

Increasing funding for TB R&D in 2023, an emergency

Despite increased international mobilization in recent years, tuberculosis (TB) continues to be one of the deadliest diseases of our time. It ranks as the 13th leading cause of death, and the second leading cause of death due to an infectious disease worldwide. Progress to eradicate the disease is slow¹: between 2015 and 2020, the cumulative decrease in disease incidence amounted to 11%, only half of the target set in the WHO Strategy to End TB². However, TB is a disease that can be prevented, treated, and cured. However, the diagnostics, treatments, and vaccines currently available are still not sufficiently effective, fast, and appropriate.

Albeit these gaps, international funding for research and development (R&D) of new tools remains inadequate (I). Increasing investments in this area is effective and even more urgent as we are facing a worrisome global rise in antimicrobial resistance (AMR) (II). For this reason, we call on the EU to capitalize on its historical leadership in the fight against TB (III) and to seize the opportunity offered by the latest advances in medical technologies, as well as the upcoming United Nations High-Level Meeting (UNHLM) on TB in September 2023, to announce new ambitious political and financial commitments (IV).

I. Insufficient international funding for R&D, despite the burden of the disease

Slow progress despite increased international mobilization in recent years

- Recent years have been marked by increased international mobilization. The third Sustainable Development Goal (SDG 3) and the WHO Strategy to End TB³ have set clear goals for the eradication of the disease by 2030. The organization of the first TB UNHLM in 2018 also established new international targets, particularly in terms of R&D funding to fight the disease by 2022⁴.
- Despite increased mobilization, progress is slow, and the targets set by the WHO are still far from being achieved⁵. The Covid-19 pandemic has further impeded these modest improvements by causing not only the interruption of essential health services and care,⁶ but also by diverting research primarily towards Covid-19 at the expense of others.

¹ Unfinished business: the challenge of ending tuberculosis in the European Region, WHO, 2023. Available <u>here</u>.

² The end TB strategy, WHO, 2015. Available <u>here</u>.

³ Ibid.

⁴ 2018 TB HLM scorecard, GFAN, 2022. Available <u>here</u>.

⁵ Deadly Divide: Priorities to Close the Deadly Divide - Call to Action, Stop TB Partnership, 2023. Available <u>here</u>.

⁶ Global Tuberculosis report 2022, WHO, 2023. Available <u>here</u>.

Insufficient international funding for R&D

- According to the WHO, \$13 billion USD per year was necessary by 2022 for TB prevention, diagnosis, treatment, and care in order to achieve the global target agreed during the UNHLM on TB in 2018. In 2020, total expenditures amounted to \$5.3 billion USD, which is less than half of the global funding target for TB control.
- Regarding R&D specifically, funding reached the symbolic threshold of \$1 billion in 2021, largely thanks to the contribution of public institutions. While this is an unprecedented amount, it represents only half of the target set by countries for 2022 during the UNHLM on TB in 2018. As a comparison, a recent report from the European Parliament⁷ shows that, from 2020 to early 2022, combined support in various form by external funds⁸ for R&D and the expansion of production capacity for the nine Covid-19 vaccines included in the study was in the range of €9 billion⁹. Additionally, almost €21 billion was allocated to companies through Advance Purchase Agreements (APAs). While the information about R&D expenditures sustained by companies for Covid-19 vaccines is not publicly available, their estimate is in the range of €4-5 billion for the period 2020-2021.

II. Increasing R&D funding to fight TB: a necessary and efficient investment

The world needs new and effective diagnostics, drugs, and vaccines that are universally accessible to effectivelly reduce the incidence of TB

• The only effective way to reduce the incidence of TB is rapid detection. However, to this day, we still do not have a sufficiently rapid, reliable, easy-to-use, and affordable diagnostic tool. Access to this diagnostic tool remains severely limited or even impossible in certain regions of the world. According to the WHO¹⁰, 40% of people with TB are not detected by healthcare systems every year. Additionally, the diagnosis is not always reliable as it is complicated to perform on certain populations such as children, or individuals with extrapulmonary or immunocompromised TB. Latent TB, which could affect up to a quarter of the global population, is particularly poorly detected and managed. Furthermore, only 38% of people were diagnosed using rapid molecular tests in 2021, meaning that most patients with the disease were tested using smear microscopy, an outdated technology with a sensitivity of only 50% to detect TB. The modernization of analytical practices still faces considerable difficulties related to high costs, lack of required infrastructures, or the complexity of use and the healthcare personnel's expertise to employ them.

⁷ Florio, M, Gamba, S. and Pancotti C., 2023, Mapping of long-term public and private investments in the development of Covid-19 vaccines, publication for the special committee on Covid-19 pandemic: lessons learned and recommendations for the future (COVI), Policy Department for Economic, Scientific and Quality of Life Policies, European Parliament, Luxembourg.. Available <u>here</u>.

⁸ External funds include mostly funds from governments, but also from some philanthropic entities, third private parties, international public-private partnerships and multilateral development banks

⁹ The study made a mapping of funds contributed by different actors for the R&D and the expansion of the production capacity of Covid-19 vaccines, with a focus on those authorized in the EU.

¹⁰ WHO standard: universal access to rapid tuberculosis diagnostics. Geneva: World Health Organization; 2023. Available <u>here</u>.

- Despite recent progress, treatment regimens for TB are burdensome. They need to be administered in large quantities, without interruption, over a period ranging from 6 months for drug-sensitive TB to up to 30 months in the case of severe drug resistance. Unfortunately, WHO recommended six-month regimen is not accessible to all those who need it. Moreover, these treatments are poorly tolerated and present various toxicities, especially when treating drug-resistant TB. This complexity increases the risks of discontinuity in treatment, which itself leads to the development of drug-resistant forms¹¹. Developing treatments, both conventional (antibiotics) and unconventional (host-targeted therapies), that are short, simple, and affordable is essential if we want to significantly reduce the incidence of the disease.
- To this day, we still do not have vaccines that are sufficiently effective and adapted to all populations at risk. Only one vaccine is currently approved, and while it offers moderate efficacy in preventing severe forms of TB for infants and young children, it does not provide sufficient protection to adolescents and adults, who represent nearly 90% of disease transmission worldwide. Developing a more effective, affordable, and better-suited TB vaccines would significantly reduce the need for antibiotics and thereby help curb the progression of antimicrobial resistance.

The progression of antimicrobial resistance: a major public health challenge

- Drug-resistant forms of TB, such as multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), are a major public health concern due to their increasing prevalence, and due to the greater mortality and the complexity of their treatments. Approximately two-thirds of individuals with XDR-TB do not recover. The treatment for drug-resistant TB has devastating side effects, and can cost up to many times more than the treatment for drug-sensitive TB. In addition to "classic" resistance to treatment, there is also the issue of phenotypically drug-tolerant bacteria, which contribute to persistent populations of mycobacteria and relapses.
- Currently, around half a million people develop drug-resistant TB each year, and its prevalence has increased by 3% between 2020 and 2021. The Stop TB Partnership¹² estimates that by 2050, drug-resistant TB will have killed 75 million people and will have cost the global economy a cumulative amount of USD 16.7 trillion if no sufficiently efficient new treatment is developed. The success rate of TB treatment is currently estimated at only 39% for individuals with extensively drug-resistant TB.

Increasing funding for R&D to fight TB: an effective investment

• The Covid-19 pandemic has demonstrated that with sufficient political and financial mobilization, the development and rapid production of new medical tools is possible due to technological advancements and historical research in the field. R&D in the field of TB has also made notable progress in the past 20 years: 16 vaccine candidates are now undergoing clinical research worldwide, including 6 in Phase III, 6 in Phase II, and 4 in Phase I of clinical trials¹³. These

¹¹ Ibid.

¹² Pharmacoresistant TB : the world deadliest super bacteria, TB Alliance Available <u>here</u>.

¹³ Tuberculosis Research Funding Trends, 2005-2021, TAG, page 18, 2023. Available <u>here</u>.

recent improvements in the development of new vaccines present a major opportunity that we must collectively capitalize on and invest in to eradicate the disease by 2030.

- Increasing funding for R&D to fight TB is also a cost-effective investment. For the TB vaccine alone, a recent study commissioned by the WHO estimates that over a 25-year period, an effective vaccine with a 50% efficacy rate in preventing the disease among adolescents and adults could prevent up to 76 million new cases of TB, avert 8.5 million deaths, eliminate the need for 42 million antibiotic treatments, and save \$6.5 billion USD in costs borne by households affected by the disease, particularly the poorest and most vulnerable. An effective vaccine with a 75% efficacy rate could prevent up to 110 million new cases of TB and 12.3 million deaths. Furthermore, this study reveals that every dollar invested in the delivery of a 50% effective vaccine could generate a return on investment of \$7 due to the avoided healthcare costs and increased productivity.
- Lastly, additional investments in the development of new tools not only benefit patients, but also contribute to health systems strengthening (HSS) overall and advance research on infectious diseases more broadly. For example, the tools, concepts, capacities, and infrastructure resulting from investments in R&D to combat TB have informed and supported research and responses to the Covid-19 pandemic. Expanding support for R&D to fight TB can help us fight new coronaviruses and better prevent and prepare for future pandemics.

III. The EU, a Historic Ally in the Fight against TB

- The EU has historically been highly involved in the fight against TB. Indeed, the EU played a significant role in the creation of the Global Fund to Fight AIDS, TB, and Malaria in 2001, and remains one of its main contributors to this day. In the last replenishment conference, the EU pledged €715 million to the Global Fund for the years 2023-2025.
- Regarding research and development (R&D), the EU has been a strong leader, investing in TB research with innovative approaches through the EU's framework programs for research and innovation. The EU has provided over €500 million to TB research under Horizon 2020, including funds from the European and Developing Countries Clinical Trials partnership (EDCTP), as well as the Innovative Medicines Initiative (IMI).
- Despite clear political leadership, the EU can and should be investing much more on TB R&D.
 Following the reassessment of financial needs to address current TB challenges, the Treatment Action Group (TAG) estimates that countries will need to allocate at least 0.15% of their gross domestic expenditure to TB R&D until 2030. The proposed fair share contribution of Team Europe (the European Union and it Member States) amounts to an annual investment of \$706 million.

IV. 2023, a pivotal year for advancing the fight against TB

With the new UNHLM on TB taking place this year, 2023 represents a major opportunity to mobilize the international community, secure new political and financial commitments, and hope to make significant progress in the field of R&D to end the disease by 2030. Therefore, we call upon EU policymakers and institutions to seize this opportunity to renew the EU's 's historic commitment to the fight against TB. We particularly urge the EU to:

- Facilitate the development and adoption of new ambitious targets and goals for TB R&D within the framework of the UNHLM Political Declaration on TB in September.
- Announce new ambitious financial commitments for TB R&D over the period of 2023-2030 at the upcoming UNHLM on TB, in order to contribute to the target of \$5 billion in annual funding for each year of the period 2023-2030.
- Ensure that the development of TB medical tools is a priority on the agenda of HERA in terms of global health R&D, pandemic prevention and preparedness, and antimicrobial resistance.
- Ensure that R&D dedicated to fighting poverty related and neglected diseases, including TB, is a priority in the upcoming strategic plan of the Horizon Europe framework program and that it is reflected in the implementation of its projects.
- Increase its financial contribution to the European & Developing Countries Clinical Trials Partnership (EDCTP) and other appropriate mechanisms to accelerate the clinical development of TB vaccines.