Roundtable Discussion: TB and HIV Trials & Research Infrastructure At-Risk in South Africa

15 May 2025

AGENDA

Opening Remarks, Dr. Marcus Low, Spotlight

Presentation of Analysis of At-Risk Trials & Research Infrastructure, Lindsay McKenna, TAG

Expert Panel

- Prof. Ntobeko Ntusi, SAMRC
- Prof. Linda-Gail Bekker, UCT
- Prof. Ian Sanne, Wits RHI
- Dr. Tom Ellman, Southern Africa Medical Unit MSF

Question & Answer

Wrap Up & Summary, Marcus Low, Spotlight

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FEATURED SPEAKERS

Dr. Marcus Low, Editor of Spotlight

Dr. Marcus Low is a public health specialist, epidemiologist, and journalist based in Cape Town. He is the editor of the public health magazine SPOTLIGHT. Previously, he was policy director at Treatment Action Campaign, the activist organization credited with forcing the South African government to expand access to antiretroviral treatment for HIV.

Lindsay McKenna, TB Project Co-Director at Treatment Action Group

Lindsay McKenna is the co-director of the tuberculosis (TB) project at Treatment Action Group, a research and policy advocacy organization based in New York. Lindsay works with community advocates, researchers, policy makers, developers, and donors to expedite the development of and access to novel TB treatment, diagnostic, and prevention technologies.

Prof. Ntobeko Ntusi, President and CEO of the South African Medical Research Council

Professor Ntobeko Ntusi is the President and CEO of the South African Medical Research Council (SAMRC). He joined SAMRC from the University of Cape Town and Groote Schuur Hospital where he was the Chair and Head of the Department of Medicine. Prof. Ntusi obtained a BSc(Hons) degree in Cellular and Molecular Biology from Haverford College, USA, and an MBChB degree from the University of Cape Town. He is a physician and cardiologist.

FEATURED SPEAKERS

Prof. Linda-Gail Bekker, Director of the Desmond Tutu HIV Centre at the University of Cape Town

Professor Linda-Gail Bekker is a leading clinician-scientist, CEO of the Desmond Tutu Health Foundation, and the Director of the Desmond Tutu HIV Centre in the Institute of Infectious Disease and Molecular Medicine at the University of Cape Town. She has dedicated her career to advancing HIV research, prevention, and treatment, and to advocating for health equity and innovative solutions to South Africa's greatest health challenges with a primary focus on community-led and integrative HIV/TB prevention and treatment.

Prof. Ian Sanne, Co-Principal Investigator of the Wits HIV Research Group Clinical Trials Unit

Professor Ian Sanne is a South African-born infectious disease doctor whose research focuses on an integrated program of HIV, HIV co-infectious diseases, TB and COVID-19 research from prospective phase I to IV clinical trials, conducted predominantly through international collaborations. He is the founding member of CHRU and of the health non-profit organisation, Right to Care. He is the Principal Investigator of the Wits HIV Research Group Clinical Trials Unit and was the previous International Vice-Chair of the ACTG to 2024.

Dr. Tom Ellman, Director of the Southern Africa Medical Unit of Medécins Sans Frontières

Dr. Tom Ellman is an infectious disease doctor and epidemiologist, and the director of the Southern Africa Medical Unit (SAMU) – a technical, research, and training unit – supporting MSF's global HIV, TB, hepatitis, and NCD work. Since training in Edinburgh and London he has over 25 years of experience in humanitarian medical work, mostly with Médecins Sans Frontières. His focus has been on HIV, TB, and malaria in Africa, apart from a three-year 'break' working on Chagas disease in Bolivia.

ANALYSIS OF TB & HIV TRIALS & RESEARCH INFRASTRUCTURE AT-RISK IN SOUTH AFRICA

LINDSAY MCKENNA, TAG

CHRISTOPHE PERRIN, MSF

15 MAY 2025

DAIDS-FUNDED TB RESEARCH IN SOUTH AFRICA: BY THE NUMBERS

25 **Research Sites**

12 **Clinical Trials**

30% **Participants from South African Sites***

*The proportion is even higher for trials focused on pediatric and pregnant populations (50-90% of participants).

$12K **Estimated Cost Per Participant***

*Per participant costs vary by site, type of intervention, e.g., treatment vs. vaccine, and labs and monitoring requirements and other trial design elements.

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DAIDS-FUNDED HIV RESEARCH IN SOUTH AFRICA: BY THE NUMBERS

22 **Research Sites**

24 **Clinical Trials**

25-50% **Participants from South African Sites***

*The proportion is even higher for trials focused on pediatric and pregnant populations (50-90% of participants).

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DIRECT IMPACTS: ACTG, HVTN, IMPAACT TB TRIALS AT RISK

- **new drugs**
  - next generation oxazolidinones (sutezolid, TBI-223)
- **shorter, safer regimens for treatment of drug-sensitive TB**
  - 2-to-6-months of treatment with isoniazid, rifapentine, moxifloxacin, and pyrazinamide, with duration tailored according to severity of disease (2-6HPMZ)
- **an optimized regimen for TB meningitis**
  - 6-months of treatment with high dose rifampicin, high dose isoniazid, pyrazinamide, and linezolid ($6R_{hd}H_{hd}ZLz$)
- **preventive treatment for contacts of drug-resistant TB**
  - 6-month preventive treatment using delamanid (6D)
- **therapeutic and preventive vaccines**
  - ID93 + GLA-SE
  - MTBVAC (safety and immunogenicity in PLHIV to enable inclusion in IAVI phase IIb+/III trial)
- **data to expand access to life-saving TB innovations to children and pregnant women**
  - 4-month rifapentine- and-moxifloxacin-containing regimen endorsed by WHO for treatment of drug-sensitive TB in non-pregnant, adults and adolescents (4HPMZ)
  - 6-month bedaquiline- and pretomanid-containing regimen endorsed by WHO for treatment of drug-resistant TB in non-pregnant adults and adolescent (6BPaLM)
  - 1-month rifapentine-based regimen endorsed by WHO as TB preventive treatment for adults and adolescents (1HP)

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DIRECT IMPACTS: ACTG, HVTN, IMPAACT HIV TRIALS AT RISK

- **Treatment**
  - dolutegravir in neonates
  - oral cabotegravir in children and adolescents
  - long-acting injectable cabotegravir and rilpivirine in children, adolescents, and pregnant women
- **Prevention**
  - preventive vaccine modalities designed to induce bNab production
  - mRNA vaccines
    - mRNA-1645-eODGT8
    - mRNA-1645-CoreG28v2
    - mRNA-1645-N332GT5
  - Injectable cabotegravir as PrEP
- **Cure**
  - broadly neutralizing antibodies (bNAbs)
    - 3BNC117-LS-J and 10-1074-LS-J - largest HIV cure-related trial on the African continent (planned n=135), following up on encouraging evidence that bNAbs can promote post-treatment control of viral load in some individuals
    - PGT121.414.LS +/- VRC07-523LS
  - analytical interruptions of antiretroviral therapy for adults and infants
- **Co-morbidities**
  - HBV: Oral TLR8 Agonist Selgantolimod
  - MDD: pramipexole vs. escitalopram
  - Hormone therapy for transgender & menopausal women with HIV

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DIRECT IMPACTS: OTHER USG-PROPOSED OR -FUNDED TB STUDIES AT RISK: USAID, CDC, AND NIH-SUPPORTED INVESTIGATOR INITIATED TRIALS

- shorter, safer regimens for TB treatment
  - 3-month bedaquiline- and delamanid-containing regimen for treating drug-sensitive TB (3BDCZ)
  - 4-month bedaquiline, moxifloxacin, and pyrazinamide-based regimens for treating drug-sensitive TB (4BMZ-based regimens)
  - 3-to-6-months of treatment with bedaquiline, pretomanid, linezolid, and moxifloxacin for drug-resistant TB, with duration tailored according to severity of disease (3-6BPaLM)
- an optimized regimen combining new drugs for XDR-TB (necessary to inform optimal treatment of patients with bedaquiline resistance)
- shorter, safer regimens for TB prevention
  - 1-month preventive treatment using bedaquiline (1B)
- shorter, safer regimens specifically for children
  - 2-months of treatment with isoniazid, rifapentine, moxifloxacin, and pyrazinamide for drug-sensitive TB in children (2HPMZ)
  - 4-to-6-months of treatment with bedaquiline, delamanid, levofloxacin, and linezolid for drug-resistant TB in children, with duration tailored according to severity of disease (4-6BDLxLz)

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POTENTIAL INDIRECT IMPACTS: TB TRIALS SPONSORED BY NON-USG FUNDERS

- Public funding from USG to South Africa is the scaffold on which pharma, philanthropies, and other governments invest in transformative TB science.
- Trials sponsored by other research funders build on top of core and other funding provided to clinical trials units and research sites through NIH awards.
- Anticipated ripple effects of NIH funding cuts could affect studies focused on advancing:
  1. vaccine candidates MTBVAC and M72/AS01E;
  2. new TB drugs, including ganfeborole, DprE1 inhibitors quabodepistat and BTZ-043, and next-generation diarylquinolones and oxazolidinones; and
  3. registrational pediatric pharmacokinetic and safety work for bedaquiline.
- In addition to imperiling specific studies and innovations, USG cuts risk infrastructure, staff/talent, training the next generation of scientists, community engagement, data sharing, biorepositories, etc.
- If South African study sites and participants are excluded from enrollment, follow-up, study completion, and data collection and analysis, ongoing and planned trials are likely underpowered to produce meaningful results, wasting years of work and tens or hundreds millions of dollars in investment.
- Trials no longer able to continue enrollment in South Africa will face delays and increased costs as they seek new sites and study participants elsewhere.

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PRIORITY TB INNOVATIONS AT RISK

Preventives	Therapeutics	Special Populations
• Shorter, safer regimens for TB prevention (6-month delamanid and 1-month bedaquiline regimens) • TB vaccines **MTBVAC** and **M72/AS01E** and next-generation TB vaccine candidates at earlier stages of clinical testing	• New drugs, including **ganfeborole**, DprE1 inhibitors (**quabodepistat** and **BTZ-043**), and next generation diarylquinolones (**TBAJ-876**) and oxazolidinones (**TBI-223**) • Shorter, safer treatment regimens, including for TB meningitis and XDR-TB • Therapeutic vaccine **ID93 + GLA-SE**	• Pretomanid and 6BPaLM for treating children with drug-resistant TB • 4HPMZ for treating drug-sensitive TB during pregnancy • 1HP for preventing TB among children exposed to drug-sensitive TB

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LIMITATIONS OF ANALYSIS

- Focused on NIH-funded/DAIDS HIV Clinical Trials Network studies and research infrastructure — trials funded by other governments or donors that may be put at risk by withdrawal of USG funding are not captured.
- List of other USG-proposed or -funded TB studies with sites in South Africa is not comprehensive as it doesn't capture trials or studies supported through other extramural NIH funding mechanisms and only includes one TB diagnostic trial; an analysis of TB diagnostic trials funded by USG with South African sites was not performed.
- Not included here, but potentially helpful for donors to have access to, is information regarding capabilities, core costs, and costs per participant per site.

To help us capture a more complete picture of affected TB and HIV trials, please consider sharing information about USG grants that have been terminated or that are under active threat using the secure form accessible at the following link and QR code:
https://cryptpad.fr/form/#/2/form/view/Q4Luco0lx+Rszmc5P+hwKOa0EtGAu3SXvdeOWZO7Mok/.

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SCAN ME

You can also contact us directly:

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AVAILABLE NOW: ISSUE BRIEF

- Provides information about TB and HIV clinical trials and research programs impacted by U.S. government funding disruptions
- Proposes urgent actions that donor agencies, governments, and philanthropies can take to preserve scientific advances underway and prevent the collapse of TB and HIV medical research in South Africa
- Identifies 39 clinical research sites and at least 20 TB trials and 24 HIV trials at risk
- Includes tables with the specific research sites and TB and HIV studies that will be affected should the U.S. government terminate research awards to South African institutions.

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SOUTH AFRICA'S TB AND HIV RESEARCH AT RISK:
A CALL TO CATALYZE URGENT ACTION BY FUNDERS

May 2025

Since January 2025, a series of United States (U.S.) executive orders, funding suspensions, and grant terminations have thrown South Africa's tuberculosis (TB) and HIV programs into crisis, threatening lifesaving research, prevention, and treatment programs. The stop-work order issued on January 24, 2025 affected all projects funded by the U.S. Agency for International Development (USAID), the Centers for Disease Control and Prevention (CDC), and the President's Emergency Plan for AIDS Relief (PEPFAR). South Africa had been one of the largest beneficiaries of PEPFAR, which contributes approximately 17% to the national HIV/AIDS response, supporting access to antiretroviral therapy (ART) for 5.5 million people.[1] Along with to the national TB response, including essential National TB Pr in South Africa.[2] Research conducted in South Africa — muc supported with funding from the U.S. National Institutes of Health (USAID — has helped to bring forward most of the innovations i ades and shaped global health policies that have revolutionized t tment and care, benefiting both the local population and commun live in the United States.

This issue brief provides info als and research programs impacted by U.S. governmen urgent actions that donor agencies, government serve scientific advances underway and prevent the co ch in South Africa.

According to the latest data, over 3 million people are living with HIV.[3] Of these, about 6.2 million are receiving ART, at least prior to the recent USAID/PEPFAR program cuts. In 2023/2024 there were an e ns and 105,000 deaths among people with HIV.[4] TB is the leadin HIV, but also affects people without HIV. According to the Wo 23 there were 270,000 new cases of TB in South Africa, 145,00 ing with HIV. Thirteen thousand cases of rifampicin-resistant and multidrug-resistant TB were reported, and 56,000 deaths from TB overall, 31,000 of them (55%) among people with HIV.[5]

SCAN ME

South African research institutions have played a central role in advancing global TB treatment, prevention, diagnostics, and vaccine development. Contributions include key trials that led to the registration and defined the optimal use of new medicines for drug-resistant TB (bedaquiline, pretomanid, delamanid), and introduced short-course regimens for the prevention (3HP, 1HP, 6L) and treatment of both drug-sensitive and drug-resistant TB (4HPMZ, 6BPaLM). South Africa has led pediatric investigations for nearly all TB medicines and generated most of the available dosing and safety data for TB prevention and treatment during pregnancy. Diagnostic breakthroughs, including validation of rapid TB tests like GeneXpert and urine LAM, relied heavily on South African study populations. Furthermore, the country has contributed to every major TB vaccine trial over the past 25 years, including the first infant efficacy trial of a novel TB vaccine candidate (MVA85A) and other ongoing trials of candidates including: M72/AS01E, BCG revaccination, MTBVAC, ID93/GLA-SE, and the first mRNA TB vaccines.

1

Available from: https://www.treatmentactiongroup.org/publication//south-africas-tb-and-hiv-research-at-risk

ACKNOWLEDGEMENTS

Tanya Nielson
Managing Director
Clinical Research Division
Aurum Institute

Richard Jeffreys
Basic Science, Vaccines, and Cure
Project Director
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Mike Frick
TB Project Co-Director
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And the DAIDS networks PIs / Leadership Teams and Network Coordinating Centers, and PIs of individual ACTG, IMPAACT, HVTN, HPTN trials.