# POLITICAL OPPORTUNITIES AND R&D TO COMBAT MDR-TB

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In 2015, TB overtook HIV as the number one infectious disease killer with 1.6 million people dying from this curable disease in 2016. 2018 is a pivotal year for TB, representing an opportunity to build on the commitments from the first high-level ministerial summit on TB in 2017. New funding and political commitments, particularly for TB R&D, must be secured at the upcoming UN high-level meeting on TB and the AMR R&D discussions at the G20. Drug-resistant forms of TB has been highlighted as a cornerstone in the response to AMR and it is vital that the importance that drug-resistant TB will play in future morbidity and mortality for AMR is recognized.

In April 1993, WHO declared a global tuberculosis (TB) emergency, and in 2015 TB overtook HIV to become the number one infectious disease killer. In 2016, 10.4 million new cases of tuberculosis were reported with 1.6 million people dying from this curable infectious disease *(1)*. In addition, the emergence of drug-resistant forms of TB since 1993 means that over 600,000 people were diagnosed with TB that is resistant to the two most effective drugs (Rifampicin and Isoniazid) in 2016 *(1)*. With the increased political attention on antimicrobial resistance (AMR), the importance that drug-resistant TB will play in future morbidity and mortality for AMR cannot be under estimated. The 2014 AMR review commissioned by United Kingdom Prime Minister David Cameron stated that if nothing changes, TB could represent a quarter of the 10 million deaths expected from drug-resistant infections by 2050 *(2)*.

*The Global Burden of Disease Study* shows that deaths caused by tuberculosis in 2016 were down by nearly 21%, since 2006, and the incidence of tuberculosis was down by 1.7% *(3)*. However, this rate of decline is not nearly sufficient enough to meet the target set in SDG 3 *(4)* or the WHO END TB strategy *(5)*, which aims to end the epidemic by 2030. For these targets to be achieved the annual decline in global TB incidence rates must reach 10% per year by 2025.

The strong link between TB and achieving the SDG goals has been recognized at the highest political level with the first WHO Global Ministerial Conference on TB entitled "Ending TB in the Sustainable Development Era: A Multisectoral Response". The call for a multisectoral response is due to the fact that the impact of TB does not only affect SDG 3 but has an impact for a number of other SDGs (see Figure 1).

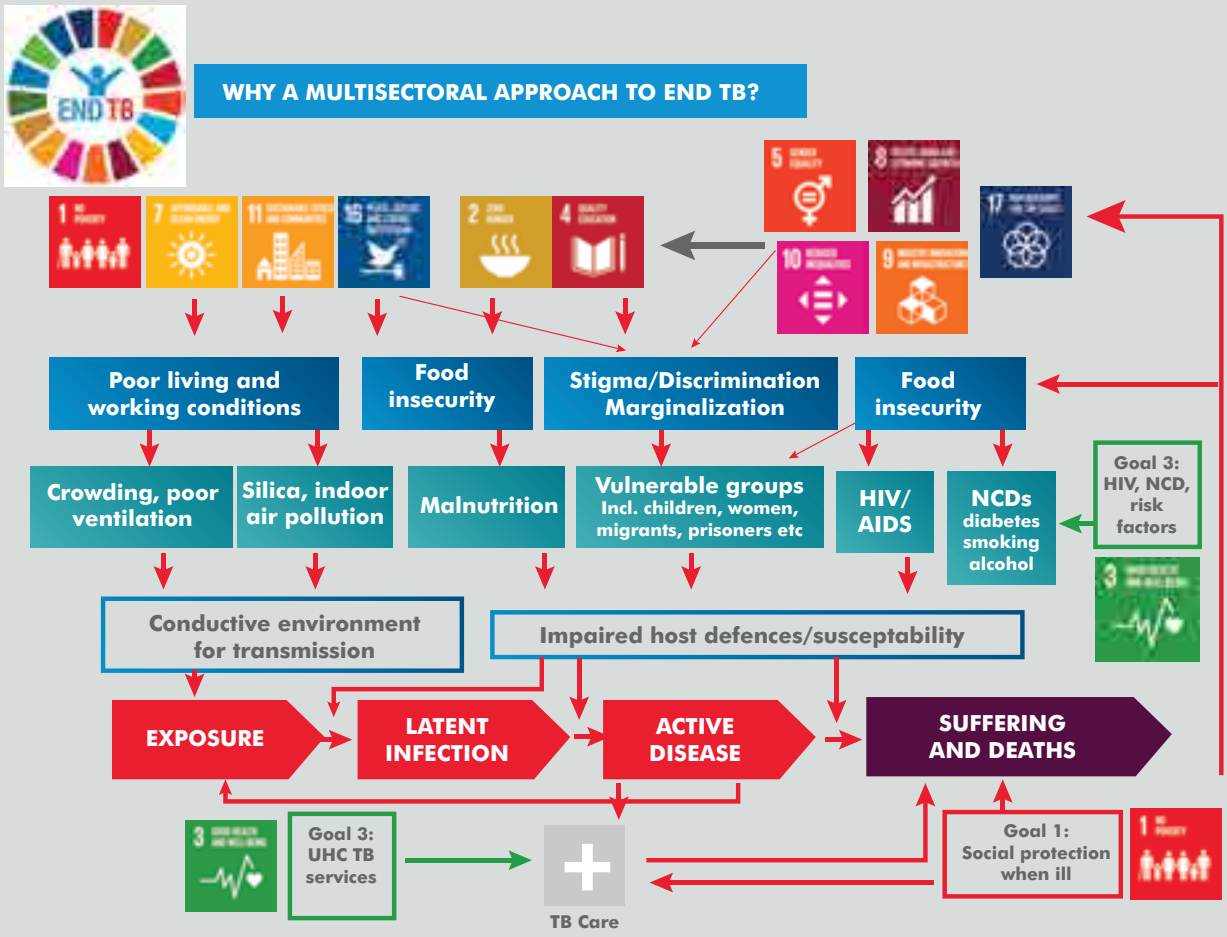
The Moscow Declaration *(6)* reaffirmed the commitment to end the TB epidemic by 2030 as envisaged in the Agenda 2030 for Sustainable Development and the SDGs, the WHO End TB Strategy, and the Stop TB Partnership Global Plan to End TB 2016–2020 *(7)*. The Declaration broke the multisectoral response for TB into four broad areas:

- Advancing the TB response within the SDG agenda;
- Ensuring sufficient and sustainable financing;
- Pursuing science, research and innovation;
- Developing a multisectoral accountability framework.

As part of advancing the TB response within the SDG agenda, the importance of MDR-TB as a priority within the AMR context was highlighted. The declaration had countries commit to implement measures aimed at minimizing the risk of the development and spread of drug resistance taking into account global efforts to combat AMR and to address MDR-TB as a global public health crisis including through a national emergency response in at least all high MDR-TB burden countries, while ensuring that robust systems are sustained in all countries to prevent emergence and spread of drug resistance. The declaration called for WHO, other UN agencies, funding agencies and technical partners to address MDR-TB as a major threat to public health security by supporting implementation of the Global Action Plan on AMR in all countries, and referenced the political declaration of the high-level meeting of the UN General Assembly on antimicrobial resistance.

The importance of MDR-TB as a priority AMR pathogen

Figure 1: **TB and the SDGs**




*Source: Knut Lönnroth and Mario Raviglione, WHO Global TB Department. Source: Knut Lönnroth and Mario Raviglione, WHO Global TB Department.*

was again highlighted in the declaration's commitment focused on science, research and innovation. The declaration called for WHO, in collaboration with global health and research partners and countries, to make further progress in enhancing cooperation and coordination of TB research and development, considering where possible drawing on existing research networks to integrate TB research, such as the new AMR Research and Development Collaboration Hub proposed in the 2017 G20 Leaders' Declaration *(8)*.

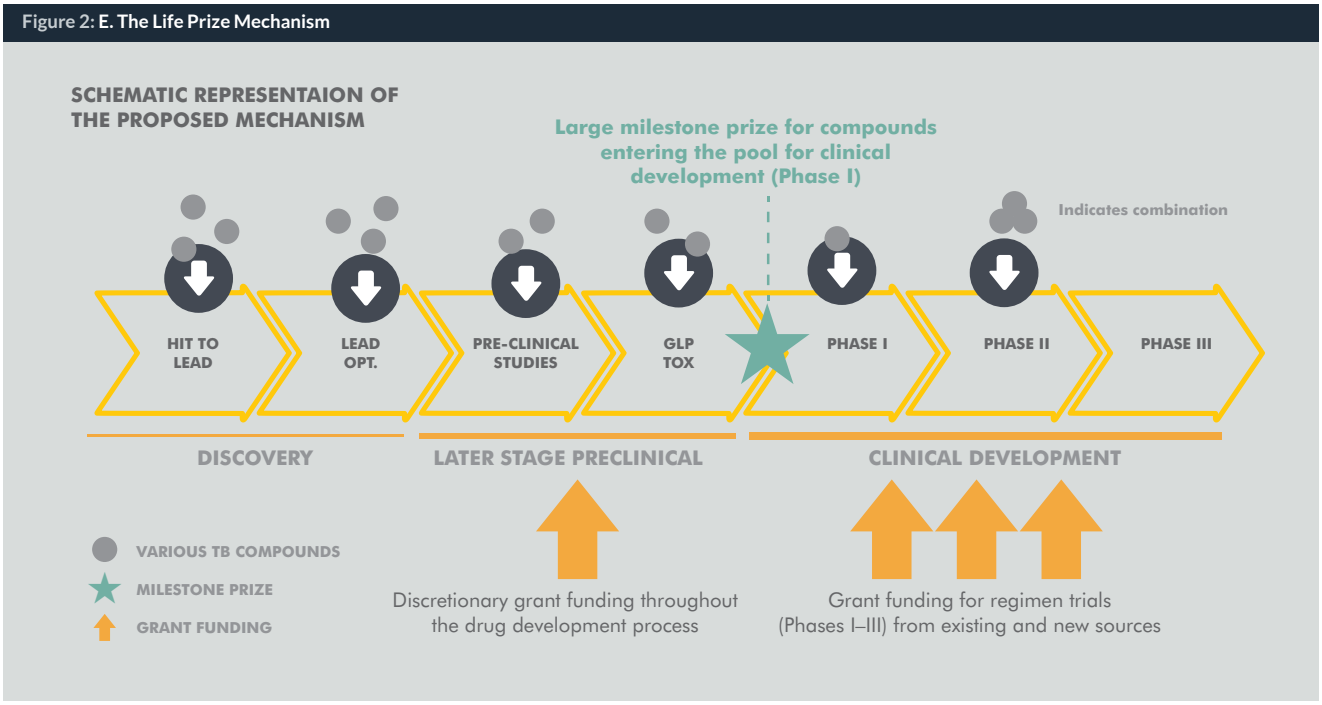
Leaders from more than 120 countries have endorsed the Moscow Declaration, which also called for countries to prepare for and follow-up on the first UN General Assembly High-Level Meeting on TB in 2018 where the link to the SDGs and AMR will be continued.

The SDG and WHO END strategy targets rely on the development of new tools for TB, and the WHO END TB strategy has a whole pillar focused on research and development. TB suffers from the market failure that has been well articulated for AMR. This lack of perceived market to recoup R&D investment has meant that TB R&D funding has never been more than a third of what is required, and in 2016 investment in R&D from the pharmaceutical industry was the lowest since 2009 *(9)*. This sustained lack of investment has resulted in a lack of innovation in all areas of R&D from diagnostic, treatment and vaccine development and without new innovations in these areas, the ambitious SDG and END TB goals will remain unmet.

There have been a number of reports looking at ways that the market failure that exists for antibiotic development (including antibiotics that are used to treat TB) can be overcome and it has been discussed at a number of high level political fora such as a United Nations General Assembly High Level meeting on AMR in 2016 and in recent G7 and G20 meetings. In all the declarations from these meetings, TB was included as a priority pathogen to be included in the resulting commitments.

The declarations included discussions around delinking the costs of research and development from the end product as a path forward. These de-linkage models promote the development of affordable medicines based on the needs of

Figure 2: **E. The Life Prize Mechanism**




patients rather than profits.

One delinkage model for R&D for TB drug and regimen development is The Life Prize *(10)* – a new and innovative funding mechanism, being developed incorporating the de-linkage principle as outlined in the UN declaration on AMR *(11)*. The Life Prize innovates, not just at the level of the traditional WHO definition of innovation (namely, new chemical classes) but also looks to change the current incentives to ensure that not only are the right incentives in place to promote innovation but that new treatments for TB developed within this framework are affordable and accessible to all who need them. The Life Prize consists of three elements: prize funding for drugs entering clinical trials that fulfil predefined criteria, additional grant funding to finance the development of a pan-TB regimen in line with target regimen profiles with all funding to require sharing of intellectual property and pre-clinical and clinical data. This enables open collaborative research and fair licensing for the competitive production of the final treatments. (Figure 2)

The recently launched "G20 Global R&D Collaboration Hub" *(12)* on AMR is intended to pinpoint important gaps in the development of tools to combat AMR, such as antibiotics, diagnostics and vaccines. The Global R&D Collaboration Hub on AMR referenced in the Moscow Declaration could be considered as one possible approach to achieving high-level coordination for new financing mechanisms like The Life Prize and although it is not clear yet how this hub will incorporate TB R&D, it is clear that TB should be a key pathogen for the hub.

Achieving decline rates required by 2020 requires increased political and financial commitments to strengthen member states' TB policies and practices and to close funding gaps, including for research and development for new TB tools appropriate for all ages. A recent report from the Global TB Caucus showed that closing the research and development funding gap could have a transformative impact on TB, and cost less than 1% of the total economic cost of the disease *(13)*.

With all the attention on AMR and TB, 2018 is a pivotal year for TB. The attendance and focus at the Moscow Ministerial Summit and the inclusion in G20 and BRICS declarations shows that TB is rising up the political agenda. It is vital that all member states and relevant stakeholders support the implementation of the Moscow Declaration to End TB and ensure that the political focus of this global killer is raised to the head of state level at the upcoming United Nations General Assembly high-level meeting on TB in 2018. It is vital that the highest level of political participation is secured for the HLM and that the required new funding and political commitments for ending TB are achieved. As the experience from 1993 shows, declaring TB a global emergency was not enough to stop the deaths from a curable infectious disease. It requires concrete actions. ■

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*Prior to this, JL. Castro advised WHO and the Government of India on the implementation of the Revised National TB Control Programme and was Director of Operations for New York City's*

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*Grania studied medicine at the University of Aberdeen, Scotland and continues to work in an ad hoc basis for the NHS as an honorary consultant at the Royal Free Hospital, London. She is based in Geneva, Switzerland.*

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