

BRICS TB Research Network

Background and context

The problem of TB in the BRICS: In 2016, there were an estimated 10.4 million new (incident) TB disease cases worldwide, of which 90% were adults, 65% were male, 10% were people living with HIV (74% in Africa) and 56% were in five countries: India, Indonesia, China, the Philippines and Pakistan. The same year, there were 600 000 new cases with resistance to rifampicin (RRTB), the most effective first-line drug, of which 490 000 had multidrug-resistant TB (MDR-TB). The countries with the largest numbers of MDR/RR-TB cases (47% of the global total) were China, India and the Russian Federation.

Moreover, up to 40% of the estimated 10.4 million new TB cases in 2016 were either not diagnosed or not formally notified to health systems. These "missing 4 million" people with TB were either treated late or not treated at all, allowing for continued TB transmission. Ten countries accounted for 76% of the "missing" people; the top three were **India** (25%), Indonesia (16%) and Nigeria (8%). Moreover, only 22% of the estimated 600 000 cases of rifampicin-resistant TB and DR-TB globally started treatment; **India** and **China** accounted for 39% of the global gap.

Brazil, Russia, India, China, and South Africa (BRICS) accounted for 40% of the global TB disease burden and mortality, and at least 50% of the global MDR/RR-TB cases. BRICS have spent at least 20 billion USD during the past decade in TB control efforts alone $(\underline{1})$.

• The need for TB R&D: Despite significant achievements, the scientific advances of the past 15 years will not be sufficient to reach the SDG targets. Mathematical modeling indicates that major reductions in TB incidence will require the development and introduction of drastically new technologies (2).

The End TB Strategy highlights the need for an affordable, effective and rapid-point of care diagnostic, vaccine that is effective pre- and post-exposure, and safer and shorter treatment for all forms of the disease (3). The current pipelines for new TB diagnostics, drugs and vaccines can meet some – but not all – of these needs, so progress in product development will depend on continued and increased support for basic science and discovery. Given the longstanding underfunding of TB research, "greatly enhanced and immediate investment in research and development will be required" to introduce new tools by 2025, the world can meet the goals and targets of the SDGs and the End TB Strategy by 2030 (4).

• The role of TB R&D in achieving SDG goals: Innovation to address the TB epidemic supports and advances the quest to achieve the following SDG goals (from *Global TB Report 2017, TABLE 2.3B TB-SDG monitoring framework: indicators to monitor beyond SDG 3*):

- SDG goal (1) End poverty in all its forms everywhere
 - Poverty is a strong risk factor for TB, operating through several pathways. Reducing poverty should also facilitate prompt health-care seeking. Countries with higher levels of social protection have lower TB burden. Progress on both indicators will help to achieve the End TB Strategy target to eliminate catastrophic costs for TB patients and their households.
- SDG goal (2) End hunger, achieve food security and improved nutrition and promote sustainable agriculture
 - Under-nutrition weakens the body's defence against infections and is a strong risk factor for TB at the national and individual level.
- SDG goal (3) of ending Tuberculosis, reducing mortality and morbidity from HIV; reducing smoking and alcohol use; achieving Universal Health Coverage; and reducing premature mortality among women and children:
- SDG goal (7) Ensure access to affordable, reliable, sustainable, and modern energy for all
 - Indoor air pollution is a risk factor for TB disease at the individual level. There
 has been limited study of ambient air pollution but it is plausible that it is linked
 to TB incidence.
- SDG goal (8) Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all
 - Historic trends in TB incidence are closely correlated with changes in the absolute level of GDP per capita (but not with the growth rate).
- o SDG (10) Reduce inequality within and among countries
 - TB is a disease of poverty, and deceasing income inequalities combined with economic growth should have an effect on the TB epidemic.
- SDG (11): Make cities and human settlements inclusive, safe, resilient and sustainable
 - Living in a slum is a risk factor for TB transmission due to its link with overcrowding. It is also a risk factor for developing TB disease, due to links with air pollution and undernutrition.
- SDG goal (17) of enhancing cooperation and access to science, technology and innovation, as well as their sound dissemination in congruence with the necessary capacity building.
- Funding gap for TB R&D: Despite some progress in the pipeline for new vaccines, diagnostics, drugs and regimens, TB R&D remains severely underfunded. TB is one of the top 10 causes of mortality globally, but receives only 0.25% of the estimated US\$ 265 billion spent on medical research annually (5). According to estimates in the Global Plan, at least US\$ 1.8 billion per year is needed for TB R&D, less than 50% of the projected needs are currently available. BRICS contribution totals to less than 5% of global contribution, not commensurate with its global burden of the disease.

- Overview of TB R&D initiatives among the BRICS countries: In recent years, the BRICS countries have individually taken steps to accelerate knowledge and technology in TB nationally through strategic plans and initiatives focused on TB (<u>6</u>, <u>7</u>, <u>8</u>). For example, science and technology features prominently in China's new national spending plan (<u>9</u>). In recent years, the BRICS countries have each taken steps to organize and promote TB research at the country level. In 2016, the Government of India launched the India TB Research Consortium, which aims to bring together all major national and international stakeholders to develop new tools for TB (<u>10</u>). In 2015, Brazil established its National TB Research Strategy, which builds on the decade-long experience of the Brazilian TB Research Network (REDE-TB), a group whose members represent universities, industry, the public health system and civil society (<u>11</u>). In South Africa, the Strategic Health Innovation Partnerships, a special product-development initiative managed by the SAMRC, has flagged TB as a priority research area (<u>12</u>)
- Political declarations: The BRICS ministers of health have called for coordinated action on TB R&D on several occasions. In the 2012 Delhi Communiqué, the BRICS countries resolved to collaborate to develop "capacity and infrastructure to reduce the prevalence and incidence of TB through innovation for new drugs, vaccines, diagnostics and promotion of consortia of TB researchers to collaborate on clinical trials of drugs and vaccines" (13). These ideas were reiterated in 2014 when the BRICS ministers of health met in Brazil and agreed to cooperate on research and innovation for TB, identifying technology sharing, manufacturing capacity and TB financing as key priorities (14). In December 2016, the BRICS ministers of health returned to Delhi, where eight of the 25 points in the resulting communiqué concerned research. Most importantly, the BRICS health ministers "agreed to the setting up of a BRICS network on TB research and creation of a research and development consortium on TB, HIV and malaria including the possibility of international fund raising" (15).

These multiple resolutions by the BRICS health ministers to work together on TB research were echoed by leaders of the BRICS nations when they met in Xiamen, China, in September 2017. In the declaration released at the summit, the BRICS heads of state agreed to "foster the development and improve the availability of innovative medical products through promotion of research and development". Importantly, the declaration specifically referenced efforts to establish new global frameworks to advance TB research in line with the SDGs. BRICS leaders welcomed "the decision to set up the **Tuberculosis Research Network**", an initiative described in the recommendation section of this policy paper, and that was presented at the First WHO Global Ministerial Conference on Ending Tuberculosis in the Sustainable Development Era: A Multisectoral Response, in Moscow in November 2017.

References

- 1. World Health Organization. Global tuberculosis report 2017. Geneva: World Health Organization; 2017.
- Dye C, Glaziou P, Floyd K, Raviglione M. Prospects for tuberculosis elimination. Annu Rev Public Health. 2013;34:271-86.
- 3. World Health Organization. Global strategy and targets for tuberculosis prevention, care and control after 2015: report by the secretariat. Geneva: World Health Organization; November 29, 2013.
- 4. Fofana MO, Knight GM, Gomez GB, White RG, Dowdy DW. Population-level impact of shorter-course regimens for tuberculosis: a model-based analysis. PloS one. 2014;9(5):e96389.
- 5. WHO. Global Investments in Tuberculosis Research and Development: Past, Present, and Future. Geneva: World Health Organization; 2017.
- 6. K M. Science is a major plank in China's new spending plan Capetown: Science 2016 [Available from: <u>http://www.sciencemag.org/news/2016/03/sciencemajor-plank-china-s-new-spending-plan</u>.
- SAMRC. South African Medical Research Council. SHIP TB Projects Capetown: South Africa Medical Research Council (SAMRC); 2014 [Available from: <u>http://www.mrc.ac.za/Media/2014/SHIPTBFlyer.pdf</u>.
- 8. Lienhardt C, Lonnroth K, Menzies D, Balasegaram M, Chakaya J, Cobelens F, et al. Translational Research for Tuberculosis Elimination: Priorities, Challenges, and Actions. PLoS Med. 2016;13(3):e1001965.
- McLaughlin K. Science is a major plank in China's new spending plan. Science. March 7, 2016.
 India takes a lead in TB research in a unique mission mode to End TB [press release]. November 10,
- 2016.
- Kritski A, Barreira D, Junqueira-Kipnis AP, Moraes MO, Campos MM, Degrave WM, et al. Brazilian Response to Global End TB Strategy : The National Tuberculosis Research Agenda. Rev Soc Bras Med Trop. 2016;49(1):135-45.
- 12. South African Medical Research Council. SHIP TB Projects 2014. Cape Town.
- 13. Ministry of Health and Family Welfare, Government of India. Delhi Communiqué. Delhi: Government of India Ministry of Health and Family Welfare; 2013.
- 14. BRICS Ministry of External Relations. Communiqué of the IV Meeting of BRICS Health Ministers. Brasília: BRICS Ministry of External Relations; 2014.
- 15. Ministry of Health and Family Welfare, Government of India. 6th BRICS Health Ministers Meeting Delhi Communiqué. Delhi: Government of India Ministry of Health and Family Welfare; 2016.