

European Commitments to TB R&D Investments: Promises Made to Be Broken?

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Before the SARS-CoV-2 virus ignited the global COVID-19 pandemic, tuberculosis (TB)—another contagious respiratory disease—was the leading annual cause of death by an infectious agent. The World Health Organization (WHO) estimates that one-quarter of the world’s population is infected with latent TB. Each year, 10 million people develop TB disease, and over 1 million people die; in 2020, this number climbed to 1.5 million.ⁱ Yet, despite its massive public health and societal burden, global attention and political action to address TB is grossly inadequate. Standing in the way of better treatments, diagnostics, and vaccines for TB is the insufficient financial investment in TB research and development (R&D).ⁱⁱ

This brief looks at trends in European funding for TB research against the backdrop of political commitments to end TB, with a focus on TB vaccines. Data on TB R&D funding levels come from the annual survey conducted by Treatment Action Group and Stop TB Partnership.ⁱⁱⁱ The brief also compares European commitments and actual contributions to TB with the overwhelming investments made toward R&D for the COVID-19 pandemic response. Recommendations for European public funders to better align actual funding with their commitments and how best to channel these investments are made.

TB is chronically underfunded, in part because there are already treatments, diagnostics, and a vaccine for TB, which makes it easy to justify investing in other

areas of research. But currently available tools are inadequate to end TB, leading the WHO to name intensified research and innovation as a central pillar of its End TB Strategy. Within the TB research agenda, development of new vaccines against TB stands out as a particularly urgent need. In July 2021, the bacillus Calmette-Guérin (BCG) vaccine, the only existing vaccine against TB, turned 100 years old. One hundred years before, an infant in Paris, France, received the BCG vaccine after being born to a mother who died from TB after delivery.^{iv} The BCG vaccine has been an instrumental part of the arsenal to control TB and has been critical for the prevention of TB in infants and young children, but the celebration of this 100-year anniversary only serves to emphasize how transformative advances in medical science over the ensuing century have not delivered the new vaccines required to end the TB epidemic. BCG does not prevent TB in adolescents and adults, who are typically the populations responsible for transmission of the disease and who account for the majority of TB prevalence. Better vaccines are needed.

With greater funding for TB R&D, the barriers to develop vaccines and other tools necessary to control this disease can be overcome. In 2018, governments made explicit commitments at the UN High-Level Meeting on Tuberculosis (UNHLMTB) to increase global funding for TB R&D in order to develop innovations for TB prevention, detection, and treatment. Together with other nations, European

leaders pledged their support to increase global investments to €1.7 billion annually for TB research.^v Between 2018 and 2022, this would amount to €8.5 billion for TB R&D overall. With these funds it was hoped that TB would finally receive the financial investments so greatly needed and that the decades-long neglect would subside.

However, governments have failed to deliver on the promises they made at the UNHLMTB; the world remains woefully behind achieving the funding levels required to make real progress in TB R&D. The annual target that was set in 2018 has not once been met. Recognizing that funding shortfalls from previous periods will need to be made up for in subsequent years, in 2019 the Stop TB Partnership updated its funding ask for TB R&D to €11.4 billion between 2018 and 2022 and called for €2.7 billion of this to go toward TB vaccines. The gap between this higher aspiration and actual spending is significant. Closing this funding gap will require an additional €8.9 billion in TB R&D over the next two years, with €2.5 billion going toward TB vaccine development.^{vi} The ever-growing funding gap is particularly stark for European public funders.

European Funding for TB R&D

In 2020, European public funding for TB R&D totaled just €139.7 million; with €91.5 million coming from the European Union and the member states (MS).

Nearly one-third of total European investments were made by the United Kingdom (30%). However, in 2020, U.K. investments decreased by nearly €8 million and further funding cuts are anticipated in the coming years.^{vii} This means that the U.K. shortfall, in addition to the overall funding gap, will need to be compensated for in future years.

A comparison of funding from 2019 and 2020 shows an increase in overall investments in spite of the economic shocks of the COVID-19 pandemic. However, this increase is due primarily to a doubling of spending by the European & Developing Countries Clinical Trials Partnership (EDCTP); like in the United Kingdom, investments from many other European countries in 2020 decreased.

Table 1: EU Funding Before and During COVID-19


E.U. & MEMBER STATES	2019 TB R&D FUNDING (€)	2020 TB R&D FUNDING (€)
European Union	34.308.891	61.069.750
Denmark	482.133	358.149
Finland	--	531.570
France	6.530.145	6.327.871
Germany	21.454.952	15.262.612
Ireland	1.234.326	1.373.681
Netherlands	3.881.226	3.096.862
Spain	425.407	1.097.820
Sweden	4.012.260	2.376.323
SUBTOTAL	72.329.339 €	91.494.638 €
NON-E.U. COUNTRIES		
Norway	2.406.032	1.387.509
Switzerland	2.937.281	4.905.701
United Kingdom	49.742.567	41.939.689
TOTAL	127.415.219 €	139.727.537 €

“The UN High-Level Meeting on TB was an event with a lot of hope, a lot of political commitment, but nobody delivered. You can make up whatever excuses you want, but even the year before COVID-19 happened, nobody delivered. It’s not just about talking in a fancy event and making headlines. It’s about actually delivering.”

- Rhea Lobo, Affected Communities Board Member (Alt), Stop TB Partnership

Table 2: TB Vaccine Candidates and EU Support

PRECLINICAL	PHASE I	PHASE IIA	PHASE IIB	PHASE III
BCG-ZMP1 (U. Zurich, TBVI)	AEC/BC02 (Anhui Zhifei Longcom)	ChAdOx1 85A + MVA85A (U. Oxford, TBVI)	BCG revaccination (Gates Medical Research Institute)	VPM1002 (Serum Institute of India, Max Planck, Vakzine Projekt Management GmbH, EDCTP, Indian Council of Medical Research)
H107 (Staten Serum Institute, TBVI)	aerosol BCG (U. Oxford)		H56:IC31 (Staten Serum Institute, Valneva, EDCTP)	MIP (Cadila Pharma, Indian Council of Medical Research)
BCG + ChAdOx/MVA PP15-85A (U. Oxford, TBVI)	aerosol AdHu5Ag85A (McMaster U., CanSino)		DAR-901 (Dartmouth, Global Health Innovative Technologies Fund)	MTBVAC (Biofabri, TBVI, U. Zaragoza, IAVI, EDCTP)
CMV-6Ag (Vir Bio, Oregon Health & Science University)	TB/FLU-04L TB/FLU-01L (Kazakhstan, Russian Federation)		ID93/GLA-SE [QTP101] (Quratis, U.S. National Institutes of Health)	M72/AS01E (Gates Medical Research Institute)
CysVac2/Ad (U. Sydney, TBVI)			RUTI (Archivel Farma, TBVI)	GamTBvac (Russian Federation)
MVA multiphasic vaccine (Transgene, TBVI)				

Candidate (major partners)  = European sponsor or funding support

Vaccines are listed by stage of most advanced trial. Some vaccines are being studied in multiple trials in different stages and for different indications.

Sources: TAG Pipeline Report. Preclinical candidates taken from the pipeline maintained by TBVI.

BCG 2.0—the Next Chapter of Europe’s Legacy in TB Elimination

It is highly likely that the next major breakthrough in TB prevention will be developed in Europe, making European funders the wellspring of innovation. There are currently 15 TB clinical vaccine candidates under investigation across the world. Five are in phase III, six in phase II, and four in phase I trials. Among the 15, six are being developed by or in partnership with European research institutions (see Table 2).^{viii}

Considering the European character of the TB vaccine pipeline, it is in the interest of European innovation to support TB vaccine development. However, in 2020, only 16% of all funding from European public funders supported TB vaccine R&D. Equating to just under €15 million, this is a level of

funding that is wholly inadequate to bring these promising vaccine candidates forward. It contributes to delays in study progression and thus impedes innovation. It also risks losing excellence in European science for TB R&D, as researchers who are unable to acquire the necessary funding for their programs become unable to support their research teams, including young and early-career investigators, who may inevitably have to pivot their research priorities to other diseases and leave the field of TB.

EUROPE'S RISING STAR—THE EDCTP

The EDCTP is the largest single funder of TB R&D across the European Union. Its funding is derived from the European Union's Horizon programmes, and its purpose is to facilitate collaborative research efforts between European and sub-Saharan African countries to address poverty-related diseases. The sizeable increase in TB investments from EDCTP in 2020 was due to several factors, such as the EDCTP's focus on infectious diseases associated with comorbidities and the increasing global competitiveness of TB research proposals, including from research institutions in the Global South.

Dr. Michael Makanga, the EDCTP's executive director, indicates that in line with the EDCTP's overall objective, there has been a noticeable increase in the competitiveness of TB researchers from low- and middle-income countries. "When we look at the scientific excellence from the proposals that we are receiving from South Africa, they are very, very highly competitive globally in the TB area," he explains.

The EDCTP is also the largest single funder of vaccine research among all European funders. In 2020, €0.25 of every euro spent by the EDCTP on TB R&D went to vaccines. These investments are currently supporting the advanced clinical trials of three TB vaccine candidates mentioned above: MTBVAC, VPM1002, and H56:IC31. The MTBVAC and VPM1002 vaccine candidates are being studied in EDCTP-funded trials as potential alternatives to the BCG vaccine for use in infants. H56:IC31 is undergoing evaluation of its effectiveness and safety in preventing TB disease recurrence among adults treated for TB disease.

Dr. Michael Makanga anticipates that in the coming years, the EDCTP's investments in TB will continue to grow, which is encouraging in the face of decreased national investments of other European funders. When one looks at the trends throughout the second EDCTP programme from 2014 to 2020 (see table below), this is very clearly the case. However, regarding vaccines, there is noticeable volatility in the year-on-year funding.

Table 3: Annual EDCTP Funding for TB R&D, 2014-2020

YEAR	TOTAL FUNDING	INVESTMENTS IN VACCINES	PROPORTION OF TOTAL FUNDING	DIFFERENCE IN VACCINE FUNDING (YEAR-ON-YEAR)
2014	5.846.032 €	2.715.601 €	46%	--
2015	4.142.020 €	820.302 €	20%	-1.895.299 €
2016	3.840.773 €	0,00 €	0%	-820.302 €
2017	15.771.247 €	3.379.805 €	21%	3.379.805 €
2018	21.812.153 €	11.794.883 €	54%	8.415.078 €
2019	21.901.761 €	1.626.935 €	7%	-10.167.948 €
2020	45.539.480 €	11.485.324 €	25%	9.858.389 €
Total	118.853.466 €	31.822.850 €	27%	--

Table 4: EU Spending on TB R&D As Percentage of Fair Share Targets

	COUNTRY	FAIR SHARE ACHIEVED			
		2017	2018	2019	2020
E.U. & MEMBER STATES	European Union	24,1%	25,5%	23,2%	39,8%
	Denmark	9,1%	18,3%	12,7%	16,4%
	Finland	7,6%	19,4%	8,3%	21,9%
	France	12,5%	17,7%	23,0%	30,3%
	Germany	23,3%	24,3%	26,0%	26,4%
	Ireland	62,1%	72,2%	41,9%	53,2%
	Italy	16,6%	21,3%	15,8%	28,3%
	Netherlands	37,9%	44,7%	29,7%	30,4%
	Spain	18,7%	20,9%	21,3%	39,8%
	Sweden	20,4%	6,9%	30,5%	23,8%
NON-E.U. COUNTRIES	Norway	40,4%	34,3%	30,8%	19,0%
	Switzerland	24,5%	30,6%	14,3%	45,0%
	United Kingdom	89,8%	141,1%	120,9%	149,5%

Putting the “Fair” Back Into Fair Share

Following the 2018 UNHLMTB, civil society organizations, including Treatment Action Group and the Stop TB Partnership, developed the concept of “Fair Share” in order to define each country’s share of the overall TB research funding target and to create accountability toward meeting these spending levels and ensuring global equity in TB R&D investments. The Fair Share target was set at a minimum of 0.1% of a country’s gross expenditure in R&D (GERD) to be invested in TB R&D in order to meet the €1.7 billion annual funding target.

Only one European country, the United Kingdom, has ever managed to give its Fair Share. New calculations of Fair Share that take into account the contributions of E.U. MS to E.U. programmes that support TB R&D, like the EDCTP, show that even with this adjustment, MS are way behind

on their commitments. The Fair Share of the European Union, when calculated against the E.U. annual budget,^x also dramatically misses the mark, especially when compared with the United States, which is meeting 90% of its target.

Table 4 shows the Fair Shares achieved against the 0.1% target by the E.U., MS, and non-E.U. European countries since the benchmark was introduced.

When the €1.7 billion annual target and the Fair Share targets were set, TB activists and researchers knew it was still not enough, but the hope was that a lower, more manageable target would garner actual resource mobility. Still, there has been a collective global failure to deliver on the promises made to increase TB R&D investments, which has resulted in the funding gap widening year after year.

“Who would have thought in a year, you could have a vaccine for a disease we’d never even heard of? ... People will always say, ‘Well, there’s limited resources for public health’, but there aren’t, and COVID-19 showed that.”

- Jennifer Furin, The Sentinel Project on Pediatric Drug-Resistant Tuberculosis

Comparing TB Investments to COVID-19

In light of the massive public investments poured into R&D to respond to the COVID-19 pandemic, it is difficult to comprehend the intractability of comparably minimal funding demands for TB. While it is still too early to know the full impact of COVID-19 on TB funding, initial data show that public funding for TB R&D plateaued for the first time in 2020 after several years of steady increases, and several E.U. member states reported spending less on TB research than in 2019.

One thing is clear: COVID-19 has upended TB R&D. The pandemic and related mitigation measures, such as social distancing and lockdowns, disrupted studies everywhere. Restarting research activities, big or small, requires extra effort, time, and, of course, money. The disruptions to TB research mirror the grave setbacks to TB control. In 2021, the WHO reported that COVID-19 has led to a reversal of global progress for TB elimination. For the first time in over a decade, more people died from TB than in previous years. Furthermore, fewer people were diagnosed, treated, or immunized against TB than in 2019.^x Some of this regression can be attributed to infrastructure and human resources for TB that were redirected to help the COVID-19 response.^{xi}

The scale of financing committed toward advancing R&D of new health technologies to prevent, diagnose, and treat COVID-19, and the rapid pace of COVID-19 innovation, have shown the world what can be achieved—both in terms of the extent of financing that can be raised to respond to a public health crisis, and regarding the speed of R&D—when financing is not a barrier to progress. Imagine the possibilities if similar energy, political will, and proper financing were to be applied to TB R&D.

In the wake of the unprecedented efforts and financing to develop vaccines and treatments for COVID-19 is the outstanding injustice they highlight for other major disease areas, such as TB. Governments are estimated to have spent over €80 billion on COVID-19 vaccine R&D alone in the first 11 months of the pandemic, or close to 82 times the €979 million the world spent on TB vaccine research over the last 11 years.^{xii}

The COVID-19 pandemic has substantively altered our shared understanding of what is achievable and demonstrated that the seemingly impossible becomes possible with political will. It has also laid bare the global neglect of TB. One can only hope that the pandemic will provide an opening to expand TB R&D investments and to demand that countries find the political will to uphold their financing commitments—as they did for COVID-19.

“...Do I expect a [TB] vaccine coming up anytime soon? ... No. You can’t get a Ferrari when you only have the money [to] buy a bike.”

- Timur Abdullaev, TBpeople

Recommendations

Make Good on Existing Commitments

Since the 2018 UNHLM TB conclusions were agreed, only one European country has actually managed to deliver on its share of the commitments made. Of the E.U. MS, only one has ever managed to fulfill even half of its promises. This is not good enough. A critical impediment to realizing funding targets for TB R&D is the lack of accountability mechanisms to ensure governments actually do good on their promises. One place this can start is with European countries setting an example and holding themselves accountable to achieve their Fair Share. Therefore, as an interim step to demonstrate commitment to supporting TB innovation, European public funders must reach at least 50% of their Fair Share targets in 2022 and 100% by 2024 at the latest.

Develop a Plan to Compensate for U.K. Fall Out

In previous years, the U.K. has shown itself to be a reliable funder for TB R&D as the only country in Europe to pay its Fair Share. But the planned U.K. budget cuts to R&D across the board are already being felt, and the gap in TB funding that will be left needs to be filled. It is therefore recommended that European partners develop a joint plan to compensate for this fall out. This should be carried out in consultation and with support from leading civil society organizations, academic institutions, and the private sector.

Support for European Vaccine Candidates

Europe is home to unparalleled research excellence and some of the brightest minds in TB innovation in the world. European science and innovation have been critical to the success of the unprecedented development of multiple COVID-19 vaccines in the last two years. The unified and dedicated response offers hope that if TB vaccine research receives the needed attention and investment by European funders, then the next lifesaving, preventive TB vaccine will no longer be a thing of dreams. New and effective TB vaccines are within reach, and Europe is the stage upon which this groundbreaking progress can play out. Supporting European vaccine candidates means supporting European science, researchers, and innovation for the global good. Therefore, as part of overall increased investments to TB, European funders should prioritize investments in vaccine R&D.

Possible avenues to achieve this are including TB vaccine development in overarching R&D objectives, such as those for anti-microbial resistance, pandemic preparedness—for example, through the European Union's new Health Emergency Response Authority—and through expanded support for existing mechanisms like the EDCTP.

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- ⁱ World Health Organization. Tuberculosis deaths rise for the first time in more than a decade due to the COVID-19 pandemic. Geneva: World Health Organization; 2021. <https://www.who.int/news/item/14-10-2021-tuberculosis-deaths-rise-for-the-first-time-in-more-than-a-decade-due-to-the-covid-19-pandemic#:~:text=Globally%2C%20the%20reduction%20in%20the,the%202020%20milestone%20of%2020%25>
- ⁱⁱ World Health Organization. Global investments in tuberculosis research and development: past, present, and future. Geneva: World Health Organization; 2017. <https://www.who.int/publications-detail-redirect/9789241513326>
- ⁱⁱⁱ TAG collects the expenditure data for its annual funding trends report through a global survey of TB research funders. The survey asked recipients to report expenditures on TB research in the past fiscal year and to categorize spending into one of six research areas: basic science, diagnostics, drugs, vaccines, operational research and epidemiology, and infrastructure/ unspecified projects. Further details can be found here: Tomlinson C. Tuberculosis research funding trends. New York: Treatment Action Group; 2021. <https://www.treatmentactiongroup.org/resources/tbrd-report/tbrd-report-2021/>
- ^{iv} Lobo N, Brooks NA, Zlotta AR, et al. 100 years of Bacillus Calmette-Guérin immunotherapy: from cattle to COVID-19. *Nat Rev Urol*. 2021 Oct;18(10):611-22. <https://doi.org/10.1038/s41585-021-00481-1>
- ^v World Health Organization. Political Declaration of the High-Level Meeting of the United Nations General Assembly on the Fight Against Tuberculosis. Resolution A/RES/73/3 adopted by the United Nations General Assembly on 10 October 2018. Geneva: World Health Organization; 2018. <https://www.who.int/tb/unhlmonTBDeclaration.pdf>
- ^{vi} Stop TB Partnership. TB research in 2020 reaches only US\$915 million - less than half of investment needed to end TB [Internet]. 2021. <https://www.stoptb.org/news/tb-research-2020-reaches-only-us915-million-less-half-of-investment-needed-to-end-tb>
- ^{vii} University of Oxford. Slashing research funding is a blow to Global Britain [Internet]. 2021 Mar 22. <https://www.ox.ac.uk/news/2021-03-22-slashing-research-funding-blow-global-britain>
- ^{viii} Data are derived from TAG Tuberculosis Vaccines Pipeline Report 2021. https://www.treatmentactiongroup.org/wp-content/uploads/2021/10/2021_pipeline_TB_vaccines_final.pdf
- ^{ix} The Fair Share target for the European Union has traditionally been calculated against the E.U. GERD, which is a cumulative sum of all member state GERDs. The E.U. GERD is more than double the E.U. annual budget, making the GERD an improbable baseline for the E.U. Fair Share target. The E.U. annual budget is therefore used as the baseline.
- ^x World Health Organization. Tuberculosis deaths rise for the first time.
- ^{xi} Chapman HJ, Veras-Estévez BA. Lessons learned during the COVID-19 pandemic to strengthen tb infection control: a rapid review. *Glob Health Sci Pract*. 2021;9(4):964-77. <https://www.ghspjournal.org/content/9/4/964#ref-5>
- ^{xii} Frick M. Tuberculosis Vaccines Pipeline Report 2021. New York: Treatment Action Group; 2021. https://www.treatmentactiongroup.org/wp-content/uploads/2021/10/2021_pipeline_TB_vaccines_final.pdf