				
HPC	10 359	82 571	20	2
Non-HPC	247	418 885	10	4
MDR-TB				
HPC	228 440	24 606	200 000	4 923
Non-HPC	2 525	82 383	2 000	169
DS TB				
HPC	918 630	5 620	688 228	8 789
Non-HPC	224 681	15 707	154 202	2 587
Total				
WHO European Region				16 473
HPC				13 713
Non-HPC				2 760

References

1. Global tuberculosis report 2014. Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf, accessed 22 May 2016).

2. International drug price indicator guide [online database]. Medford (MA): Management Sciences for Health; 2016 (http://erc.msh.org/dmpguide/, accessed 24 July 2015).

3. Global drug facility [website]. Geneva: Stop TB Partnership; 2016 (http://www.stoptb.org/gdf/, accessed 24 July 2015).

4. Tuberculosis (TB). TB monitoring and evaluation: financing. TB planning and budgeting tool, version 6 [online database]. Geneva: World Health Organization; 2016 (http://www.who.int/tb/areas-of-work/monitoring-evaluation/financing/planning-tool/en/, accessed 22 May 2016).

5. FIND-negotiated product pricing [online database]. Geneva: Foundation for Innovative New Diagnostics (FIND); undated (http://www.finddx.org/pricing, accessed 22 May 2016).

6. The vision ... "a better way to fight TB" [website]. Sunnyvale (CA): Cepheid®: 2013 (http://www.cepheidcares.com/tb/index.php/eligibility/vision/#pricing, accessed 10 May 2016).

7. Cost effectiveness and strategic planning (WHO-CHOICE). Results of unit costs for patient services for the 14 GBD regions [website]. Geneva: World Health Organization; 2016 (http://www.who.int/choice/costs/unit_regions/en/, accessed 22 May 2016).

8. CHOosing interventions that are cost effective (WHO-CHOICE). Price of local (non-traded) goods. EURO A [website]. Geneva: World Health Organization; 2016 (http://www.who.int/choice/costs/prog_costs/en/index7.html, accessed 10 May 2016).

9. CHOosing interventions that are cost effective (WHO-CHOICE). Price of local (non-traded) goods. EURO B [website]. Geneva: World Health Organization; 2016 (http://www.who.int/choice/costs/prog_costs/en/index8.html, accessed 10 May 2016).

10. CHOosing interventions that are cost effective (WHO-CHOICE). Price of local (non-traded) goods. EURO C [website]. Geneva: World Health Organization; 2016 (http://www.who.int/choice/costs/prog_costs/en/index9.html, accessed 22 May 2016).

11. Guidelines for cost and cost-effectiveness analysis of tuberculosis control. Geneva: World Health Organization; 2002 (http://www.who.int/tb/publications/tb-control-cost-effectiveness/en/, accessed 10 May 2016).

12. Data. GDP per capita (current US$) [online database]. Washington (DC): World Bank; 2016 (http://data.worldbank.org/indicator/NY.GDP.PCAP.CD/, accessed 10 May 2016).

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