

The Broad Benefits of TB Vaccine Research

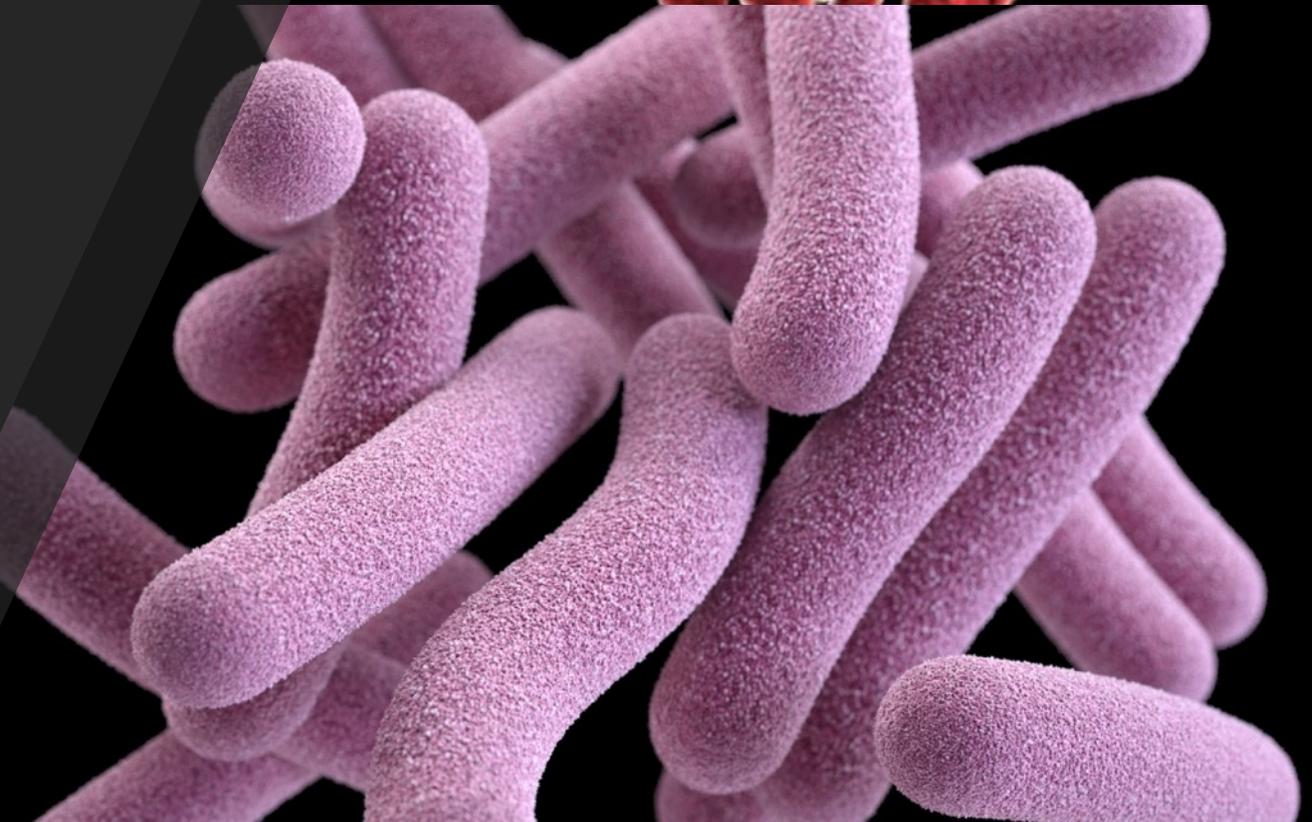
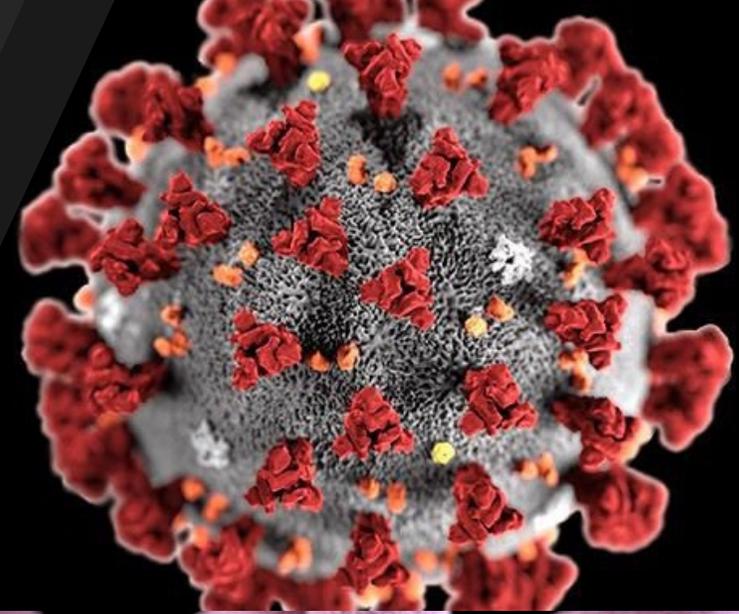
The Impact of **COVID-19** on Research and Development for TB Vaccines

TBEC Webinar Series

Mike Frick

Treatment Action Group

September 2020



Two things are true:

1. COVID-19 has disrupted TB research.
2. TB research has contributed to COVID-19 R&D.
The most obvious area of crossover is TB vaccines.

TREATMENT ACTION GROUP POLICY BRIEF

August 2020

TAG

Treatment Action Group
www.treatmentactiongroup.org

TB Research Investments Provide Returns in Combating Both TB and COVID-19:

Sustained and Expanded Financing Is Needed to Safeguard Tuberculosis Research Against COVID-19-Related Disruptions and Improve Global Epidemic Preparedness

By Catherine Tomlinson

Edited by Mike Frick, Lindsay McKenna, Suraj Madoori

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COVID-19 has disrupted TB research in myriad ways.

- Participant enrollment
- Participant monitoring and support
- Supply chain disruption
- Sample collection
- Sample export
- Laboratory capacity
- Community engagement

“TB clinical trials carry inherent challenges at the best of times. Locations with the highest TB burden often have less resilient regulatory infrastructure, complex operational environments, and more limited clinical trial experience. During an unexpected and large-scale disruption like COVID-19, the impact of these weaknesses becomes more magnified.”

—ID Rusen, Trop Med Infect Dis, June 2020

Covid-19 research in Europe needs coordination, but we must not stop European research investments in poverty related diseases

August 24, 2020

- “We must remain aware of the danger of an excess of COVID-19 exceptionalism in the planning of future research funding that would come at the expense of other urgent global health needs. Tuberculosis, malaria, and HIV have well documented research needs and any redirection of funding from these poverty-related diseases to covid-19 would be highly deleterious to global public health.”
- “The reduction of research funds to support improved TB research and control will not only ruin earlier investments made in the past decade, but also have direct consequences on the quality of programme management and the availability of better diagnostics and treatments in the near future.”

Pletschette M, et al. [BMJ Opinion](#). August 2020.

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TB research strengthens more than the movement to end TB. Investments in TB research yield broad benefits.

Cross-disease benefits for COVID-19 from TB R&D include:

- Transmission and aerobiology research
- Artificial intelligence
- Diagnostic tools (Xpert)
- **Vaccine platforms (BCG and others)**
- Research infrastructure and capacity
- Laboratory biosafety
- Implementation research (on e.g., contact tracing)

Shoring up global investments in TB R&D may deliver not only new tools to end TB in our lifetimes but also cross-disease benefits that may be leveraged in combating COVID-19 and future pandemic threats.

Crossroads: TB Vaccine Pipeline and **COVID-19**

Phase 1	Phase 2a	Phase 2b	Phase 3
AEC/BC02 Anhui Zhifei Longcom	RUTI Archivel Farma, S.L	DAR-901 Dartmouth, GHIT	Vaccae™ Anhui Zhifei Longcom
Ad5Ag85A McMaster, CanSino	MTBVAC Biofabri, TBVI, Zaragosa	M72/AS01E GSK	VPM1002 SII, Max Planck, VPM, TBVI (Phase 2/3)
ChAdOx1 85A/MVA85A (ID/IM/Aerosol) Univ of Oxford	ID93 + GLA-SE IDRI, Wellcome Trust, Quratis	H56:IC31 SSI, IAVI, EDCTP, Valneva	Immuvac ICMR, Cadila Pharmaceuticals
	TB/FLU-04L RIBSP	BCG Revaccination Gates Medical Research Institute (GMRI)	

Vaccine construct also being studied against COVID-19

BCG and COVID-19 Trials

HCWs = healthcare workers

Registry number + Sponsor	Intervention (BCG strain)	Primary endpoint	Study population	Study locations	Date of last data collection
<u>NCT04327206</u> (BRACE) Murdoch Childrens Research Institute	BCG (Danish 1331)	Incidence of COVID-19 disease and severe disease	10,078 HCWS	Australia, Netherlands, Spain	June 2021
<u>NCT04328441</u> (BCG-CORONA) UMC Utrecht	BCG (Danish 1331)	Unplanned absenteeism from work (for any reason)	1500 HCWS	Netherlands	March 2021
<u>NCT04348370</u> (BADAS) Texas A&M University	BCG (Tice strain)	Incidence of COVID 19 infection	1800 HCWS	USA	May 2021
<u>NCT04379336</u> TASK Applied Science	BCG (Danish 1331)	Incidence of HCWs hospitalized due to COVID-19	500 HCWS	South Africa	April 2021
<u>NCT04475302</u> ICMR	BCG (NA)	Mortality due to COVID-19 disease	2175 elderly	India	Jan. 2021
<u>NCT04384549</u> Assistance Publique - Hôpitaux de Paris	BCG (Danish 1331)	Incidence of documented COVID-19	1120 HCWS	France	Feb 2021
<u>EUCTR2020-002111-22-PL</u> University of Rzeszów	BCG (Moreau)	Death or life-threatening health impairment	1000 HCWS	Poland	NA
<u>EUCTR2020-001783-28-HU</u> National Korányi Institute of Pulmonology	BCG (Danish 1331)	Unplanned absenteeism from work (due to documented COVID-19 infection)	1000 HCWS	Hungary	NA

+ about a dozen more similar trials

Adapted from WHO Compendium of research projects at the interface of TB and COVID-19

VPM1002 and COVID-19 Trials

Registry number + Sponsor	Primary endpoint	Study population	Study locations	Date of last data collect.
NCT04387409 Vakzine Projekt Management	Number of days absent from work due to respiratory disease (with or without documented SARS-CoV-2 infection)	1200 healthcare workers	Germany	June 2021
NCT04435379 Vakzine Projekt Management GmbH	Number of days with severe respiratory disease at hospital and/or at home	2028 elderly individuals	Germany	May 2021
NCT04439045 University Health Network, Toronto	Self-reported incidence of SARS-CoV-2 infection (confirmed by positive test)	2626 frontline workers	Canada	July 2021
ACTRN12620000707965 Accelagen Pty Ltd, Serum Institute of India	incidence of lab-confirmed SARS CoV-2/COVID-19 infection with severe, critical or life-threatening disease severity based on medical records	3468 healthcare workers or individuals with high-risk of infection (>65 or < 18 with comorbidities)	Australia	March 2021

Adapted from WHO *Compendium of research projects at the interface of TB and COVID-19*

COVID-19 and TB vaccines: other areas of overlap

- **BCG:CoVac**: novel BCG-based COVID-19 vaccine candidate developed in Australia using earlier TB vaccine discovery work.
- **MTBVAC**: live, attenuated form of genetically weakened *M. tuberculosis*. Being studied as a TB vaccine candidate and, possibly, against COVID-19 based on mouse data that MTBVAC protects against challenge by lethal pneumonia.
- **RUTI**: TB vaccine candidate made of fragmented *M. tuberculosis*. Undergoing a clinical trial of protection from COVID-19 in healthcare workers.
- **MIP**: TB vaccine candidate consisting of whole-cell *M. indicus pranii* (sometimes called *Mycobacterium W*) and being studied in critically ill COVID-19 patients in India
- Efforts to develop COVID-19 **human challenge models** have benefitted from techniques and facilities used to develop a TB challenge model using aerosol BCG (Oxford), which have demonstrated the feasibility of aerosol pathogen challenge and built experience with monitoring immune responses in the lungs and blood.

COVID-19 and TB Vaccine Funding Disparities

USG funding for COVID-19 vaccines:

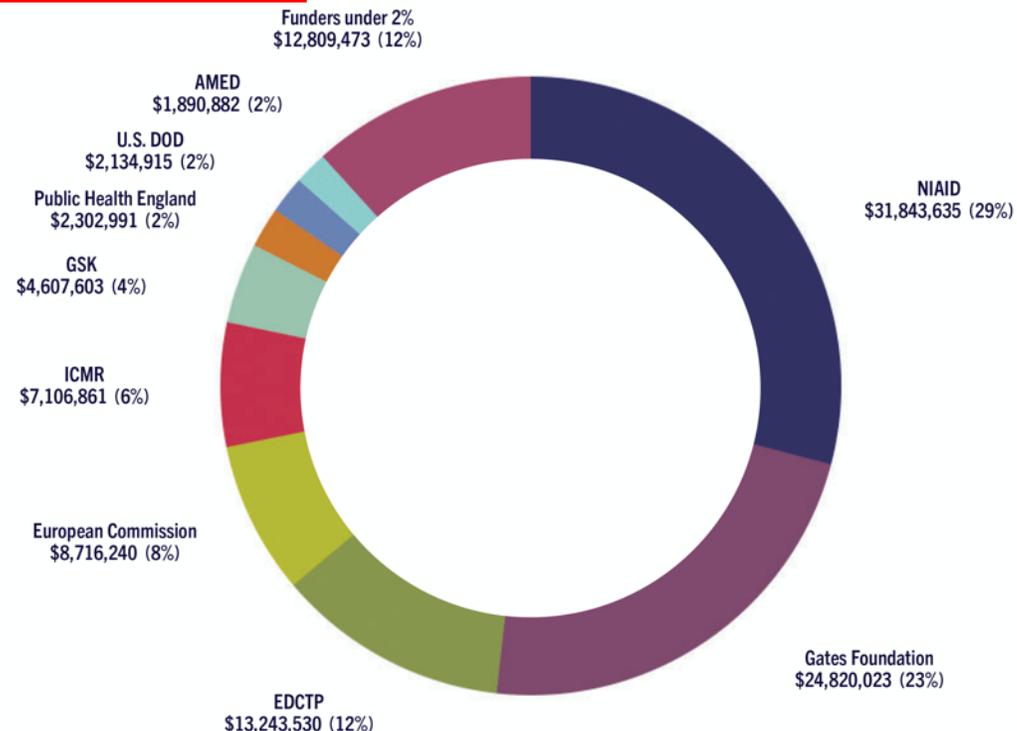
- \$1.525 billion to Moderna*
- \$1.001 billion to Janssen
- \$2.042 billion to Sanofi and GSK
- \$1.950 billion to Pfizer/BioNTech
- \$1.600 billion to Novovax
- \$1.200 billion to AstraZeneca
- \$38 million to Merck and IAVI

* Source: BARDA [COVID-19 Medical Countermeasure Portfolio](#)

** TAG and Stop TB [Report on TB Research Funding Trends](#)

TB vaccine funding 2019**

Vaccines: \$109,476,154



1/10th or less of the average USG contract to COVID-19 vaccine makers!

Longstanding issues in TB vaccine R&D

- Lack of biomarkers or correlates of protection that could act as surrogate markers in clinical trials.
- Inclusion of PLHIV and children in the TB vaccine R&D agenda.
- Need to develop better animal models to inform human trials.
- Mechanisms for regular community engagement and protocol review.
- Chronic underfunding.
- Small advocacy community.

Year	TB Vaccine R&D Funding
2018	USD\$109,476,154
2017	\$100,338,945
2016	\$95,394,136
2015	\$80,736,948
2014	\$111,340,797
2013	\$92,373,647
2012	\$92,049,229
2011	\$99,183,567
2010	\$81,280,821
2009	\$115,741,957

Emerging issues in TB vaccine R&D

- Provision of TB preventive therapy (TPT) as part of TB vaccine trials as an ethical imperative.
- Inclusion of pregnant women in TB vaccine trials.
- Trial site capacity to enable multiple large efficacy trials.
- Attention to access and benefit sharing (and understanding access as something to address at earlier stages of R&D).
- Development of human challenge models.
- **Introduction of next-generation vaccine candidates (e.g., mRNA).**
- Funding for experimental medicine, biomarker investigations, and research on stored samples from clinical trials.
- **Intersection of TB vaccine R&D and COVID-19 vaccine R&D.**

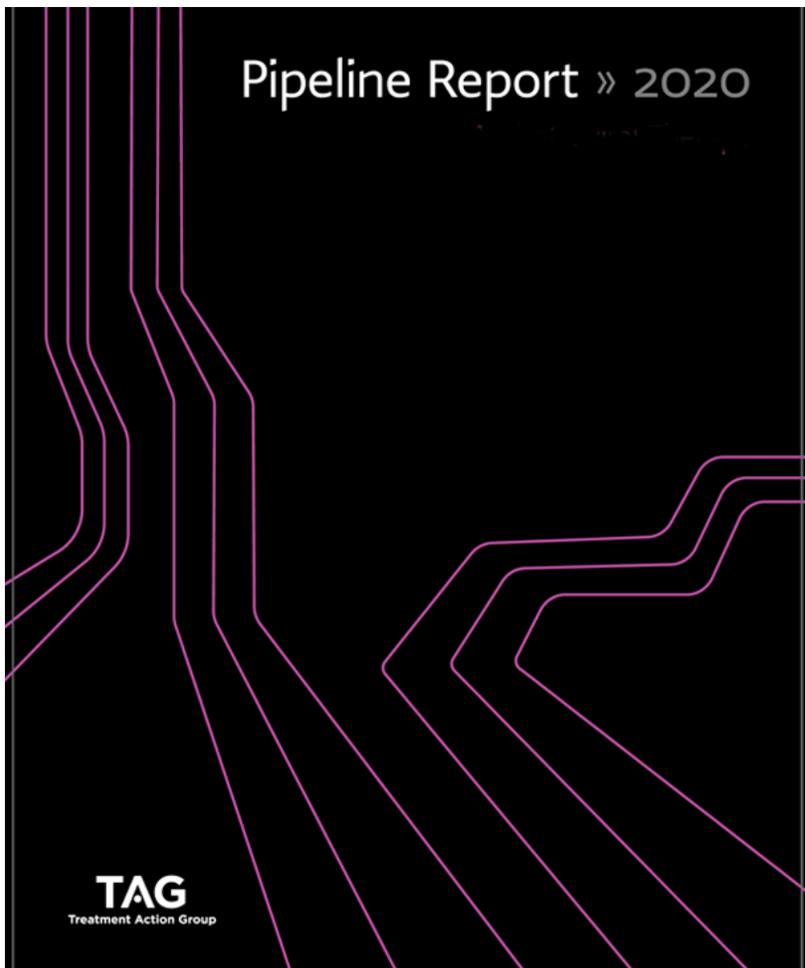
Closer look: **BioNTech**

- German biotech company developing mRNA vaccines.
- Partnering with Pfizer on a COVID-19 mRNA vaccine (BNT162b2).
- Newly working with Gates Foundation to develop mRNA vaccines for HIV and TB:
 - 2019: Gates Foundation makes \$55 million equity investment in BioNTech to develop HIV and TB mRNA vaccines (with the potential to receive up to \$100 million from the Gates Foundation via future grant funding to support clinical evaluations of the resulting candidates).
 - Under the agreement, BioNTech “will retain rights for commercialization of the vaccine candidates in the developed world, while providing affordable access to the candidates in developing countries.”

European support is essential for the future of TB vaccine research: then (BCG) / and now (below)

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	TB/FLU-04L RIBSP	BCG Revaccination Gates Medical Research Institute (GMRI)	

Vaccine developed by
European/Central Asian
institution



Thank you!

← coming soon: overview of TB vaccine clinical development