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POLICY BRIEF

Policy Brief on Revising the TB Action Plan for the WHO European Region 2016-2020: What amendments are needed to reach the UN SDG3 to eliminate TB epidemics by 2030?

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Abstract

Context:

The World Health Organization (WHO) European Region's political attention shifted to the COVID-19 pandemic from the start of 2020 onwards. A consequence of this shift has been decreased political attention towards combating tuberculosis (TB) in the WHO European Region. As a result, decreasing TB data reporting, rising death rates, and increasing antimicrobial resistance (AMR) have prevented the WHO European Region from remaining on track to reach the United Nations Sustainable Development Goal 3 (SDG3) to eliminate TB epidemics by 2030. Furthermore, the WHO tuberculosis action plan for the WHO European Region 2016-2020 has missed opportunities to mitigate TB in this region, thus exacerbating the issue and preventing the achievement of SDG3.

Policy Options:

The WHO's Roadmap to implement the tuberculosis action plan for the WHO European Region 2016-2020 provided guidance for TB management in the member states (MS), but did not sufficiently address AMR, lacking promotion of new TB vaccine rollout, nor describe national TB implementation strategies. The WHO 2016-2020 TB action plan is now overdue and WHO policymakers should consider the following recommendations when creating the new TB action plan.

Recommendations:

This policy brief addresses the urgent need for a new WHO TB action plan to integrate a national level implementation commitment, AMR programming, and WHO support in creating a vaccine strategy with aims for the WHO European Region to achieve SDG3 and eliminate TB epidemics by 2030.

Keywords: AMR, WHO European Region, SDG3, Tuberculosis Action Plan, Tuberculosis, WHO

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Abbreviations:

AMR	Antimicrobial Drug Resistance
AP	Action plan
BCG	Bacillus Calmette-Guérin vaccine
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EU	European Union
EMA	European Medicines Agency
MDR TB	Multidrug Resistance Tuberculosis
MS	Member States of the WHO European Region
TB	Tuberculosis
TB AP	Tuberculosis Action Plan
NGO	Non-Governmental Organization
SDG3	Sustainable Development Goal 3
WHO	World Health Organization
XDR TB	Extensively Drug-Resistant TB

Introduction

Tuberculosis (TB) is the second most infectious killer after COVID-19 (1). A bacterial infection caused by the mycobacterium tuberculosis, TB, most commonly resides in the lungs as pulmonary TB but can infect any part of the body (2). This illness is highly contagious as it spreads through airborne transmission. Although it is both preventable and treatable, without sufficient treatment nearly 45% of people with TB die, and this rate increases for those with compromised immune systems such as coinfection of HIV, COVID-19, etc. (2). Approximately one in four people in the world have a TB infection, and the European Union (EU) has the highest rate of drug-resistant TB in the world (3).

In 2019, the WHO European Region exceeded the 2020 milestone of reducing TB incidence by 25% instead of the targeted 20% (4). However, the COVID-19 pandemic

caused several setbacks, and the WHO European Region is no longer on track to achieve the United Nations Sustainable Development Goal 3 (SDG3) of ending TB epidemics by 2030 (5). Throughout the ongoing COVID-19 pandemic, there has been a drop in TB diagnoses, data reports, TB incidence reporting, funding, and an increase in TB deaths (1; 6). The drop in diagnoses is believed to be attributed to unreported data and not an actual drop in cases; experts believe there has actually been a rise in cases. Furthermore, TB laboratories have been burdened by social distancing measures and fewer resources (7). This is a result of resources being allocated towards COVID-19 control efforts, including personnel, equipment, and monetary resources. Mathematical modeling suggests long-lasting setbacks in TB response and an increase in deaths and incidence due to the COVID-19 pandemic (6).



Another burden for TB is antimicrobial resistance (AMR). This is the ability of bacteria and fungi to develop resistance against drugs that have been produced to eliminate them (8). Organ transplantation, cancer chemotherapy, and major surgeries can become high-risk without an appropriate answer to antimicrobial treatment. Misuse and overuse of antibiotics are the main contributors to accelerating this process (9). This is an urgent problem that affects people's lives every day and results in prolonged illness, disability, and death. This problem is especially pertinent for those with TB since antibiotics are vital to treat the infection (10).

Additionally, AMR dramatically increases the financial burden on national governments. According to the European Commission, the 3.000 deaths due to AMR cost the EU €1.5 billion per year in healthcare costs and productivity losses in 2017 (11).

In the WHO European Region, we can observe that European countries have different levels of drug resistance. EARS-Net data for 2019 displayed wide variations in the occurrence of AMR across the EU/EEA depending on the bacterial species, antimicrobial group, and geographical region (12). Moreover, a North-to-South and a West-to-East gradient could be observed in

the EU/EEA for several bacterial species–antimicrobial group combinations (12). This gradient refers to the observation that AMR rates in Western and Northern Europe are lower than in Eastern and Southern Europe. For instance, Norway is located in the North and has a lower AMR rate than Bulgaria, Greece, and Romania, situated in the East and South.

As a bacterial disease, TB demonstrates a similar pattern. Due to AMR, in 2019 only 63.7% of tuberculosis cases were treated successfully; 43.2% for Multidrug-Resistant Tuberculosis (MDR TB) cases at 24 months, and 34.9% among Extensively Drug-Resistant Tuberculosis (XDR TB) cases at 36 months (13). Countries with the highest proportion of MDR TB rates among examples with drug susceptibility (DST) results (excluding France) were Estonia (21.3%) and Lithuania (17.0%), which are situated in Central-East Europe. This fact also reflects the geographical pattern mentioned above (Figure 1). For instance, in Portugal, which is located in Western Europe, MDR TB rate was only 1% of all TB events. XDR TB was reported for 21.9% of 584 MDR TB cases tested for second-line drug susceptibility in EU/EEA region (13).

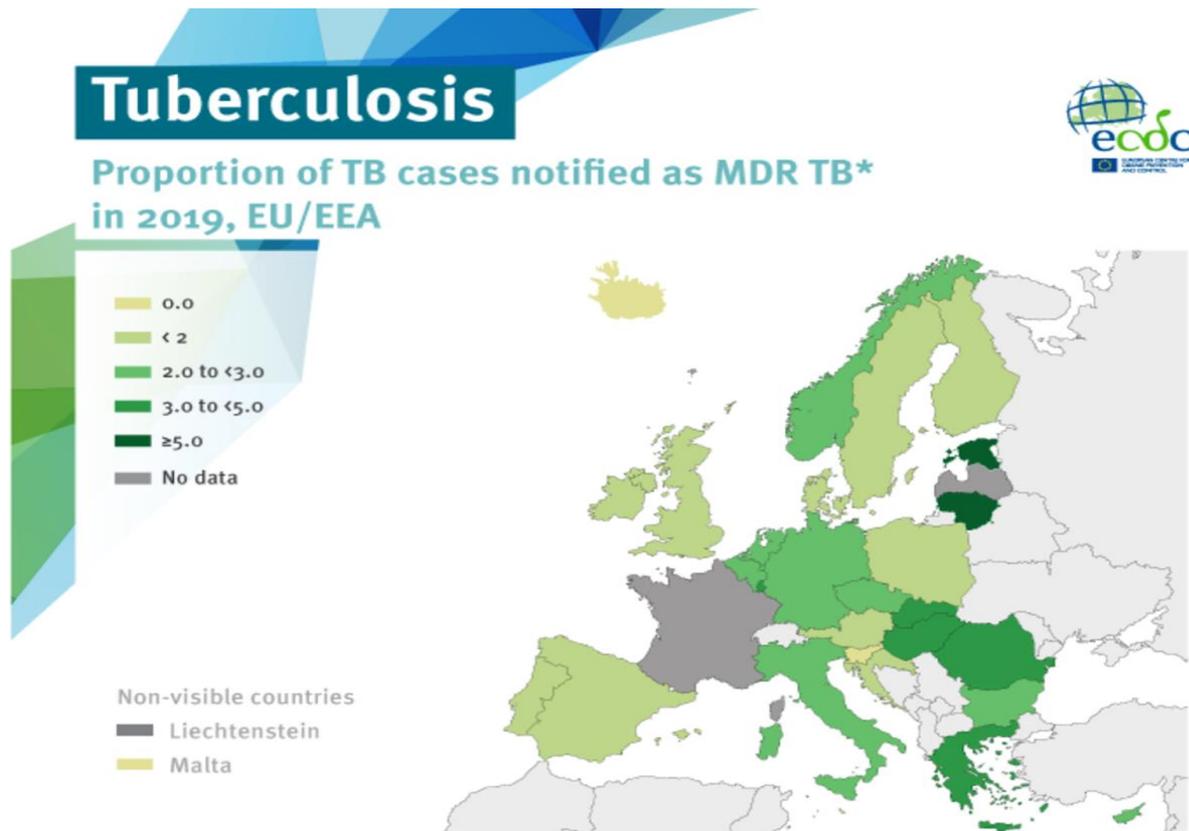


Figure 1. The proportion of TB cases notified as MDR TB in 2019, EU/EEA (retrieved from ECDC. Tuberculosis surveillance and monitoring in Europe 2021 –2019 report 13).

The United Kingdom Health Security Agency warns of a ‘hidden pandemic’ of antibiotic-resistant infections after COVID-19 due to misuse of drugs in case of viral infections (14). Considering the fact that developing new antibiotics is a difficult process with an assessed failure rate of 95% (15) and the mean cost of developing a new drug has been estimated to be between \$314 million to \$2.8 billion (16), further disregard of this problem will lead to critical consequences.

Additionally, the lack of a widespread vaccination campaign also reflects the increased number of TB cases. Currently, only the BCG vaccine is available and used

against TB. It does not provide 100% protection against the development of TB, but it does offer protection for the most serious forms and complications of TB at a young age. It demonstrates 80% effectiveness against severe forms of childhood TB (TB meningitis) and roughly 60% for pulmonary TB (17). The protection effect lasts for 20 years (17). The BCG vaccine is only included in 15 European countries' immunization program schedules.

Despite controversial data in research about the effectiveness of the BCG vaccine, another type of immunization has not been established. Currently, 15 vaccines are under development; 6 of them are at the third phase of clinical trials (re-BCG included) and are

expected to come to market soon. However, a lack of financing impedes the research of a new vaccine against TB. Statistics show that governments spent an estimated US\$90 billion on COVID-19 vaccine research and development (R&D) in the first 11 months of the pandemic; this is nearly 82 times the US\$1.1 billion the world spent on TB vaccine research in the last 11 years (18).

Context

The WHO European Region developed a tuberculosis Action Plan (AP) 2016-2020 to address TB (19). This AP was part of the policy to achieve SDG3. The AP was largely based on the framework proposed by Lönroth et al. 2015. It originally consisted of 8 priority action areas; political commitment, reaching vulnerable groups, cross-border, screening, prevention, surveillance, research, and control (20). The WHO European Region provided support to reach several goals. These goals focused on:

- Care of TB patients and preventing the spread of TB among vulnerable groups and hard-to-reach populations;
- Policies and supportive systems to address the lack of political commitment and infrastructures;
- Intensifying research and innovation to create tools and new vaccines to stop TB spread.

In the AP, the WHO European Region pointed out how screening programs, better monitoring, cross-border collaboration, and ensuring access to treatment have taken place. However, the AP omits some issues. For instance, the rise of AMR was not explained and AMR was only mentioned once in the annex of the original AP.

Moreover, vaccine research has been performed, but no clear strategy on how to organize distribution and infrastructure was described. Furthermore, the AP stated that declining TB visibility could lead to less political commitment. This happened at the start of the ongoing COVID-19 crisis when the political attention shifted to managing the pandemic. The AP did not provide a structure that ensured the above-mentioned goals would be fulfilled if an emergency occurred.

The World Health Organization monitored the AP implementation until their final report in 2020. The most important observation that emerged from their monitoring is a persistent lack of political commitment. Most reports say that politicians, policymakers, and high-level officials are responsible for making available structural national funding for TB research and methods of measurement for TB prevention and detection. If there is no commitment, the fight against TB will be inadequate. Additionally, the European Centre for Disease Prevention and Control (ECDC) produced an overview document in 2016 on why interventions for vulnerable groups are necessary. They recommended that teams should form to garner better involvement of partners to integrate services, ensure adherence to the treatment protocol, and promote TB awareness and education (21).

Furthermore, several studies have evaluated the AP interventions. For example, Rafetery et al. (22) examined a training program for strengthening European National Reference laboratories in combating TB. This program demonstrated success in developing leadership, expertise, partnerships, and networks to support TB laboratories. Additionally, a European Union Funding for Research & Innovation report (23) found the



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development of TB vaccines an accomplishment towards ending TB epidemics.

Lastly, the WHO European Region's (24) final report on the implementation of the AP acknowledged their progress prior to the onset of COVID-19. Many 'in-between' goals were reached, but since the pandemic, funding, research, and diagnosis have decreased while the TB death rate has increased. Despite the WHO European Region's accomplishments, many targets lie ahead to achieve SDG3.

Policy Options

The WHO roadmap for implementing the AP is addressed to those responsible for TB

prevention and care in the Member States (MS) (ministries of health and other government bodies, health financing, health education, Non-Governmental Organizations (NGOs), social services, and other stakeholders). According to the WHO, this roadmap is applicable for all EU/EEA MS. Nevertheless, the implementation of the AP has not been fully processed in all of the MS (25). Data about the how the AP was implemented during the COVID-19 pandemic is lacking. Therefore, data from 2017-2019 was obtained to analyze the progress of implementation of national TB strategies and the AP. The latest survey was conducted by Collin et al. (26) in 2017 and demonstrates the progress of national implementation strategies (Figure 2).

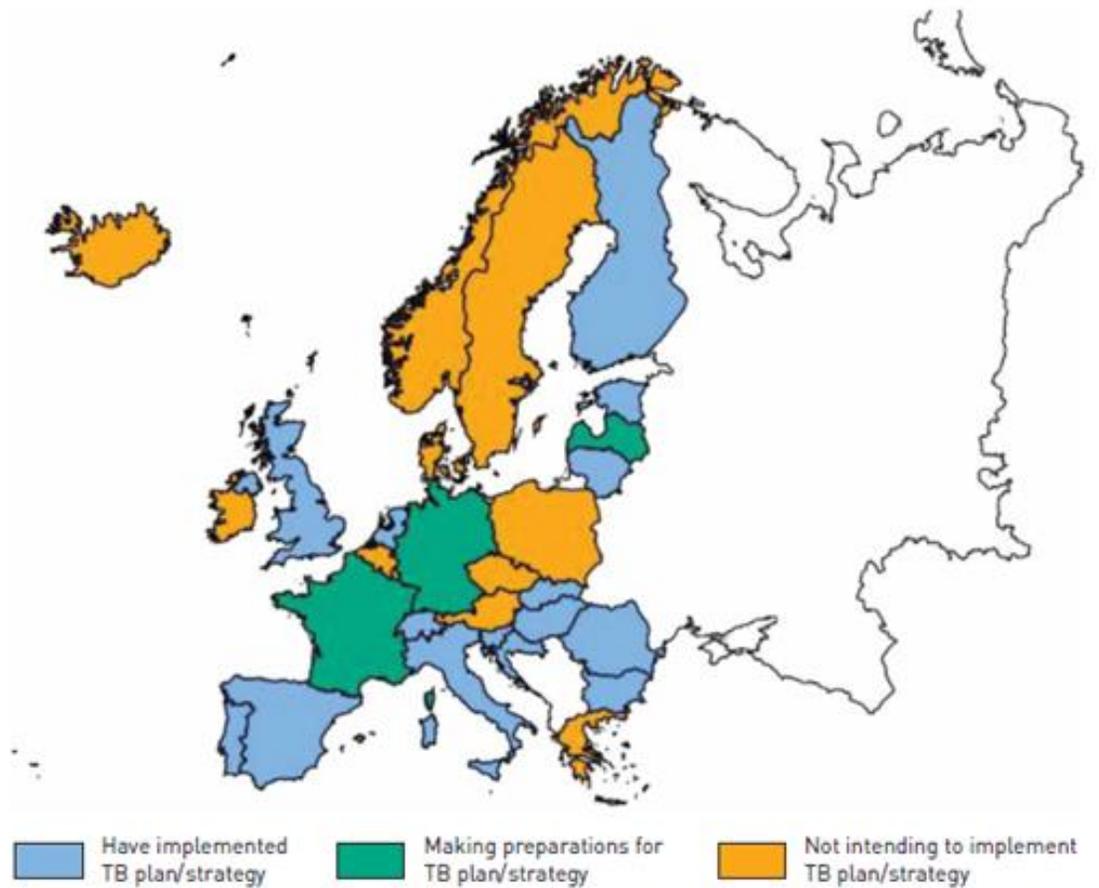


FIGURE 1 National tuberculosis (TB) control plans or strategies in European Union/European Economic Area countries.

Figure 2: National TB strategy implementation in EU/EEA countries in 2017 (25)

Collin et al. (26) identified three barriers referring to vulnerable/high-risk groups that impede TB control in the majority of EU/EEA countries: lack of knowledge, low motivation to adhere to treatment, and low motivation to seek treatment. Countries reported that special TB training is needed for health care workers at local levels and especially for nurses in TB patient care. In some countries, the low incidence of TB led to neglecting the importance of training

health care workers in adequate TB care. Additionally, political commitment for better TB control seems to be low, which results in insufficient funding. It was found that general health system constraints for TB care increase gaps in TB control between the MS. On the one hand, most of the countries rated reaching vulnerable population groups, screening for active cases, and implementation of electronic TB registers as high priority areas for action. On the other

hand, BCG vaccination and establishing or managing TB control boards were most frequently rated as low priority areas (26).

WHO End TB Strategy Implementation Progress

0%	0%-25%	25%-50%	50%-75%	75%-100%
Spain	Croatia	Italy	Hungary	Lithuania
United Kingdom	Greece	Finland	Portugal	Romania
France		Slovakia	Germany	Slovenia
Austria		Netherlands	Ireland	Estonia
Iceland		Switzerland		
Cyprus		Latvia		
		Sweden		
		Poland		
		Denmark		
		Norway		
		Czechia		
		Belgium		
		Luxembourg		

	Have implemented national TB strategy in 2017
	Prepared implementation of national TB strategy in 2017
	No intention to implement national TB strategy in 2017

Table 1: WHO End TB Strategy Implementation Progress in % in 2019, including data about national TB strategy implementation in 2017 from (25).

In Table 1, data from Figure 2 was merged with data about the implementation progress of the End TB Strategy in 2019 (27), stated in the WHO roadmap. The coloring of the national TB strategy from Figure 1 (26) was applied to the implementation progress of the AP in 2019. The percentage represents the progress of implementation of the AP related to 86 areas. The ECDC (27) did not elaborate on these 86 areas, stated in their Annex 4, which is a limitation. Most of the orange countries without a national plan

implemented under 50% of the AP, with the exception of Ireland. The implementation progress of blue-marked countries, however, is varied. The majority of countries are still scoring under 50% concerning implementation progress.

Overall, Lithuania, Romania, Slovenia, and Estonia progressed in their implementation of the AP. However, Estonia, and Lithuania show rising AMR rates, which confirms the North-to-South and the West-to-East

geographical pattern described above (27) and is demonstrated in Figure 3. Countries with the highest level of MDR TB as a consequence of AMR's geographical pattern

(Estonia, Lithuania, and Romania) have implemented a national TB strategy in 2017 and were on track with implementing the AP in 2019.

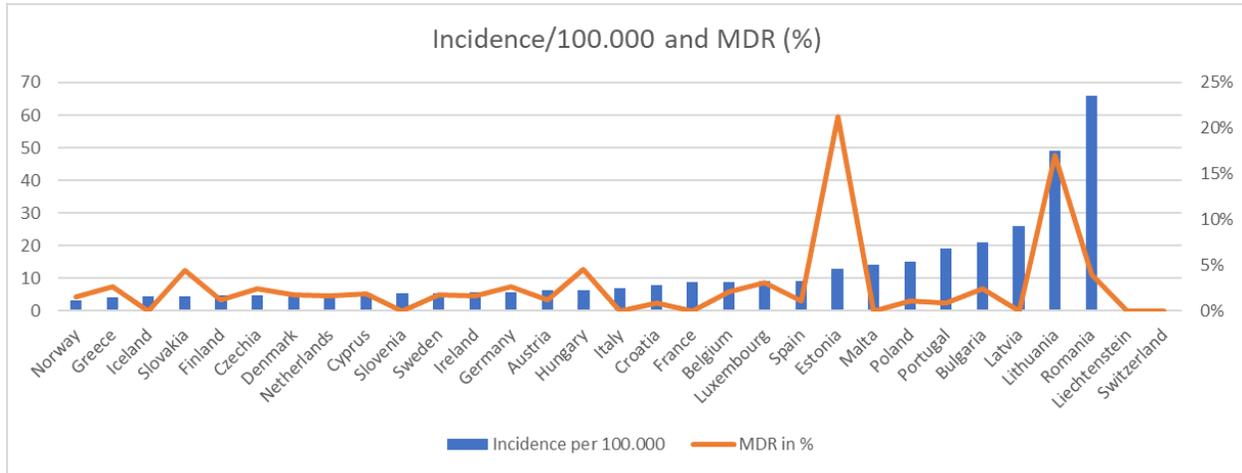


Figure 3: Incidence of TB per 100,000 and MDR rates in % based on data retrieved from (27)

The COVID-19 pandemic, rising AMR rates, and stagnant TB vaccination rates add to the burden of TB across the WHO European Region and hinder efforts to achieve SDG3 to end TB epidemics by 2030. Additionally, the AP contains several missed opportunities. The 2016-2020 AP must be amended, and a new AP created for the WHO European Region to get back on track. To achieve SDG3, the new WHO European Region TB AP should integrate the policy recommendations detailed below.

Recommendations

Our proposed upcoming 2022-2027 AP requires new guidelines that build upon existing frameworks and address pressing TB issues in order to get back on track with achieving SDG3. This new AP should

integrate both WHO European Region guidelines and country-specific national strategies to address local and regional barriers to eliminating TB epidemics. Three policy recommendations below detail specific measures the WHO can include in the new AP in order to bolster political will and mitigate barriers that hinder reaching SDG3. WHO policymakers responsible for creating a new AP should therefore consider the following policy recommendations.

1. Promote agenda setting and evaluated commitment at the national level

The WHO European Region AP includes helpful guidance for better TB control, e.g., the collaborative monitoring of TB data as well as guidance for screening programs. Vulnerable population groups were identified, and the WHO recommends more awareness to make TB care and prevention

accessible for all population groups (25). Nevertheless, Collin et al. (26) demonstrated that the MS set different priorities in TB control and are facing different barriers concerning the implementation of TB strategies. This leads to problems regarding the commitment and implementation of the AP and highlights the importance of clear guidance in a new plan. Therefore, TB needs to be reintroduced into the political agenda with clear guidelines concerning common goals and progress evaluation. A strong commitment from all WHO European Region countries is needed to achieve SDG3. Country-specific guidance is needed for providing support for the implementation of the AP. Therefore, the WHO European Region should amend the new AP to make it applicable for all EU/EEA MS TB situations and other territories, including the incidence, mortality, treatment guidelines, and vaccination rates. Standardized goals applicable for all MS can prevent implementation differences through common goal setting and evaluation of progress. The new guidance should recommend educational interventions for health care workers and TB patients in ministries of health and local health services to educate physicians and nurses working in TB care settings. Evaluation guidelines can promote regular monitoring and help identify gaps in the education of healthcare workers as well as communication problems between the EU/EEA MS, at national and regional levels.

Management structures of TB care need to be implemented at national levels. This can be assured through binding guidelines that are based on the recommendations of the WHO and set out by health ministries. The WHO should also refer to the “TB Strategy Toolkit”, which gives recommendations on the development and implementation of

national TB strategies (28). This toolkit focuses on adjusting a TB strategy to country-specific TB situations and aims to create consistency with national health policies and national health plans. Guaranteed TB care resources need to be provided and should not be used for other crisis management situations. Technical assistance and funding must be guaranteed in all MS, which can be planned and calculated with the “TB Strategy Toolkit” (28). Combining the toolkit with guidance from the WHO for the new AP should help reintroduce TB and especially MDR TB into the political agenda of the EU/EEA MS.

2. Include AMR into the new Action Plan

AMR issues were not deeply integrated into the previous AP. For instance, rising AMR rates through EU/EEA countries have become visible, and the prevalence of MDR TB forms increased as a result. Therefore, this problem has to evolve into a new milestone for the WHO European Region in combating TB. A strong engagement between MS to increase observational, informational, educational, and resilience resources in case of TB treatment needs to be established.

First of all, national governments should appropriately revise and update their medical protocols for antibiotic prescription in case of bacterial infection along with TB and include novel medicines for MDR TB care. Secondly, proper education and communication for the medical and public health workforce need to be established to ensure that the AMR-combating strategy will be successfully implemented. Thirdly, national governments should inform the medical staff about the new AP goals and how to achieve these goals (e.g., goals that



measure AMR rate decrease and MDR TB successful treatment percentage increase), and develop digital instruments for strong monitoring of antibiotic prescription according to the protocol. Lastly, wide-ranging information campaigns about the misuse of antibiotics and the harmful consequences of their overuse need to be developed and presented for patients by national and local governments to increase population awareness of AMR. These steps could decrease antibiotic consumption and provide a reduction of AMR rates. Therefore, an AMR combating strategy needs to be part of the new AP.

3. Vaccination Strategy

TB is a vaccine-preventable disease, and wide vaccination campaign could decrease the incidence of TB cases. However, a vaccination strategy was not included in the previous AP, and this is a lost opportunity for the WHO European Region.

The COVID-19 pandemic demonstrated how European Region countries could promptly arrange vaccination campaigns and immunize a considerable part of the population. Therefore, TB vaccination could rely on a similar scheme once new vaccines become available. Additionally, the WHO and national governments need to allocate funding for researching new vaccines against TB, as due to the COVID-19 crisis a lot of resources were relocated. For instance, new research grants should be provided for scientists to boost clinical trials. Furthermore, while new vaccines are under development, national governments should organize their own medical infrastructures to allow for quick vaccine distribution after approval is granted by European Medicines Agency

(EMA) or equivalent organizations in the region. Moreover, preparations for creating a vaccination partnership for TB could make immunization affordable for the most vulnerable countries. These actions will facilitate delivering new vaccines to the most susceptible population groups and help reach SDG3. In sum, an appropriate immunization strategy against TB, sufficient funding for novel vaccine development, and adequate market distribution needs to become a part of the new AP.

Conclusion

The WHO European Region is no longer on track to reach SDG3 to end TB epidemics by 2030. This is a combined result of the COVID-19 pandemic deviating political attention and resources away from TB, increasing AMR rates, and an outdated AP with several missed opportunities to facilitate achieving SDG3. WHO policymakers should urgently focus on creating a new 2022-2027 AP, taking the following recommendations into account:

- Promote agenda setting and evaluated commitment at the national level
- Include an AMR-combatting strategy
- Promote research towards new TB vaccine development and rollout

By bolstering political will towards TB with the new AP, the WHO can facilitate a more robust TB strategy aimed at mitigating TB epidemics in the WHO European Region. By including the above policy recommendations, TB will hopefully be reduced and the WHO European Region can get back on track with achieving SDG3.



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