TB Vaccine Roadmap for People Living with HIV

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IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

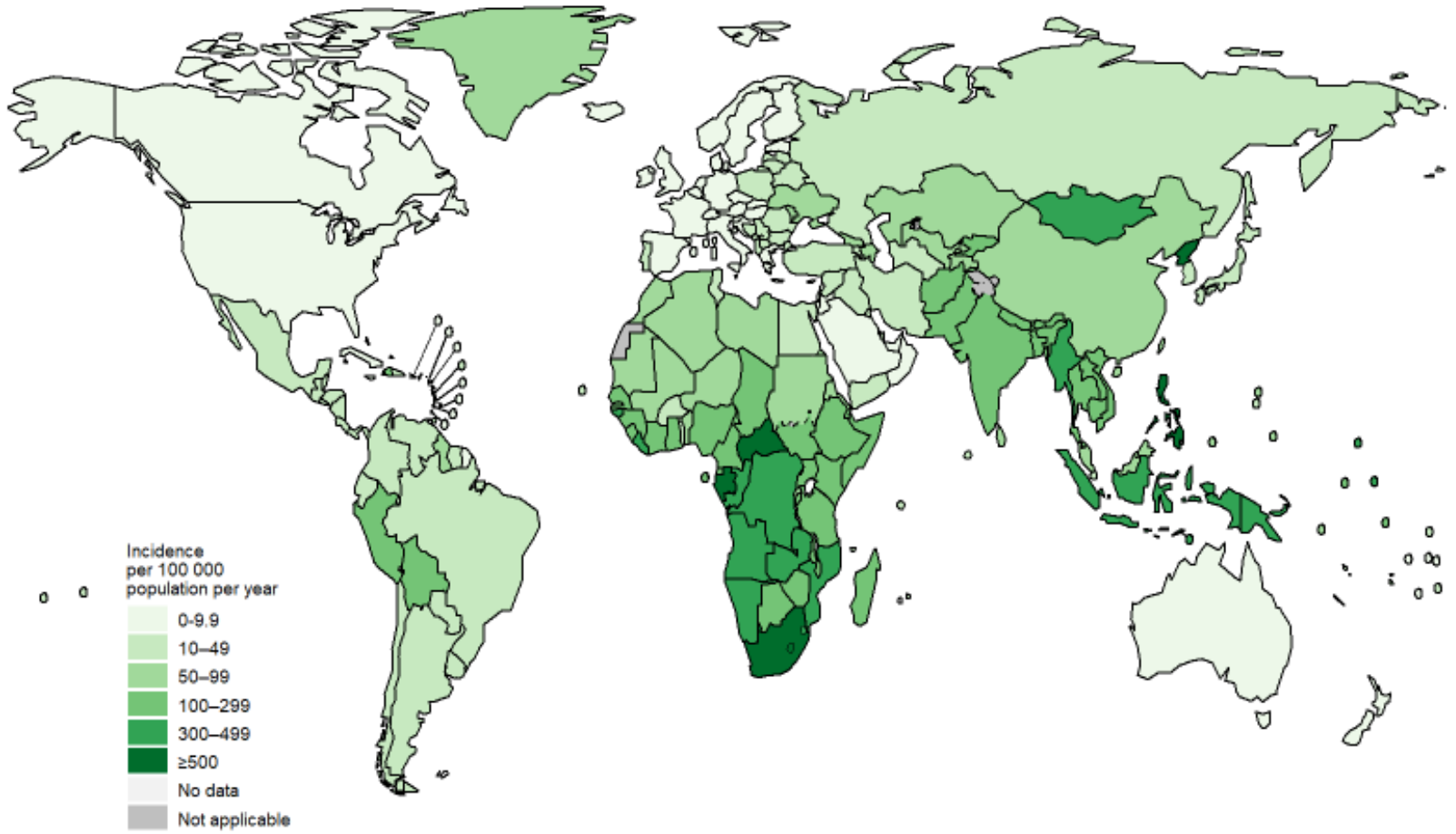
ACTG
AIDS CLINICAL TRIALS GROUP

HIV VACCINE TRIALS NETWORK

Overview

- Background of TB and PLWH
- Symposium roadmap description and methods
- What’s ahead

Global TB incidence



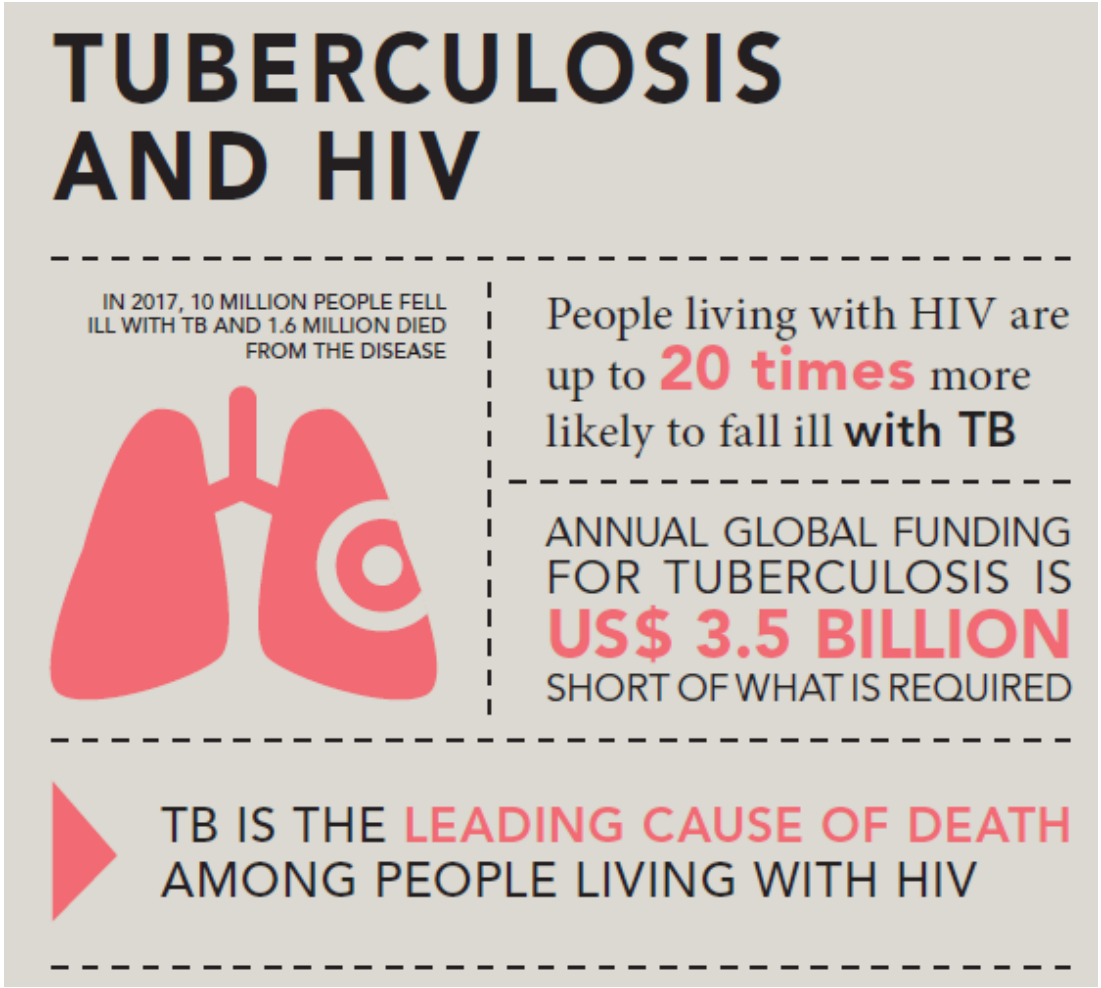
Estimated TB incidence rates, 2021

HIV VACCINE TRIALS NETWORK

Global TB Report 2022, WHO

People living with HIV and TB

- Estimated 10 million TB cases in 2020; 1.5 million deaths
- Large population is people living with HIV (PLWH)
  - At high risk of TB acquisition
  - TB is leading cause of death
  - Historically been excluded from TB vaccine trials
- TB vaccines may not be as immunogenic / efficacious in PLWH



UNAIDS 2018

Modeling suggests exclusion of PLWH from TB vaccination campaigns reduces ability to control transmission

Incidence rate reduction for an efficacious vaccine:

Harris et al., Sci. Transl. Med. 12, eaax4607 (2020)

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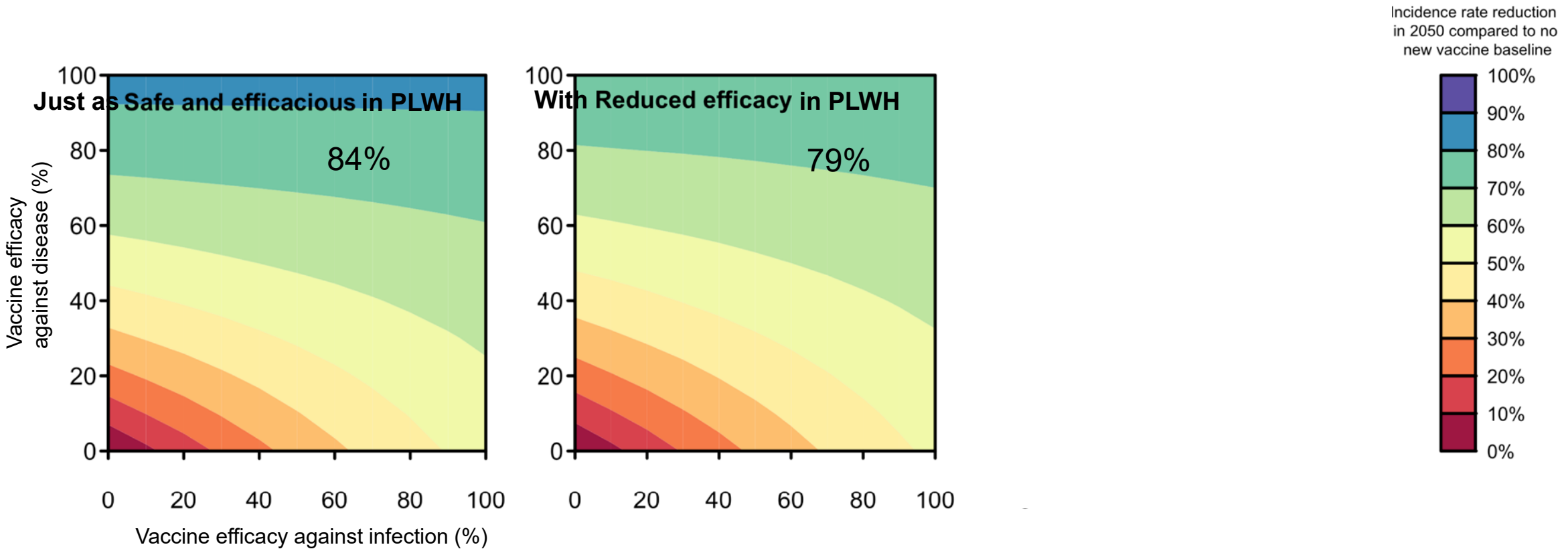

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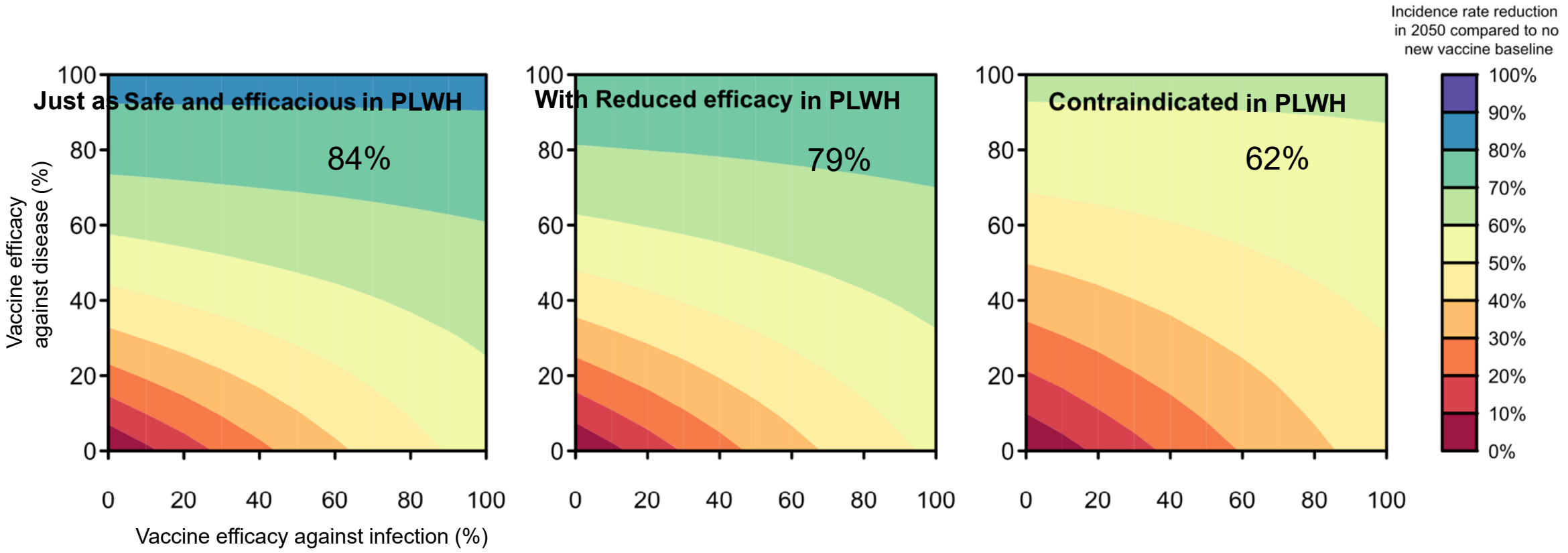

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Purpose of the symposium

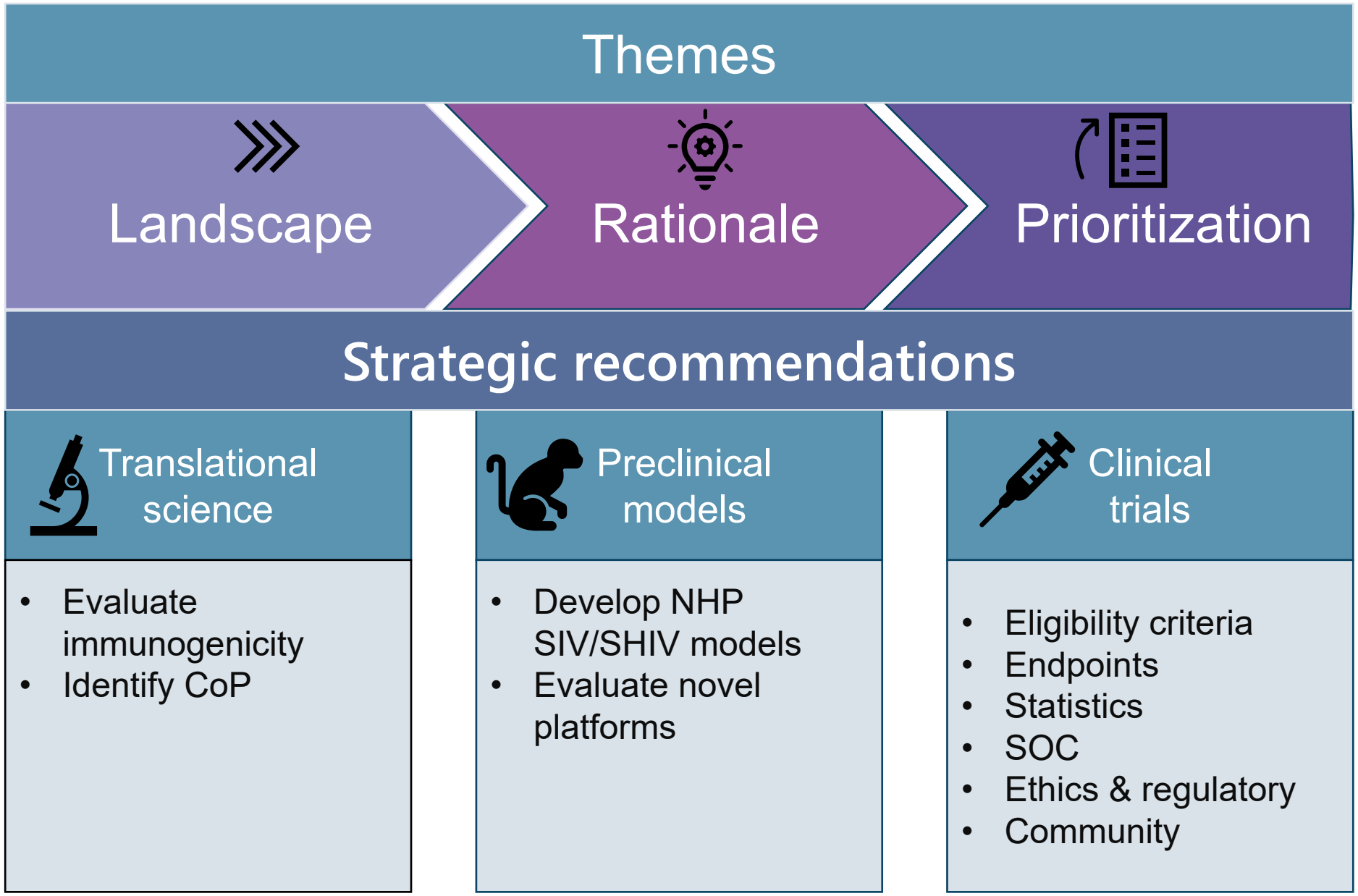
- To accelerate development of TB vaccines for PLWH by identifying gaps and priorities with respect to:
  - Basic & translational studies
  - Preclinical models
  - Vaccine candidate selection
  - Clinical trial designs

Description of the symposium for inclusion of PLWH in TB vaccine trials

- NIAID Cross-Network TB Vaccine Working Group recognized need for a roadmap for TB vaccines in PLWH

- Jan-Feb 2021, presentations and discussion sessions based on six framing questions
- Organizers and panelists generated consensus statements supporting priorities and pathways
- Experts in TB and HIV immunology, vaccinology, ethics, regulatory affairs, epidemiology, community engagement, and modeling

TB vaccine roadmap for PLWH



Symposium framing questions

1. **What is the landscape of TB vaccines and potential risks of administering these to PLWH?**

2. **What is the use case or rationale for developing TB vaccines for PLWH?**

3. **Which vaccine candidates should be prioritized for study in PLWH?**

Symposium framing questions

4. **What is the role of immunological correlates of protection in PLWH?**

5. **Trial design considerations**

- When should PLWH be included in TB vaccine trials?
- What should the standard of care (SOC) be?
- What are the HIV specific eligibility criteria?
- What are the HIV specific efficacy endpoints?
- What are the statistical considerations?
- What are the ethical considerations?
- What are the regulatory considerations?
- How should community be involved?

6. **What are the gaps in preclinical models for studying TB vaccines in PLWH?**

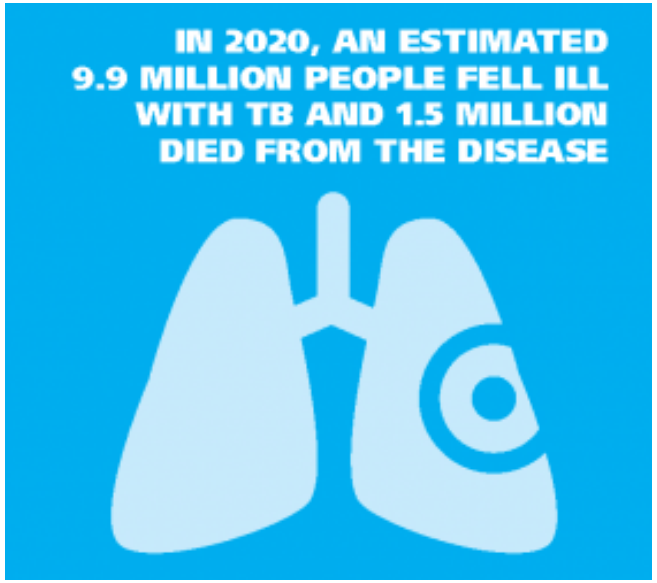
What is the rationale for developing TB vaccines for PLWH?

Background:

- TB remains leading cause of death in PLWH
- 14% of TB deaths are among PLWH
- PLWH have poorer outcomes than general population
- Models show importance of vaccine efficacy in PLWH

Consensus statement:

- Trials of TB vaccines among PLWH are required to demonstrate safety, immunogenicity and efficacy
- Inclusion early in clinical development avoids unnecessary delays



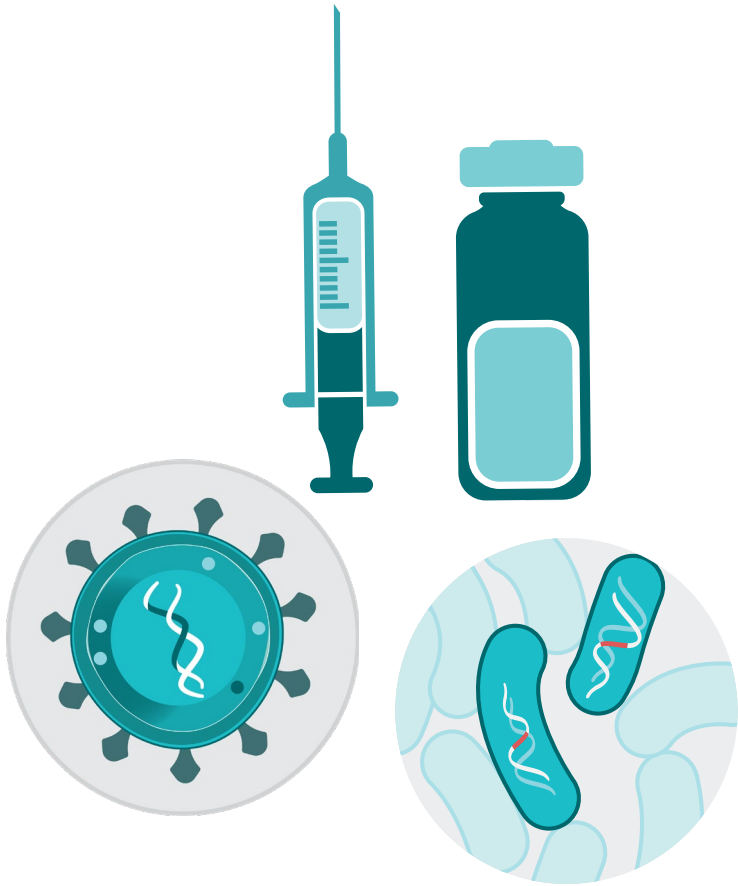
People living with HIV are up to **18 times** more likely to fall ill with TB

UNAIDS 2022

Which vaccine candidates should be prioritized for study in PLWH?

Background:

- PLWH can have impaired immune responses, even while on ART
- Based on the pre-ART era, PLWH historically have not been given live attenuated TB vaccines



Consensus statement:

- Adults/adolescents, infants/children
  - Subunit or inactivated mycobacterial vaccines
  - Non-replicating viral vectored vaccines
  - Followed by viral vectored and live attenuated
  - mRNA and DNA vaccines prioritized once in development

What should the standard of care be for PLWH in TB vaccine trials?

Background:

- An effective TB vaccine for PLWH would complement existing tools for TB prevention
  - early disease detection
  - prompt diagnosis and treatment
  - infection prevention and control
  - TB preventive treatment (TPT)

Credit: WHO Global TB Report 2022

Consensus statement:

- All PLWH participating in TB vaccine trials should be on ART
- TB preventive treatment should be offered to PLWH as the standard of care either prior to or post enrollment

How should community be involved with TB vaccine trials including PLWH?

Background:

- Trial designs should include input from community engagement and deliberations with Community Advisory Boards and local leaders
- Community Advisory Boards and other community stakeholders significantly enhance enrollment and retention
- For example, recent HIV vaccine trials were re-designed after community engagement to offer PrEP

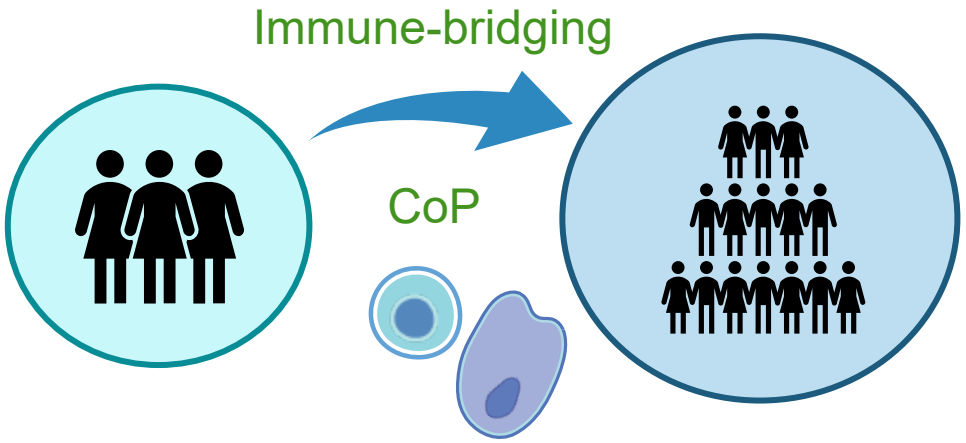
Consensus statement:

- This type of community focused trial design should be applied to TB vaccine trials to ensure PLWH are included safely
- Community stakeholders should be involved early in the process to ensure best outcomes and provide input into study design, trial conduct and results dissemination

What is the role of immunological correlates of protection (CoP) in PLWH?

Background:

- Currently no known CoP have been identified
- Immune-bridging: immune responses to an efficacious vaccine in one population can accelerate vaccine development in another population



Consensus statement:

- Standardized sample collection and endpoint measurements is encouraged to enable immune-bridging
- Identified CoP should be applied to PLWH using immune-bridging studies
- Immunogenicity studies should be done in PLWH to maximize potential to identify CoP

Consensus roadmap

Key gaps and priorities

Basic & translational studies

- Analyse responses from TB vaccine clinical trials showing efficacy to identify CoP
- Use immune-bridging studies to apply CoP identified in people without HIV to PLWH

Preclinical models

- Invest in NHP SIV/SHIV models (with and without ART)
- Novel vaccine platforms should be evaluated in NHP SIV/SHIV models

Vaccine candidate selection

- Subunit, inactivated, viral vectored, live attenuated vaccines
- Novel vaccine platforms such as mRNA and DNA should be prioritized once they enter clinical trials

Clinical design considerations

- PLWH (on ART) should have completed TPT prior to enrollment or be offered TPT during the study
- PLWH CD4+ T-cell counts >100 cells/uL or HIV RNA <200 copies/mL may be included
- The timing of when to include PLWH should be based on risks (safety) versus need to reduce “time-to-evidence”

Looking ahead

- Three HVTN TB vaccine protocols will open for enrollment in 2023
- Each is a collaboration with ACTG or IMPAACT networks

HVTN 603 / ACTG 5397: ID93/GLA-SE for prevention of recurrence	HVTN 604 / IMPAACT 2035: VPM1002 safety and immunogenicity	HVTN 605 / ACTG 5421: MTBVAC safety and immunogenicity
• Ph 2a/2b for prevention of recurrence in adult South Africans (n = 1500) • Will enroll adults undergoing TB therapy, including PLWH	• Ph 1/2 in pre-adolescent South Africans (n = 480) • Includes IGRA+/- and PLWH+/- randomized to VPM1002, BCG and placebo	• Ph 2a in adolescent and adult South Africans (n = 276) • Includes IGRA+/- and PLWH+/- (w/ and w/o advanced HIV at HIV diagnosis)

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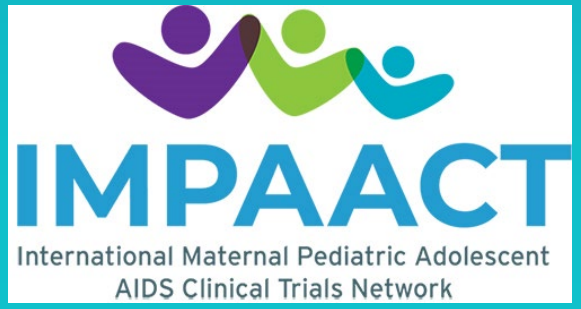
THANK YOU


NIH
National Institute of
Allergy and
Infectious Diseases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