

# TB preventive therapy: recent advances and future prospect

23rd June 2020, 10:00 EST

Moderator: Karin Turner

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# Presentation

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## **TB preventive therapy: recent advances and future prospects**

Moderator: Karin Turner

### **1. TB preventive therapy: recent advances and future prospects**

Prof Gavin Churchyard , Aurum Institute, South Africa

### **2. The South African experience**

Dr Lindiwe Mvusi, Department of Health, South Africa

### **3. TB Preventative Therapy, continuing scale up during the COVID-19 pandemic**

Mr Bill Coggin, CDC, USA

Questions and Answers will follow the presentations.



## Disclaimer

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# TB preventive treatment: recent advances and future prospects

**Gavin Churchyard**

**MBBCh (WITS), FCP (SA), MMED (Int  
Med), FRCP (Edin), PhD (WITS)**

*Union webinar*

*TB preventive treatment: recent  
advances and future prospects*

**23 June 2020**



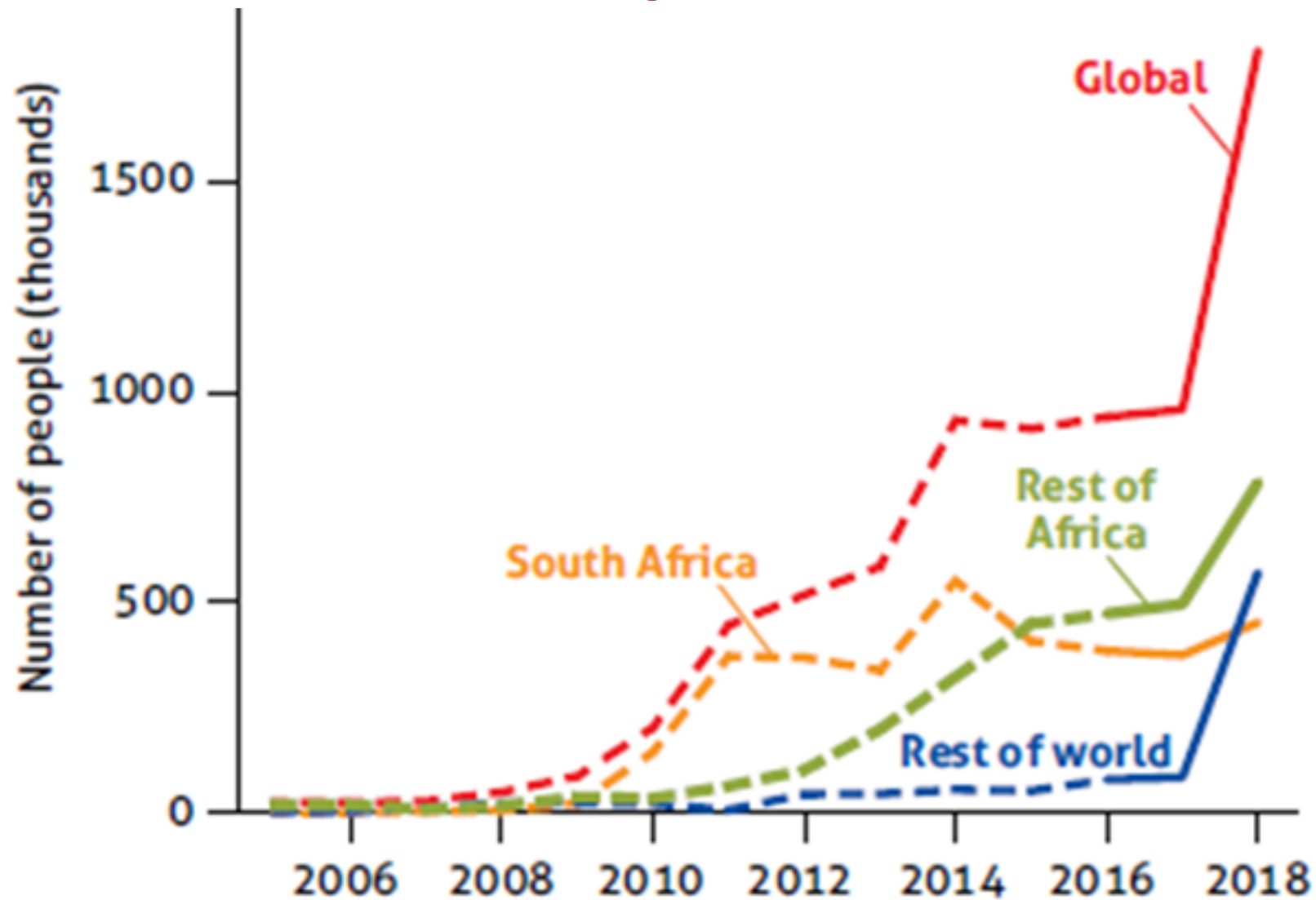
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# Overview

- Background
- Long TPT
- Short-course TPT
- Ultra-short course TPT
- Periodic short-course TPT
- Conclusion



# Global uptake of IPT



(Global TB Report 2019)



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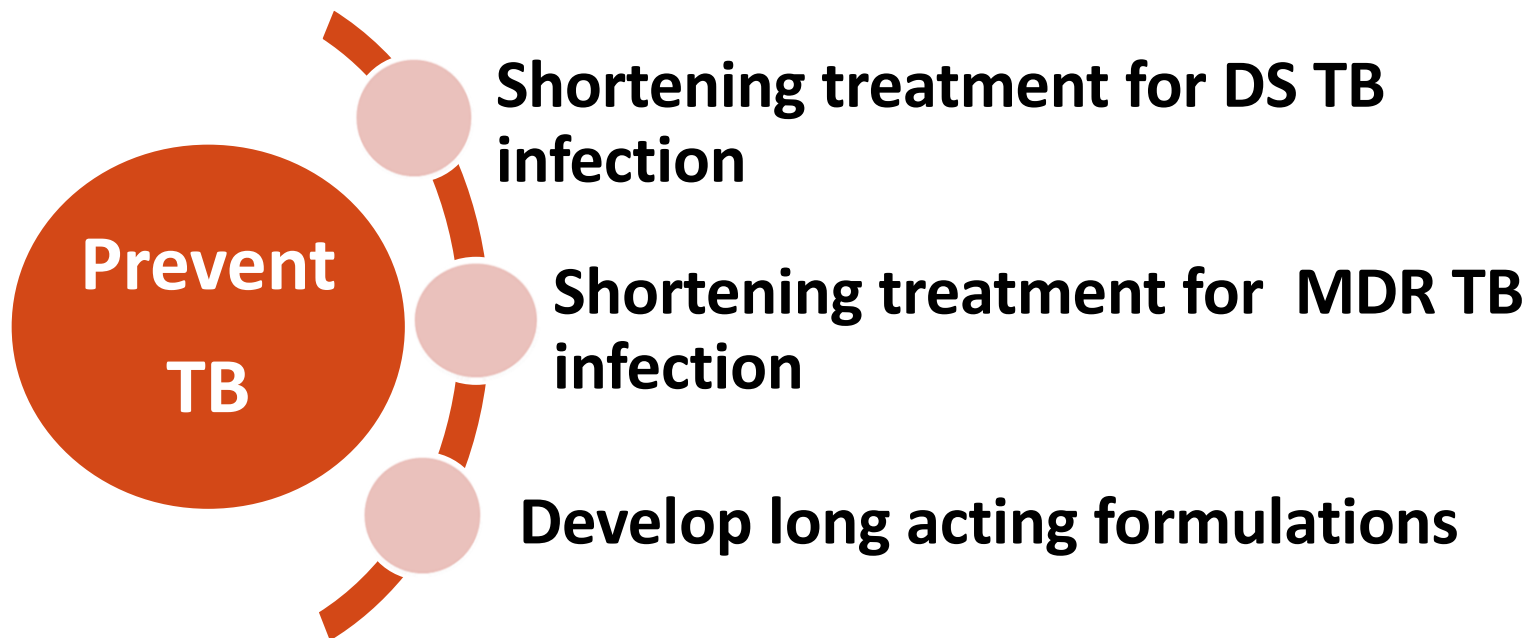
# United Nations High-Level Meeting on TB

- UNHLM was held in New York, September 2018
- Heads of State committed to meeting End TB targets by 2030 by
  - Scaling up effective interventions, including starting at least 30 million people on TPT by 2022
    - 4 million children under 5 years of age
    - 20 million other household contacts
    - 6 million people living with HIV





## Research priorities



# Long TB preventive treatment

*6-12 months of IPT*



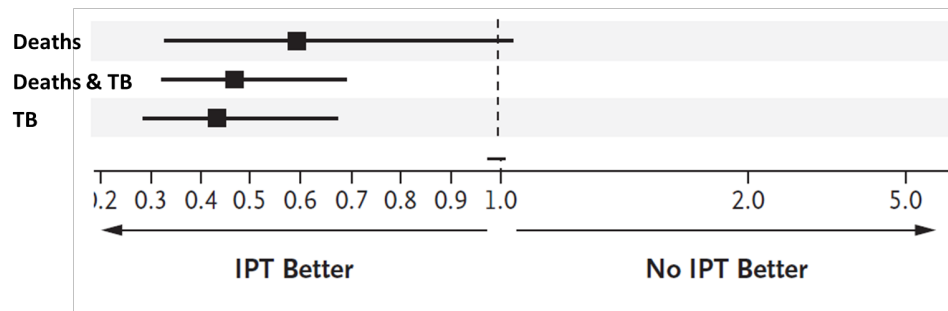
## IPT with ART

IPT with ART is effective in reducing the risk of TB disease and death

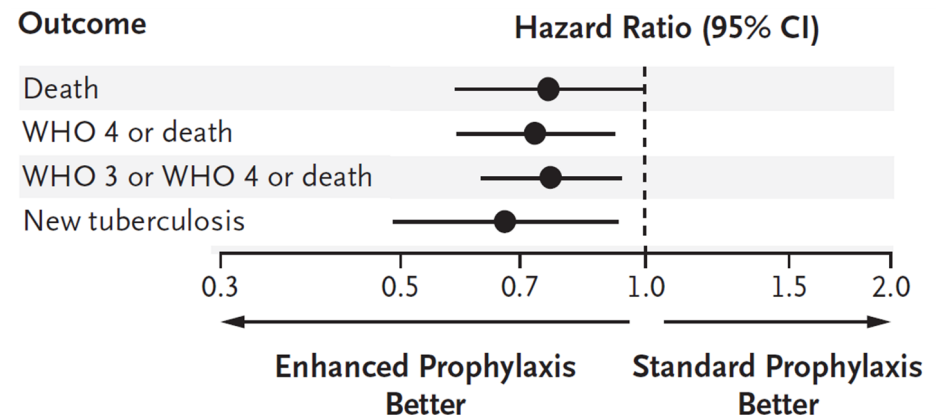
- Among those already on ART<sup>1</sup>
- When started immediately with ART, including those with CD4 count > 500 cells/mm<sup>3</sup><sup>2</sup>
- Among patients with advanced HIV disease<sup>3</sup>

### Temprano study

Immediate ART+ 6H reduced TB and deaths\*

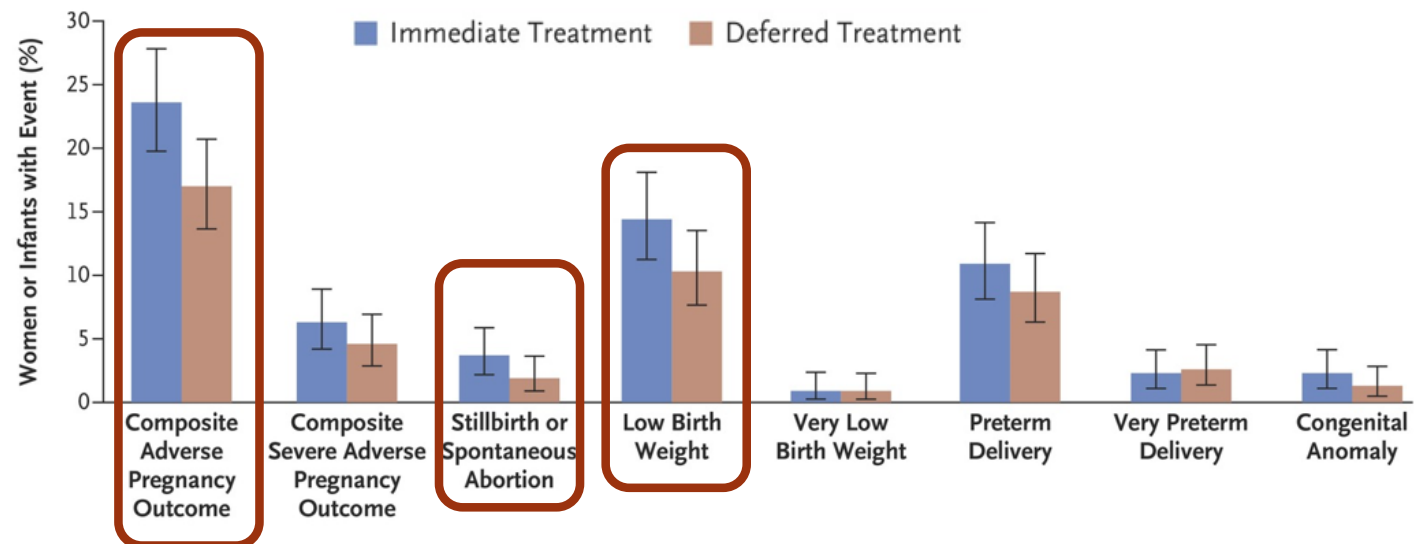


### Enhanced prophylaxis + ART reduces death and TB



## IPT in pregnant HIV-positive women

- IPT during pregnancy vs. postpartum initiation in HIV-positive women was associated with
  - low birth weight and fetal demise<sup>1</sup>
  - 1.6x increased odds of adverse pregnancy outcome in adjusted analysis<sup>2</sup>
- WHO does not recommend deferring IPT to the postpartum period<sup>3</sup>



# iTIPS Trial: IPT in HIV-exposed uninfected infants

- Compared IPT for 12 months vs. no IPT in HEU infants
- Non-blinded RCT in Kenya, 2016-2019
- Mtb infection rates were not significantly lower in the IPT arm
  - IPT arm (7.0%) vs. no IPT arm (13.4%),  $p=0.11$
- No INH-related SAEs

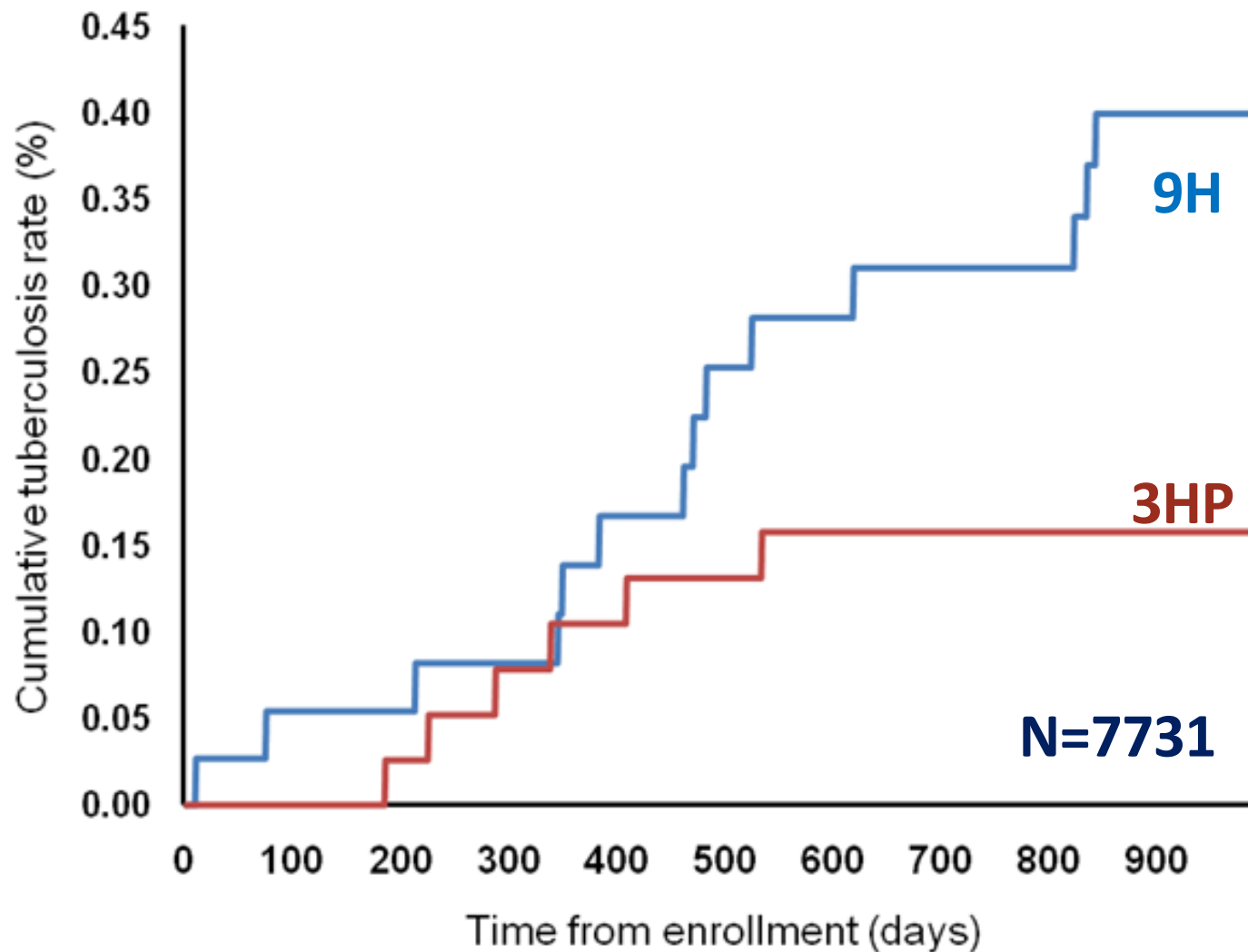


# Short-course TB preventive treatment



# Weekly high dose 3HP is non-inferior to 9H

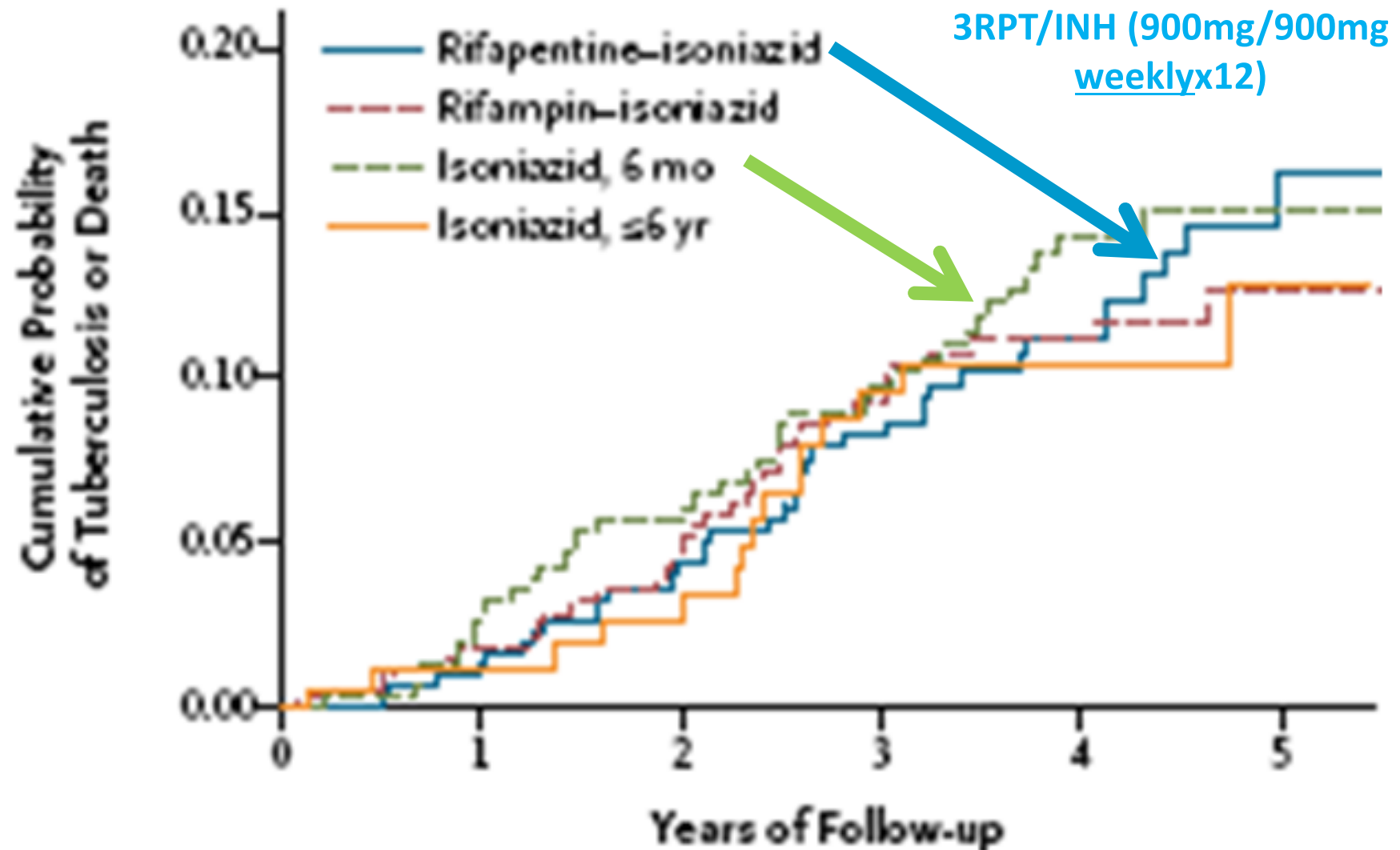
Study 26: High risk persons in US, Canada, Brazil & Spain



Sterling NEJM 2011;365:2155

# Short course rifamycin based regimens have similar efficacy as 6-months IPT in PWHIV

TST+ South Africans



(Martinson NEJM. 2011)

# Cost effectiveness of short TPT regimens

3HP vs 9H<sup>1</sup>

- 3HP likely to be cost-effective if
  - Price of RPT can be greatly reduced (to ~\$20 per course)
  - High treatment completion (85%) can be achieved

(1. Johnson. CID. 2018)

# Pragmatic dosing recommendations for rifapentine based TPT

- Weight-based dosing of rifapentine for 3HP & 1HP initially recommended, but is not aligned to
  - Dosing algorithm
  - Available formulations
  - Results in lower rifapentine exposures in persons with low weight or HIV
- Flat rifapentine dosing recommended in adults to avoid under exposure in people with low weight or HIV<sup>1</sup>
- WHO now recommends flat dosing for rifapentine based TPT

(1. Radke. CROI 2020)



# Rifapentine safety & PK in pregnant women with or without HIV on 3HP

- IMPAACT2001: Phase I/II study
- N=50 (20 had HIV)
- No drug related SAEs
- No TB in women or infants
- Tolerability and safety looks promising
- Pregnancy did not increase rifapentine clearance
  - Therefore no need to dose adjust rifapentine
- Among pregnant women with HIV taking EFV, rifapentine had higher than expected clearance

(Mathad. CROI 2020)

# 4R vs 9H for TB infected adults

- 3443 adults randomised
- Efficacy
  - 4R non-inferior to 9H
- Better safety (all AEs)
  - 2.8% vs. 5.8% (Risk difference:  $-3.0$  ( $-4.1$  to  $-2.0$ ))
- Higher treatment completion
  - 78.7% vs 62.8% (*Risk difference: 15.6% (13.4%-17.8%)*)

(Menzies. NEJM. 2018)

# 4R vs 9H in children: safety & treatment completion

- 844 children <18 years randomised
- Treatment completion rates
  - 85.3% vs 76.4%
- AE rates similar & low (<5%)
- Treatment efficacy similar
  - Rate difference: -0.37 cases/100 py (-0.88-0.37))

(Diallo. NEJM. 2018)

# Rifamycin based TPT with dolutegravir

## **DOLPHIN<sup>1</sup>**

- 3HP with DTG was well-tolerated with no viral rebound
- Trough DTG concentrations were reduced by ~ 50%, median values > 300 ng/mL at all time points
- DTG dose adjustment is not required with 3HP

## **TBTC 35**

- Evaluating safety & PK in children

## **INSPIRING<sup>2</sup>**

- Twice-daily DTG was effective and well tolerated with rifampicin based TB treatment
  - DTG dose should be doubled with rifampicin based TPT

# Ultra-short-course TB preventive treatment





# One month of isoniazid and rifapentine (*Ultra short*)

## 1HP vs 9H

- 1HP non-inferior to 9H
- Better
  - Safety & tolerability
  - treatment completion
- Unknown whether dose adjustment of DTG is required
  - A5372: DTG given QD or BD
- No evidence yet for use in HIV-uninfected persons, children & pregnant women

### The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MARCH 14, 2019

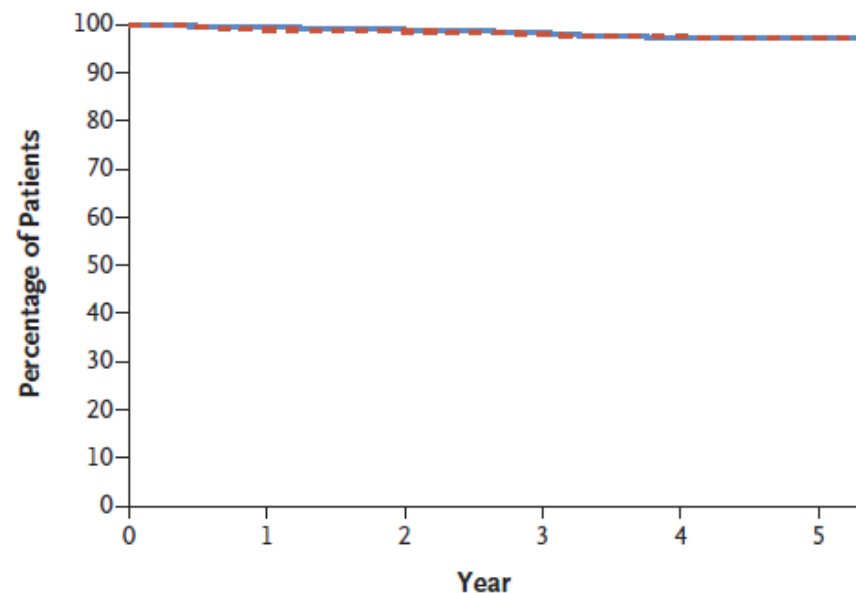
VOL. 380 NO. 11

#### One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis

S. Swindells, R. Ramchandani, A. Gupta, C.A. Benson, J. Leon-Cruz, N. Mwelase, M.A. Jean Juste, J.R. Lama, J. Valencia, A. Omoz-Oarhe, K. Supparatpinyo, G. Masheto, L. Mohapi, R.O. da Silva Escada, S. Mawlana, P. Banda, P. Severe, J. Hakim, C. Kanyama, D. Langat, L. Moran, J. Andersen, C.V. Fletcher, E. Nuernberger, and R.E. Chaisson, for the BRIEF TB/A5279 Study Team\*

— 1-Month    - - - 9-Month

#### A Freedom from Primary End Point in All Patients



# Cost effectiveness of short TPT regimens

1HP vs 3HP<sup>1</sup>

- Cost effectiveness of 1HP vs 3HP, is driven by 1HP completion rates relative to 3HP, cost of rifapentine, and LTBI prevalence

(1. Ferguson et al, Union 2019)

# 2R2: Higher Dose Rifampin for 2 Months vs Standard Dose Rifampin for Latent TB

**PI:** Dick Menzies

## **Aim**

- To determine if rifampin at double or triple the standard dose for 2 months is as safe and effective as 4R

## **Design**

- 1:1:1 randomized
- Phase 2b, partially blind, controlled trial
- The two higher doses (intervention arms) will be administered double-blind: participants and providers will be blinded to dose (i.e. 20 or 30 mg/kg/day)

# Assessment of the Safety, Tolerability, and Effectiveness of Rifapentine Given Daily for LTBI (ASTERoid)

**PI:** Tim Sterling

## **Aim**

- To compare the safety and effectiveness of 6-weeks of daily rifapentine (6wP) with 12-16 weeks of rifamycin-based treatment

## **Design**

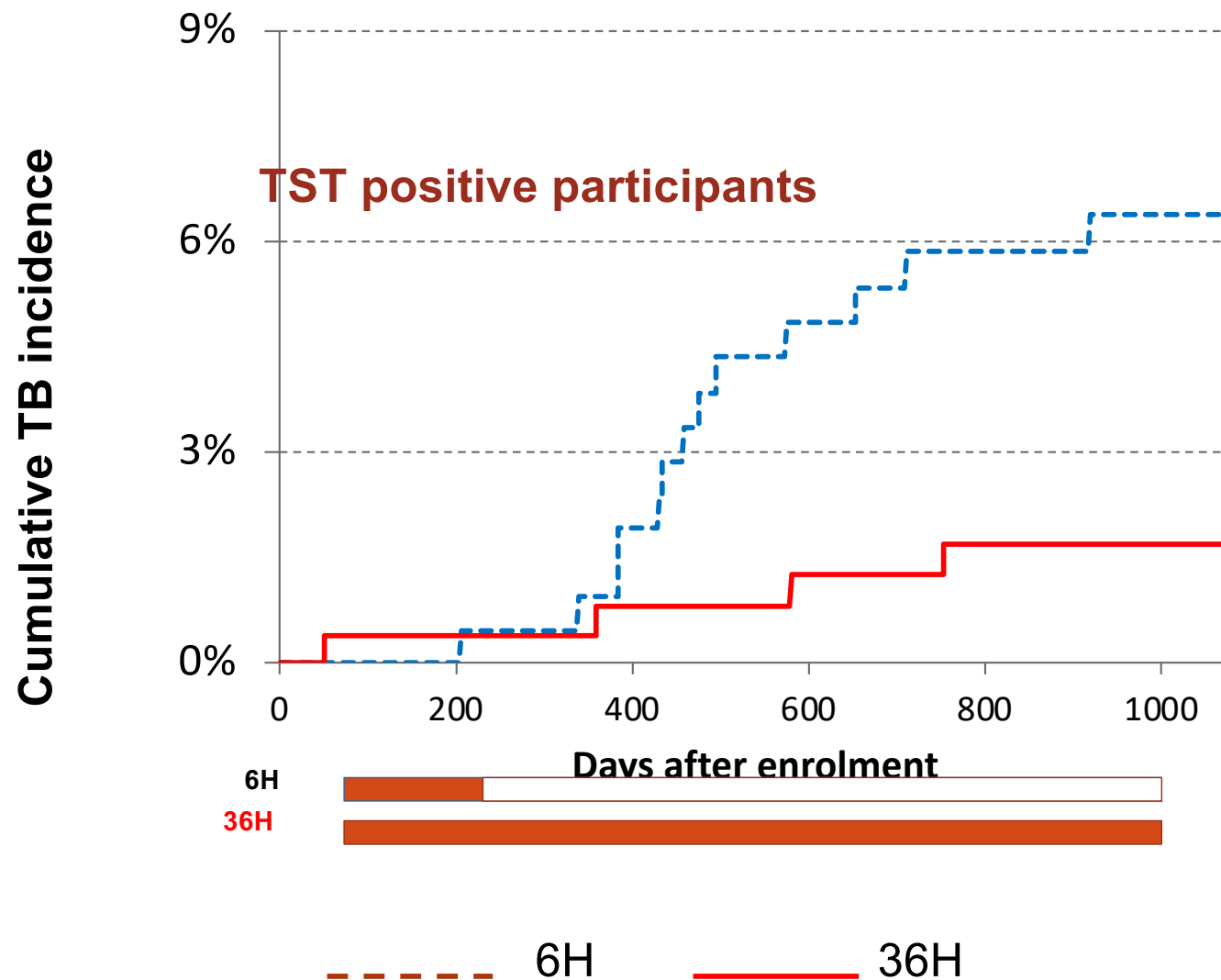
- RCT
- 1:1 randomisation

# The ultra-long and periodic short course TB preventive treatment



# 36 months of IPT

## *Ultra long*





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**CHALLENGE** **TB**

## **Effectiveness of 3HP Annually vs Once for HIV-Positive People: The WHIP3TB Trial**

**Gavin Churchyard<sup>1</sup>, Vicky Cardenas, Violet Chihota, Kathryn Mngadi, Modulakgota Sebe, William Brumskine, Salome Charalambous, Neil A. Martinson, Getnet Yimer, Alberto L. Carcia-Basteiro, LeeAnne Masilela, Susan Van Den Hof, Richard E. Chaisson, Alison Grant, Katherine Fielding, for the WHIP3TB Team**

<sup>1</sup>The Aurum Institute, South Africa

School of Public Health, University of Witwatersrand, South Africa



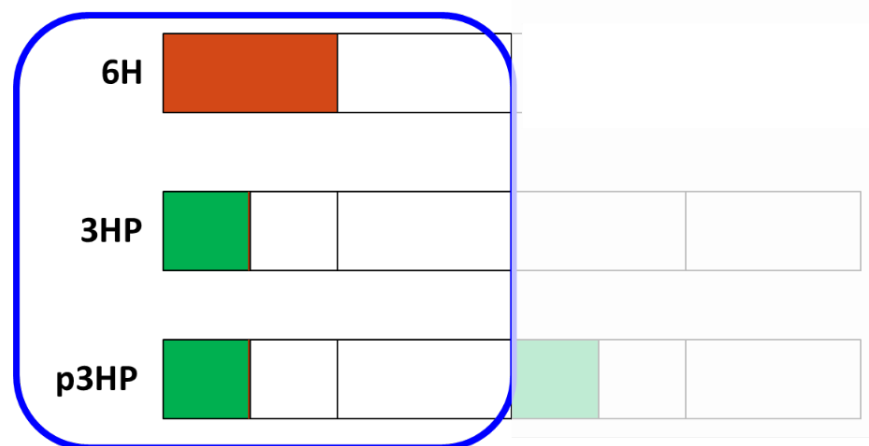
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# Part A: An observational randomised comparison of 3HP vs 6H

## Primary objective:

- To compare treatment completion in HIV-positive participants taking 3HP to those taking 6H



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## Part A: primary outcome

### *Treatment completion*

|                        | Arm | n/N       | % treatment completion | Risk difference, % (95% CI) | Risk Ratio (95% CI) |
|------------------------|-----|-----------|------------------------|-----------------------------|---------------------|
| Primary outcome        | 3HP | 3264/3610 | 90.4                   | 39.9 (35.0-44.9)            | 1.79 (1.62-1.97)    |
|                        | 6H  | 204/404   | 50.5                   | 0                           | 1                   |
| Sensitivity analysis * | 3HP | 3199/3279 | 97.6                   | 34.9 (29.5-40.3)            | 1.56 (1.43-1.70)    |
|                        | 6H  | 198/316   | 62.7                   | 0                           | 1                   |

\* restricted to participants who had pill counts recorded at the month 3 visit for the 3HP arm and at the month 6 visit for the 6H arm



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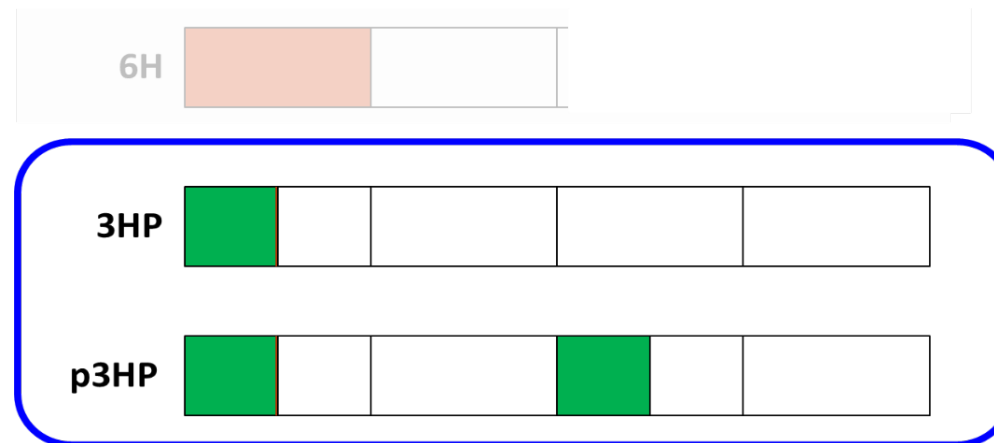


**CHALLENGE** TB

# Part B: A randomised controlled trial of p3HP vs 3HP

## Primary objective:

- To compare TB incidence among individuals randomised to two periodic (annual) rounds of 3HP (p3HP) vs a single round of 3HP



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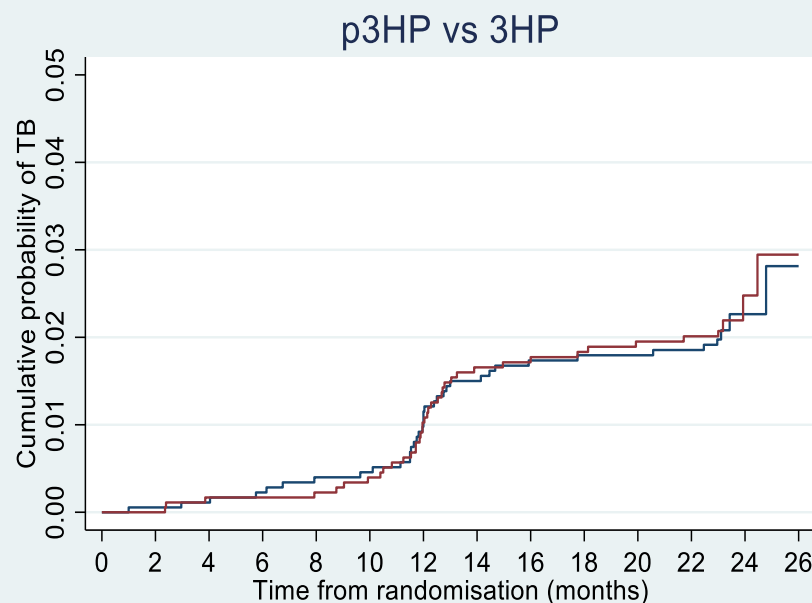


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**CHALLENGE TB**

# Part B: primary outcome *TB incidence over 24 months*



No. at risk (TB events):

p3HP: 1808 (2) 1742 (5) 1725 (10) 1708 (13) 1659 (1) 1642 (5) 292

3HP: 1802 (3) 1755 (1) 1748 (14) 1731 (12) 1662 (4) 1648 (4) 326



| Arm  | n    | # TB/pyrs,<br>Rate/100pyrs | HR (95% CI)*         | P-value |
|------|------|----------------------------|----------------------|---------|
| p3HP | 1808 | 37/3070,<br>1.21           | 0.96 (0.61-<br>1.50) | 0.85    |
| 3HP  | 1802 | 39/3094,<br>1.26           | 1                    |         |

pyrs person-years, HR hazard ratio, CI confidence interval

\* Adjusted for country

TB events (n=76):

definite 68% (n=52)

probable 4% (n=3)

possible 28% (n=21)



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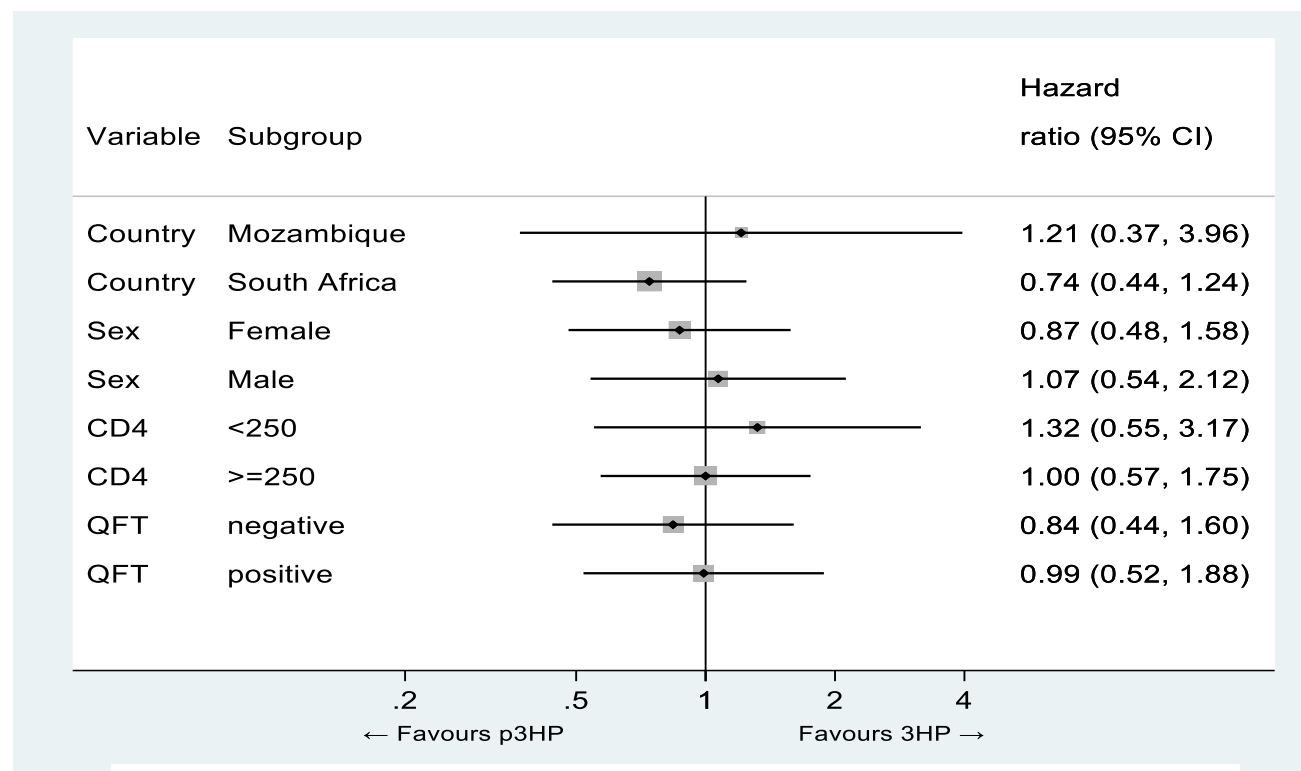
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**CHALLENGE TB**

# TB incidence

## *Sub-group analyses (p3HP vs 3HP)*



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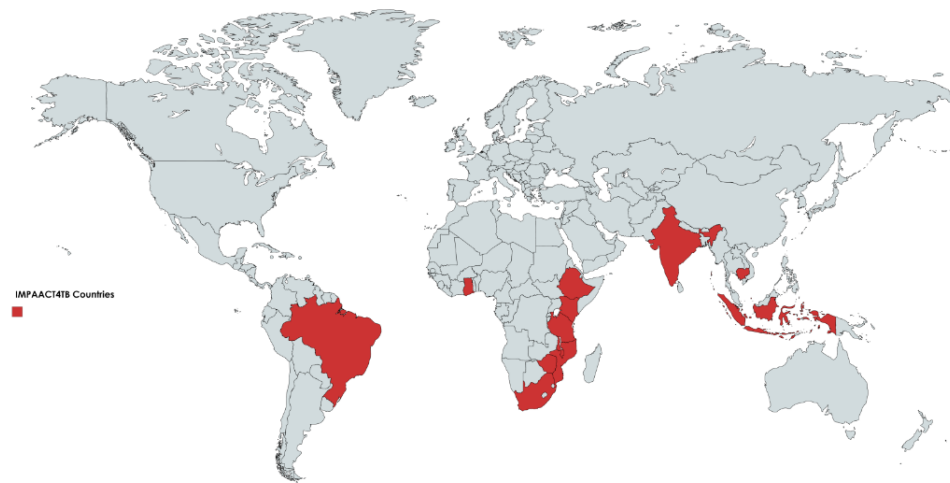


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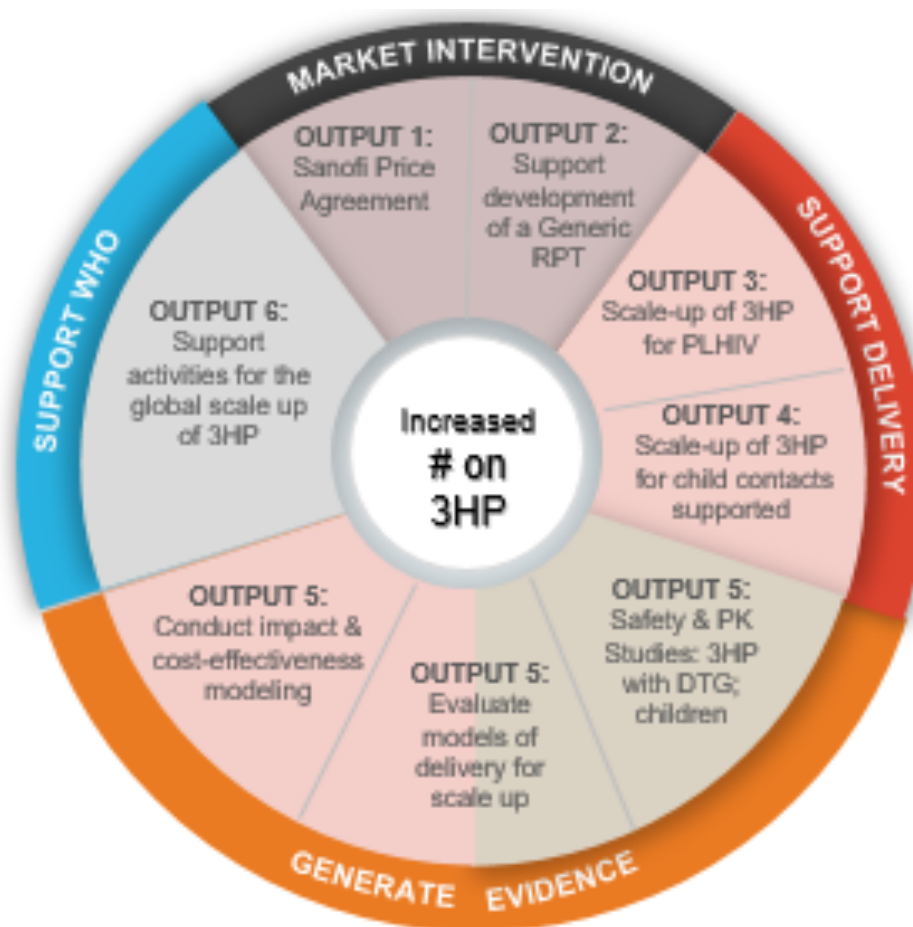
**CHALLENGE TB**

*Increase Market and Public health  
outcomes through scaling up Affordable  
Access models of short Course  
preventive therapy for TB*



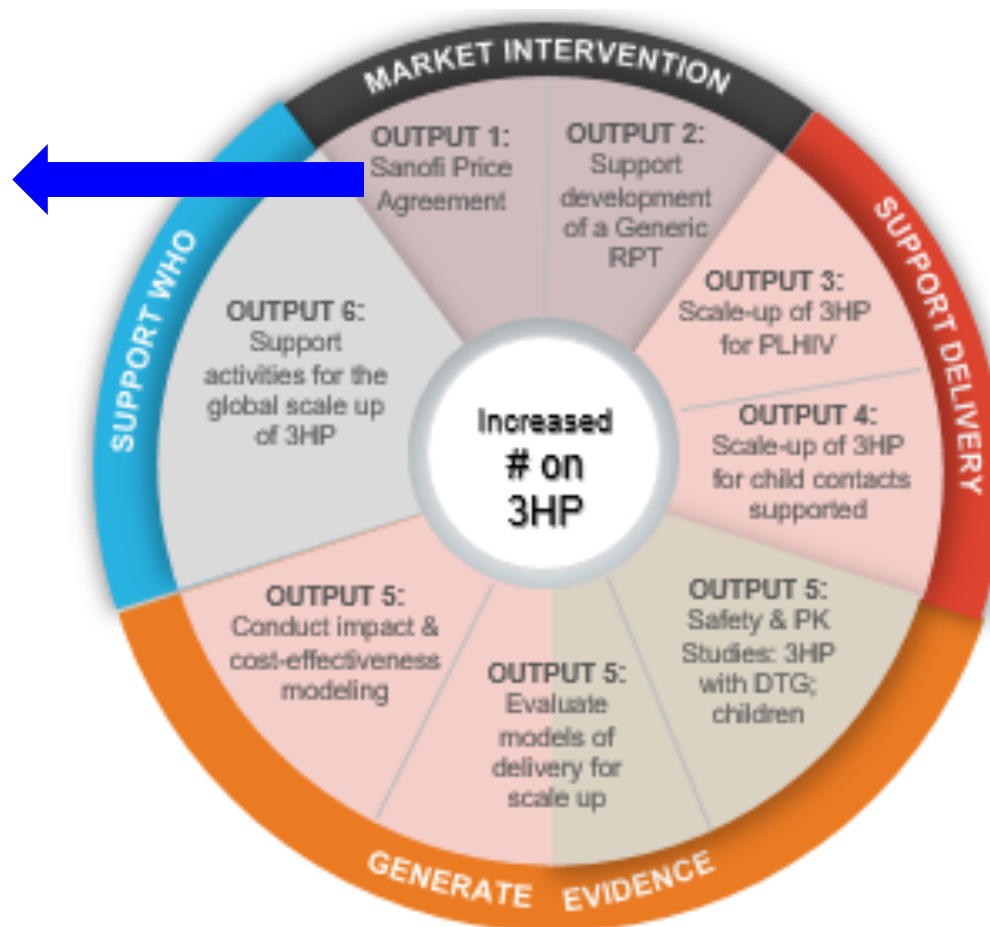
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# IMPAACT4TB: Activities & Outputs

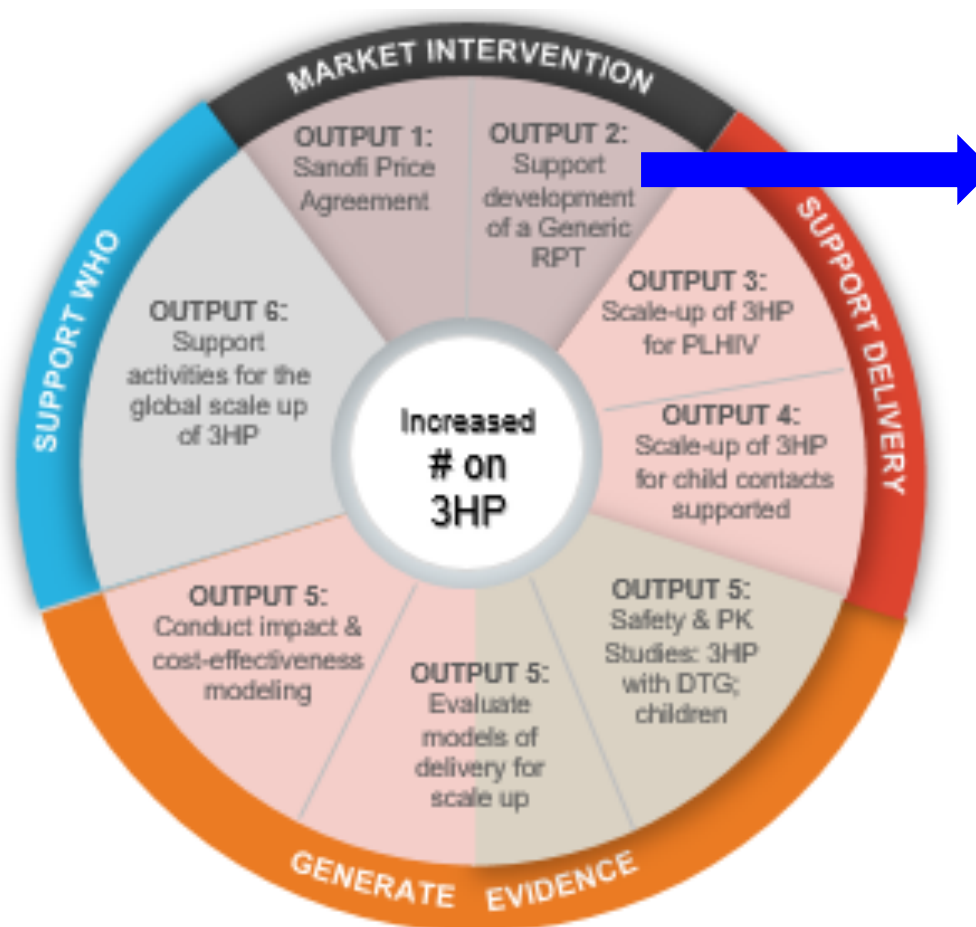


# IMPAACT4TB: Activities & Outputs

Price of  
rifapentine  
reduced from \$48  
to \$15 / patient  
course



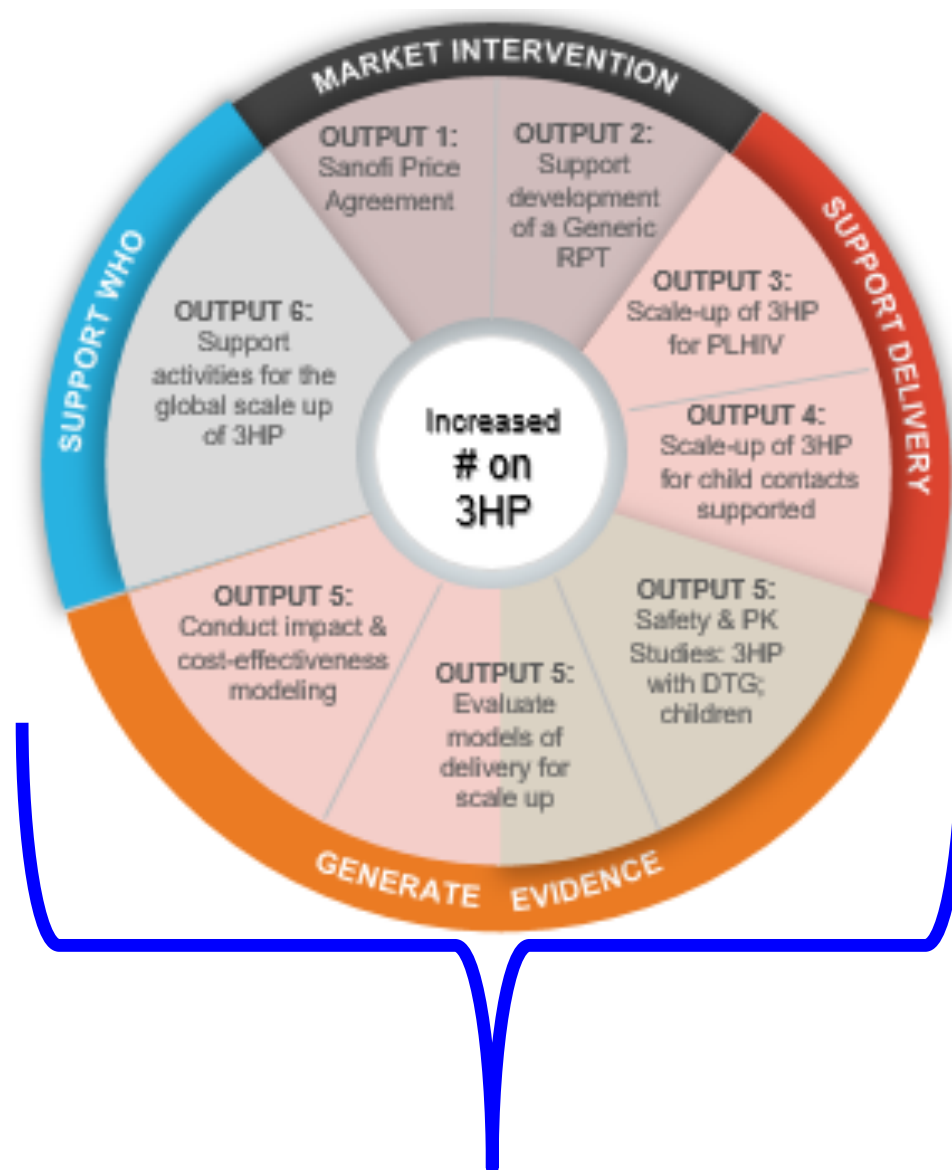
# IMPAACT4TB: Activities & Outputs



Generic FDC  
developed



# IMPAACT4TB: Activities & Outputs



## DOLPHIN TOO

- **DOLPHIN** showed that 3HP+DTG is safe and dose adjustment of DTG not required
- DOLPHIN protocol amended to describe the rate of decline of plasma HIV-1 Viral load among ART naïve participants starting either IPT (n=25) or 3HP (n=50) with a DTG based ART regimen
- Protocol approved and ready to open but on hold due to COVID19

# Choice architecture based TB preventive therapy prescribing



- **Primary objective:** To test whether the choice architecture approach of a “default” to prescribing TPT substantially increases 3HP prescribing
- **Study design:** Pragmatic Cluster-Randomized Trial
  - Standard implementation within IMPAACT4TB project: clinic training on 3HP along with posters and other standard medication material
  - Choice architecture/ “opt-out” 3HP prescribing: where prescription of 3HP will be automatically included with HIV medications unless clinicians write order not to prescribe
- **Sample size:** 30 clinics per arm; mean cluster size of 150 HIV patients (Malawi, Mozambique, Zimbabwe)
- **Duration:** 24 months

## Community vs. facility based child contact investigation

- **Aim:** to compare the effectiveness and cost-effectiveness of community-based versus facility-based child contact investigation and delivery of TPT care
- **Design:** A pragmatic cluster-randomized trial of community-based contact investigation and initiation
- **Sites:** South Africa and Ethiopia
- **Sample size:** 32 clinics (16 clinics per arm)
- **Qualitative study:** nested with cluster-randomized trial
  - Will describe the social context for delivering community-based TPT
  - Develop context-specific adaptations to the intervention to maximize its effectiveness,

## 1HP vs. 3HP (One to Three) trial

- **Aim:** To compare treatment completion in HIV-positive participants on ART taking **1HP** compared **to 3HP**
- **Design:** A cluster-randomized trial
- **Sites:** Brazil, South Africa and Cambodia
- **Sample size:** 24 clinics (12 clinics per arm)

# TB preventive treatment for MDR TB

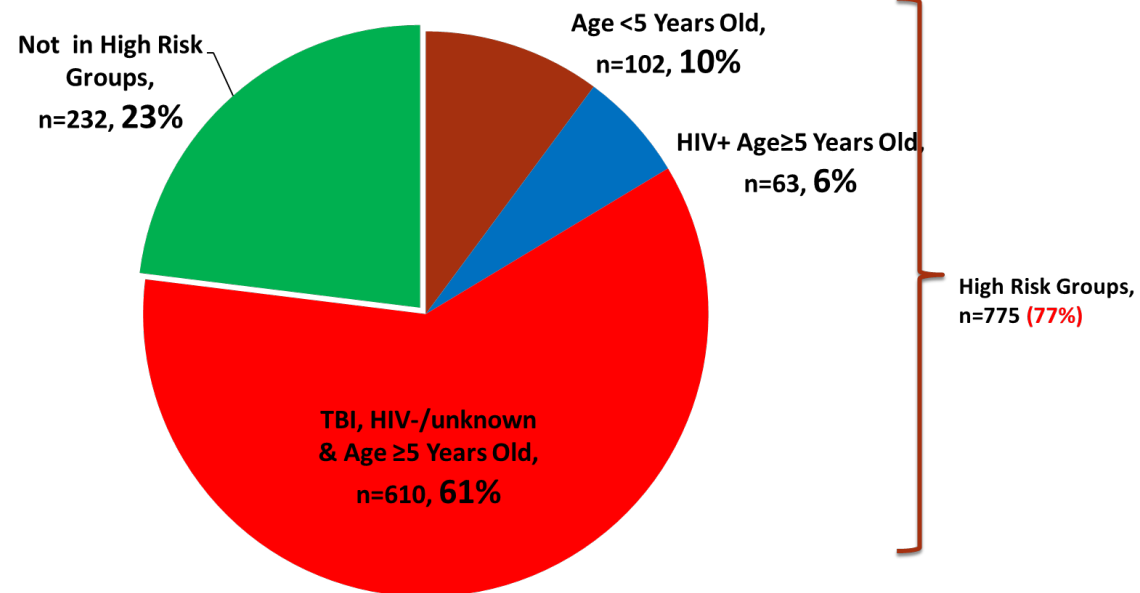


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## Protecting MDR TB exposed households

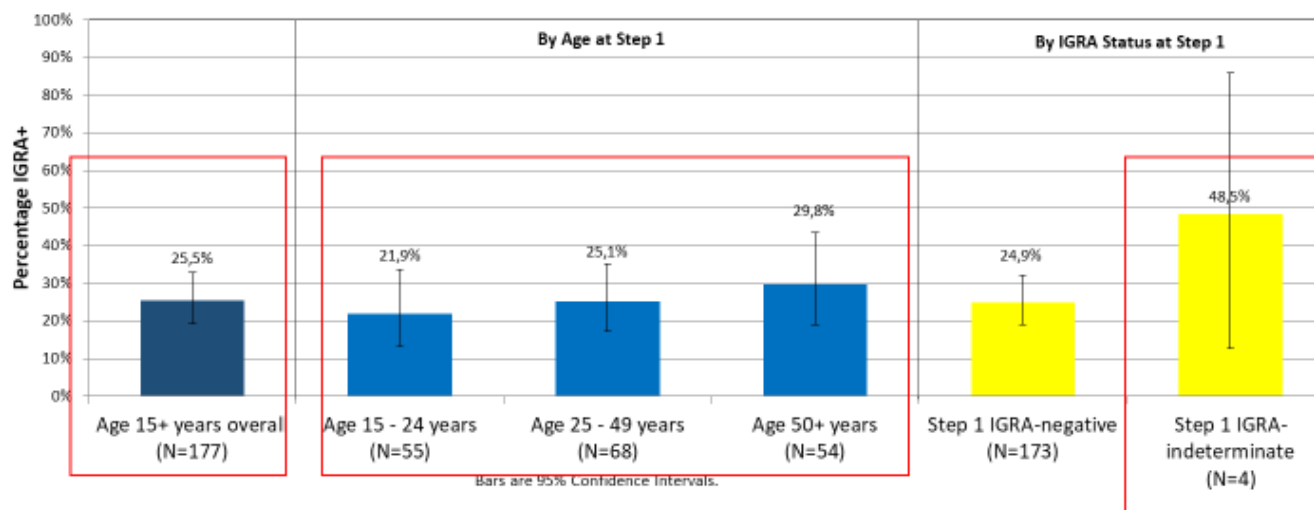
- A5300B/IMPAACT2003B/PHOENIX is evaluating DLM vs INH to prevent TB in household contacts of MDR TB patients

The vast majority of household contacts are eligible for TPT



# Protecting MDR TB exposed households

Newly IGRA+ after 1 Year among HHCs age  $\geq 15$  of Pulmonary MDR-TB Patients



- 68.8% of HHCs  $\geq 15$  years of age of MDR-TB cases had evidence of TB infection
- A further 25% of HHCs age  $\geq 15$  years became TB infected over one year



# Trials of treatment for MDR TB infection

|                          | <b>TB-CHAMP</b>  | <b>V-QUIN</b>  | <b>PHOENIX</b>   |
|--------------------------|--|--|--|
| <b>Intervention</b>      | LVF (paediatric dispersible tablet formulation) vs. placebo daily for 6 months | LVF vs placebo daily for 6 months                              | DLM vs INH daily for 26 weeks                                |
| <b>Design</b>            | Cluster randomized; superiority<br>Community-based                             | Cluster randomized; superiority<br>Community-based             | Cluster randomized; superiority                              |
| <b>Target Population</b> | 0-5 years of age regardless of TST or HIV status                               | All ages (including infants < 6 mo), TST +                     | 1. Children 0-5 yrs, HIV +, TST/IGRA +<br>over 5 year olds   |
| <b>Assumptions</b>       | LVF decreases incidence from 7 to 3.5%;<br>80% power                           | LVF decreases incidence by 70% from 3% untreated;<br>80% power | DLM decreases incidence by 50% from 5% to 2.5%;<br>90% power |
| <b>Sample size</b>       | 788 HH<br>1565 contacts  | 1326 HH<br>2785 contacts                                       | 1726 HH<br>3452 contacts                                     |
| <b>Sites</b>             | South Africa   | Viet Nam   | ACTG & IMPAACT sites   |

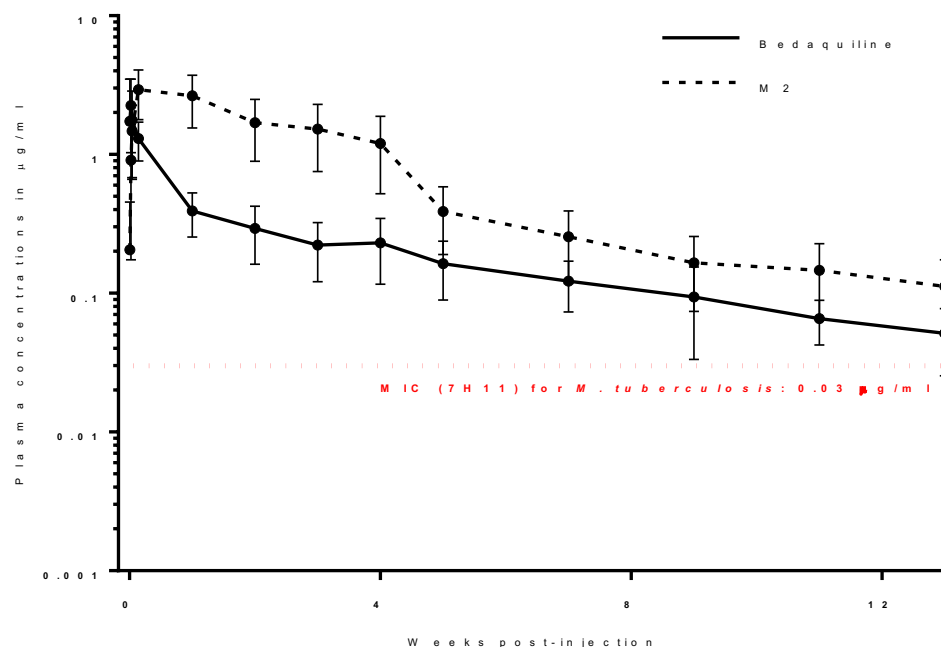
# TB preventive therapy with Long acting injectable's



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# PK of Long-Acting Injectable formulation of Bedaquiline in mice

Plasma bedaquiline and M2 metabolite concentrations after intramuscular injection of long-acting bedaquiline formulation at 160 mg/kg in male Swiss mice



**Based on PK modeling**, a 1 g single intramuscular injection of B<sub>LAI</sub> in humans is predicted to maintain plasma bedaquiline concentrations > 0.1 µg/mL for > 1 month. (Vermeulen *et al.* 2018)

Figure adapted from Kaushik *et al. Antimicrob Agents Chemother* 2019; pii: AAC.00007-19.

ECOFF from Keller *et al. Antimicrob Agents Chemother* 2015;58:4352-4355 and Rajoli *et al. Int J Tuberc Lung Dis* 2018;22:937-944.

CC from WHO. Technical Report on critical concentrations for drug susceptibility testing of medicines used in the treatment of drug-resistant tuberculosis. 2018.

Vermeulen *et al.* Oral abstract, 11<sup>th</sup> International Workshop on Pharmacology of Tuberculosis Drugs. 23 Oct. 2018. The Hague, Netherlands.

# Long acting injectable for treating TB infection

TB preventive therapy with one or two injections of long acting drugs could be transformative



(Source: Sue Swindells)

# Conclusion

- Managing the global burden of LTBI is essential to meeting the End TB targets
- INH is cheap and effective, yet IPT uptake in high burden settings remains low
- Short-course TB preventive treatment is associated with better adherence & safety
- A single round of short-course treatment is effective in TB high burden countries
- Ultra-short course (1HP) now recommended by WHO
- Further innovation is required to improve potency and further reduce the duration of treatment



# TREATMENT OF LTBI

## SOUTH AFRICA EXPERIENCE

Dr Lindiwe Mvusi  
Date: 22 June 2020



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## GOAL 2: Progressively improve TB prevention and cure

Methods of treating TB are well known and have been practiced for over 50 years. The indicators of effective implementation are:

- TB rates among adults and children compared with global targets
- Successful treatment completion

- Progressive decline in the latent infection rate among school-age children
- Decrease in TB contact indices
- Number of latently infected people receiving six months isoniazid treatment (first-line anti-TB medication in prevention and treatment).



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# NATIONAL HIV, AIDS, TB AND STI STRATEGIC PLAN 2017 - 2022

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## PREVENTION TARGETS FOR 2022

Reduce  
NEW  
INFECTIONS  
OF HIV

from **270 000**  
per year to less than  
**100 000**

Reduce  
NEW  
TB  
INFECTIONS

from **450 000**  
per year to less than  
**315 000**

Reduce  
NEW  
STI  
INFECTIONS

Reduce NEW  
STI INFECTIONS  
and Identify  
ASYMPTOMATIC  
INFECTIONS

## HIV TREATMENT TARGETS FOR 2022

**90%**  
of PLHIV  
know their status

**90%**  
of people who know their  
status receive ART

**90%**  
of those on ART have a  
suppressed viral load

## TB TREATMENT TARGETS FOR 2022

Diagnose  
**90%**  
of people with TB  
(including key populations)

Treat  
**100%**  
of people with TB

**TREATMENT SUCCESSFUL**  
Drug-susceptible **90%**  
Drug-resistant **75%**  
Decrease TB mortality by 30%

## Goal 1

Accelerate prevention in order to reduce new HIV and TB infections and new STIs

## Goal 2

Reduce illness and death by providing treatment, care and adherence support for all

## Goal 3

Reach all key and vulnerable populations with services that are tailored to their specific needs

## Goal 4

Address social, economic and cultural factors that add fuel to the HIV, TB and STI epidemics

## Goal 5

Ground the HIV, TB and STI programme in human rights principles

## Goal 6

Promote leadership at all levels and shared accountability for delivering this plan

## Goal 7

Mobilise resources to support achievement of the NSP and ensure a sustainable HIV, TB and STI programme

## Goal 8

Strengthen the gathering and use of information to make the NSP successful



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# END TB TOP INDICATORS PROGRESS: 2018



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| Indicator |   | (2018)                          |
|-----------|---|---------------------------------|
| 1         | TB treatment success rate   | 55% (MDR/RR)<br>76.3% (DS-TB)   |
| 2         | Percentage of new and relapse TB patients tested using a WRD at the time of diagnosis | 66%                             |
| 3         | Latent TB infection (LTBI) treatment coverage   | 79% (HHC <5yrs)<br>63% (PLHIV)  |
| 4         | Contact investigation coverage  | N/A                             |
| 5         | Drug-susceptibility testing (DST) coverage for TB patients                            | 64% (New)<br>68% (Prev treated) |
| 6         | Documentation of HIV status among TB patients   | 94%                             |

# PROGRESS AGAINST UNHLM TARGETS



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| INDICATOR                            | TARGET 2018 | ACHIEVED 2018 |
|--------------------------------------|-------------|---------------|
| Childhood TB diagnosis and treatment | 15 900      | 17 561        |
| MDR-TB diagnosis and treatment       | 9 600       | 9 558         |
| Preventive therapy for under 5 yrs   | 15 400      | 25 357        |
| Preventive therapy in PLHIV          | 392 089     | 455 127       |
| TB Diagnosis and treatment           | 213 600     | 235 652       |
| Total Preventive therapy             | 419 300     | 480 484       |

Data on Preventive therapy in contacts more than 5 years of age not available.



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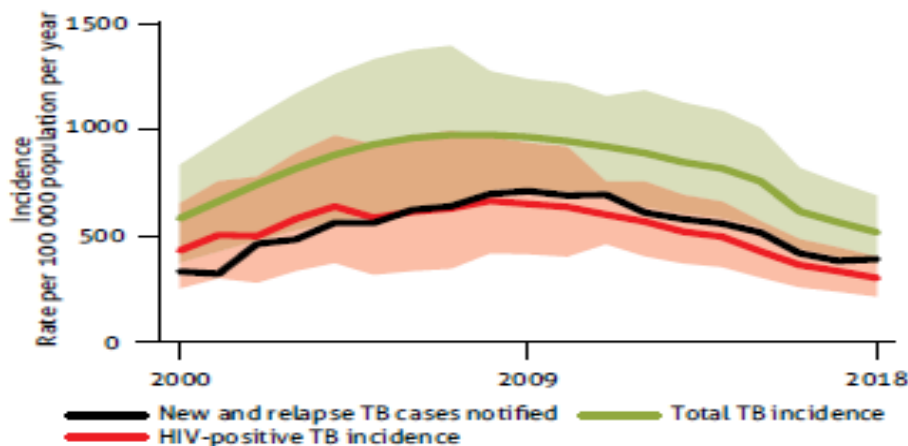
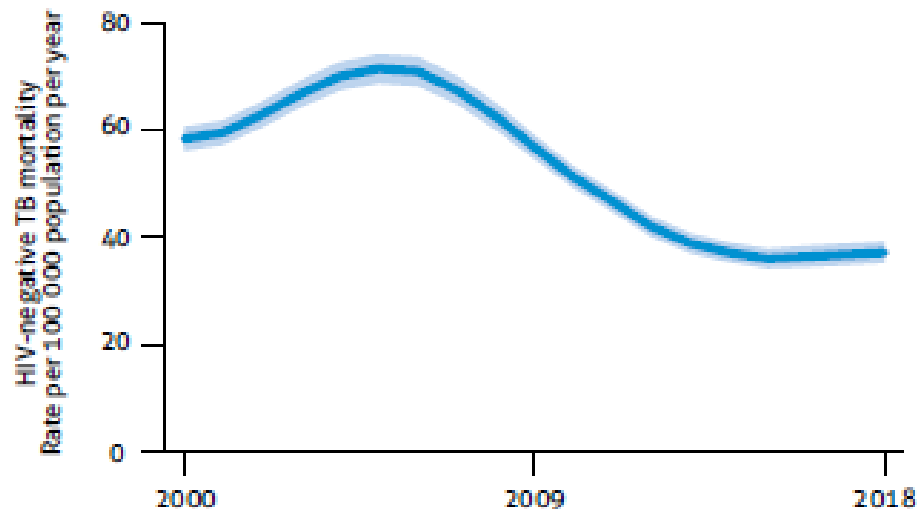


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# COUNTRY PROFILE 2018



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TB Incidence est: 520 per 100 000

HIV+TB incidence: 306 per 100 000

Mortality HIV Neg: 37 per 100 000

Mortality in HIV Pos: 73 per 100 000

Total Notifications: 235 652

New and relapse: 227 999

- HIV Status known: 90%
- HIV Positive: 59%
- On ART: 87%

TB Treatment coverage: 76%

MDR-TB Incidence: 19 per 100 000

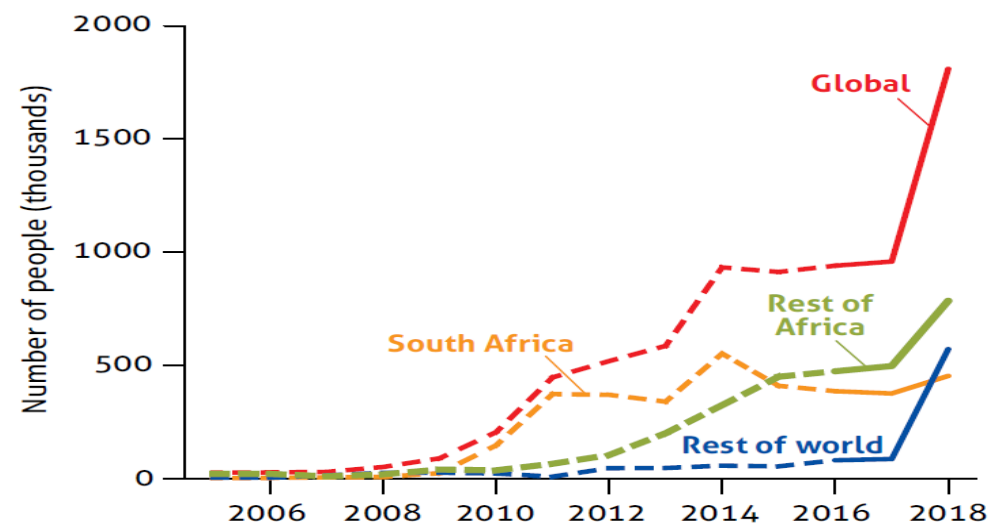
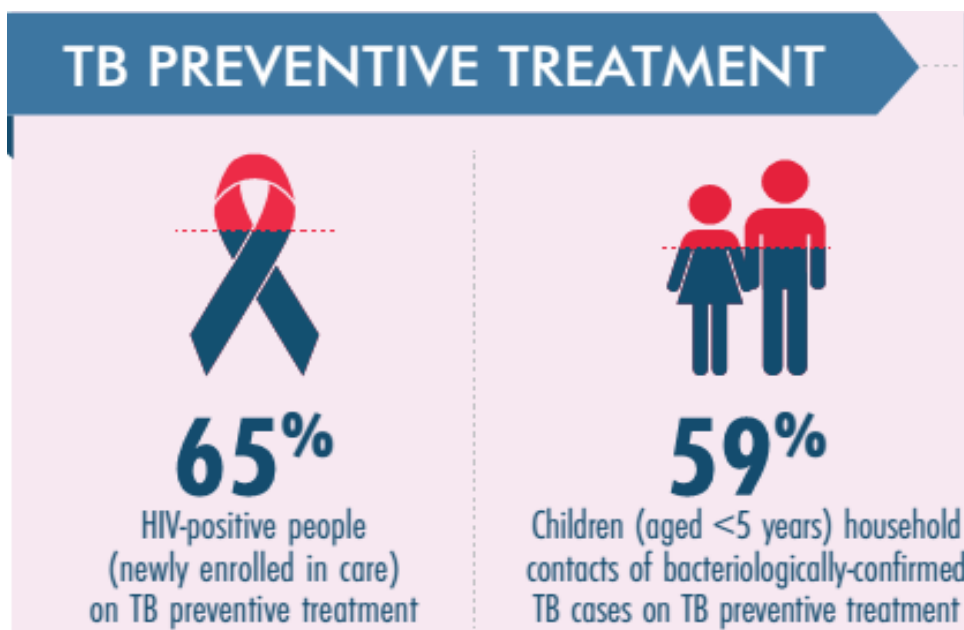


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# COUNTRY PROFILE 2018 (2)



<sup>a</sup> Prior to 2017, data were collected for PLHIV newly enrolled in HIV care (dotted lines). In 2017 and 2018, data were also collected for PLHIV currently enrolled in HIV care (solid lines).



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# TB PREVENTIVE TREATMENT (1)



- Target populations
  - People living with HIV including pregnant women
  - HH Contacts >5 yrs of TB patients
  - Child HH contacts <5 years
  - Healthcare workers
  - Inmates
  - People living with Silicosis (miners)
- No TST/ CXR for PLHIV
- IGRA is piloted in healthcare workers
- CXR and IGRA for consideration in children
- Guideline revision to be finalised by end of year



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# TB PREVENTIVE TREATMENT (2)



- Options for treatment currently
  - Isoniazid for 6 months
  - Isoniazid for 12 months
- Plan to introduce 3HP
  - High dose INH and Rifapentine for 3 months
  - Focus on HIV positive patients stable on ART and switching to TLD regimen and HIV negative household contacts
- Key considerations for implementation
  - Health Care Worker Guidance
  - Service delivery models
  - Supply planning during the scale up of 3HP.
  - Civil society engagement
  - Patient level guidance
  - Pharmacovigilance
  - M and E



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# TB PREVENTIVE TREATMENT (3)



- Cost and supplier capacity has limited scale of implementation
- Funded through Global Fund Grant

| Province               | Municipality/District | Number of patients per district |
|------------------------|-----------------------|---------------------------------|
| Gauteng                | City of Johannesburg  | 108 011                         |
| KwaZulu Natal Province | eThekweni             | 155 996                         |
| Eastern Cape Province  | OR Tambo              | 39 404                          |
| Mpumalanga             | Ehlanzeni district    | 57 968                          |
|                        | Total                 | 361 379                         |



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# 3HP DEMAND PLAN



| NDOH YR1 3HP DEMAND PLAN |                  |                                      |                           |           | Orders per province/district |              |               |              |                |
|--------------------------|------------------|--------------------------------------|---------------------------|-----------|------------------------------|--------------|---------------|--------------|----------------|
|                          |                  |                                      |                           |           | HIV Population (2018 data)   |              |               |              |                |
|                          |                  |                                      |                           |           | (108 011) 30%                | (57 986) 16% | (155 996) 43% | (39 404) 11% | (361 379) 100% |
| Year 1- 2019             | Provinces        | Districts                            | est. no. of patients/mnth | RPT Packs | COJ                          | Ehlanzeni    | eThekwini     | OR Tambo     | All Districts  |
| April                    | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 20 333                    | 60 000    | 18 300                       | 9 760        | 26 230        | 6 710        | 61000          |
| May                      | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 27 334                    | 82 000    | 24 600                       | 13 120       | 35 260        | 9 020        | 82 000         |
| June                     | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 27 334                    | 82 000    | 24 600                       | 13 120       | 35 260        | 9 020        | 82 000         |
| July                     | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 33 333                    | 100 000   | 30000                        | 16000        | 43000         | 11000        | 100000         |
| August                   | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 37 333                    | 112 000   | 33790                        | 17390        | 48431         | 12389        | 112000         |
| September                | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 46 666                    | 140 000   | 42000                        | 22400        | 60200         | 15400        | 140000         |
| October                  | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 45 333                    | 136 000   | 40800                        | 21760        | 58480         | 14960        | 136000         |
| November                 | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 48 667                    | 146 000   | 43636                        | 23273        | 62545         | 16546        | 146000         |
| December                 | GP, KZN, MP & EC | COJ, Ehlanzeni, eThekwini & OR Tambo | 47 000                    | 141 000   | 42300                        | 22560        | 60630         | 15510        | 141000         |
| Total                    |                  |                                      | 333 333                   | 1 000 000 | 300026                       | 159383       | 430036        | 110555       | 1000000        |



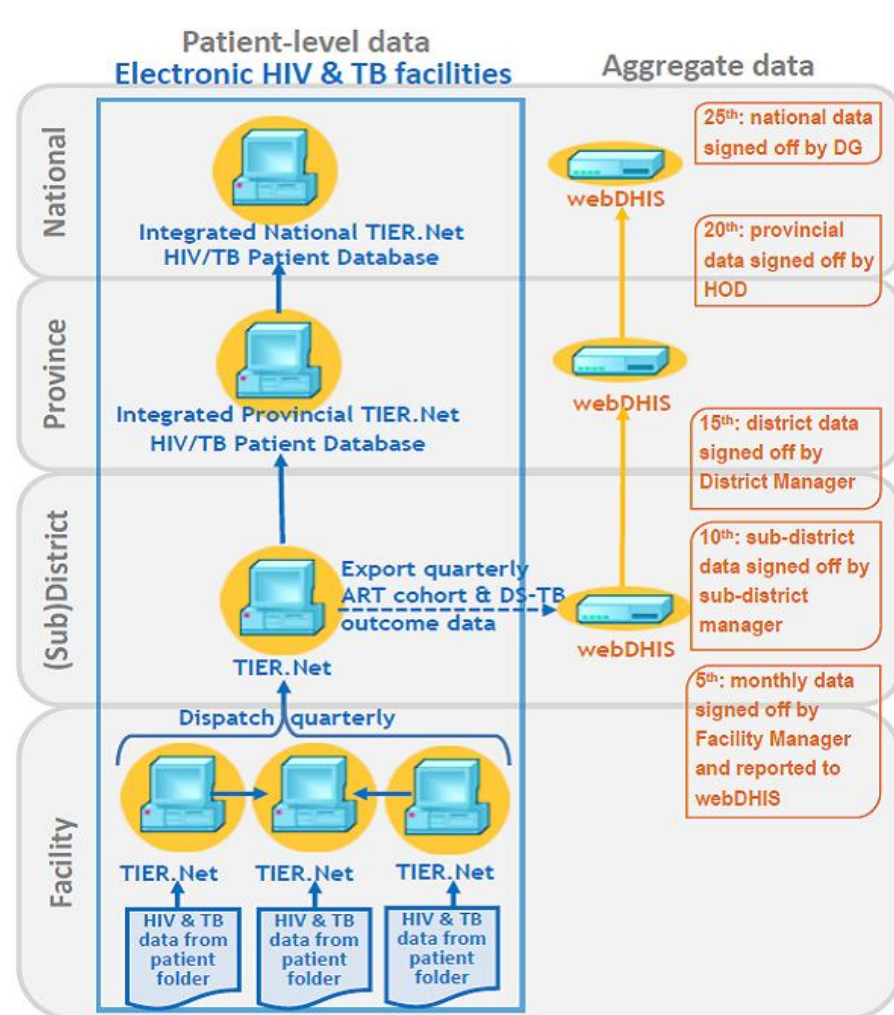
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# MONITORING EVALUATION



- DHIS
  - PHC Tick Register (PLHIV, Child contacts <5yrs)
  - TIER.Net – PLHIV
  - DHIS
- Plan to digitise TPT for all patients started on treatment and monitor outcomes



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# CHALLENGES



- Managing 4 treatment options for treatment of LTBI
- Low IPT coverage
- Poor data quality
- Confusion on indicator
  - Newly enrolled in care vs all eligible
- Negative health care provider attitudes
- Outcomes not recorded and monitored
- Shortages of TST major setback



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# TB Preventive Treatment (TPT) among PLHIV, current progress, opportunities, and challenges, including in the context of the COVID-19 pandemic

**Bill Coggin, MSA**

Team Lead, Program Support and Evaluation Team  
Global TB Branch, Division of Global HIV & TB, CDC-Atlanta

Webinar: TB preventive therapy: recent advances and future prospects

23 June 2020

Division of Global HIV & TB





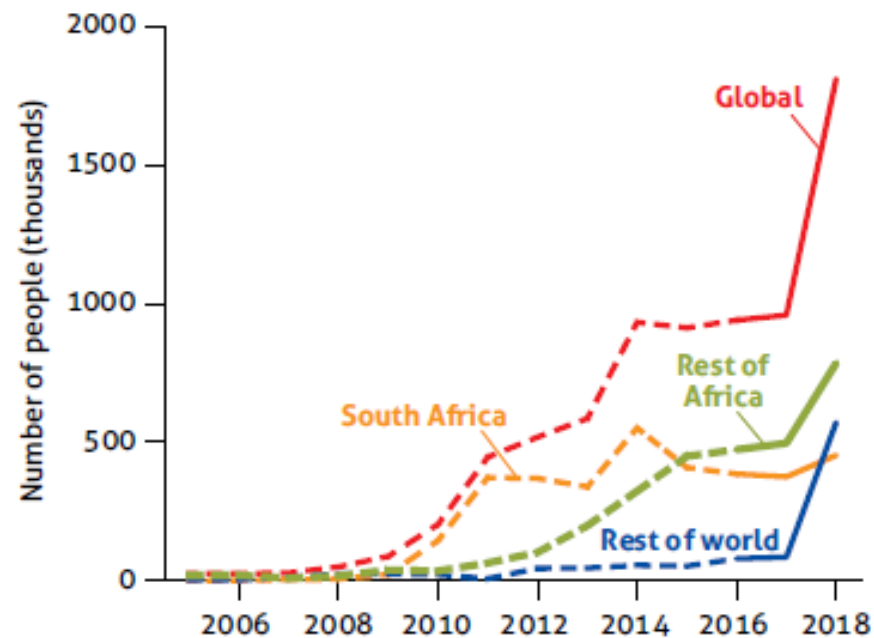
*“If a new ART regimen were shown to reduce mortality by 37%, the demand for immediate access from clinicians, programmes, international agencies, and the advocacy community would be deafening. The faint whispers for IPT must be amplified and action must be taken to reduce deaths from such an eminently preventable disease.”*

Richard E. Chaisson, Jonathan E. Golub  
Lancet Glob Health. 2017 Nov;5(11):e1048-e1049



# Recent progress in TPTScale-up

**Provision of TB preventive treatment to people enrolled in HIV care,<sup>a</sup> 2005–2018**



<sup>a</sup> Prior to 2017, data were collected for PLHIV newly enrolled in HIV care (dotted lines). In 2017 and 2018, data were also collected for PLHIV currently enrolled in HIV care (solid lines).

## PEPFAR's commitment to TPT

14 Million PLHIV to complete  
at least **ONE** course of TPT

**\$22.7 Million**

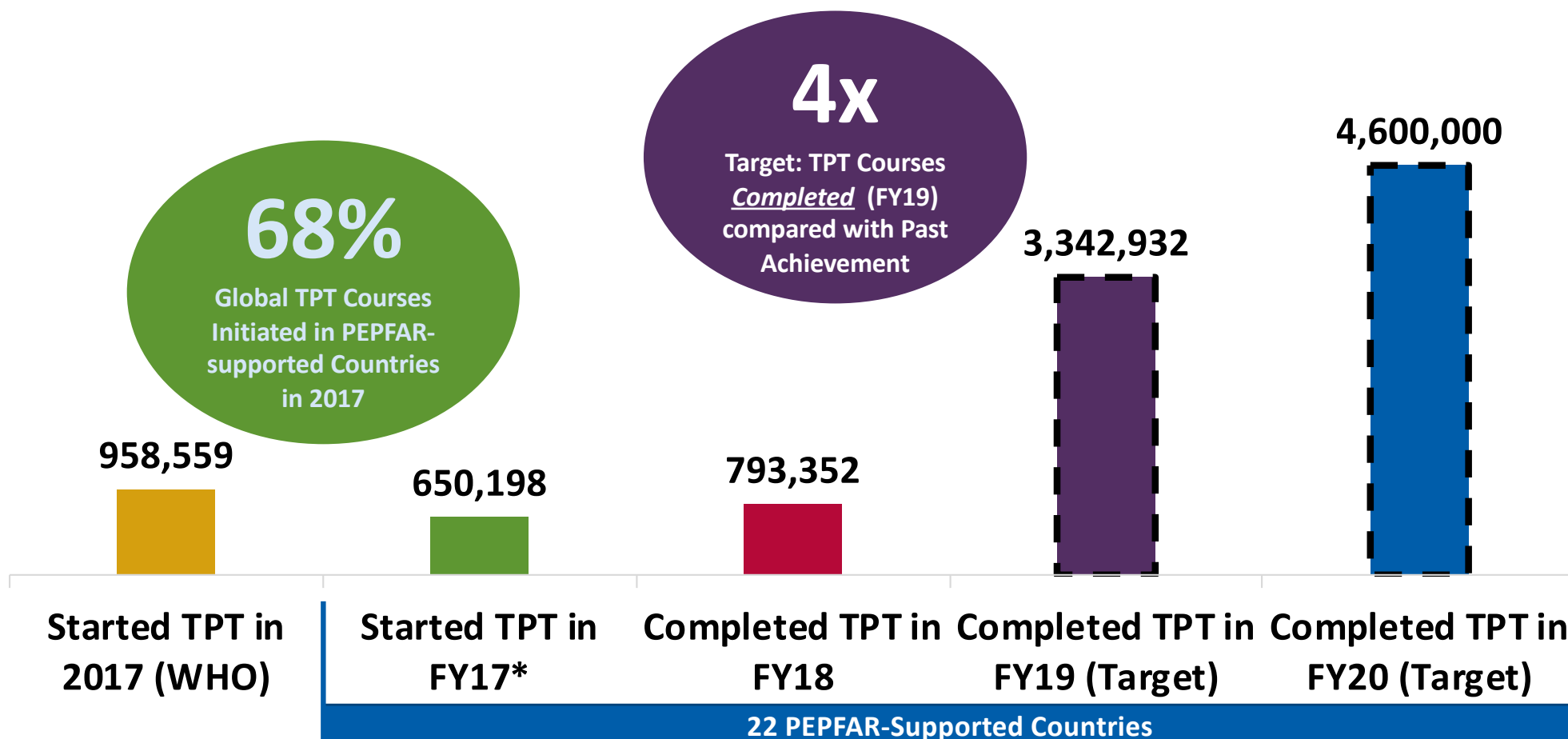
for TPT commodities



**"If immediate ART is the cornerstone of PEPFAR's TB/HIV efforts, then TB infection control and TB preventive therapy are the capstones..."**

**-Amb. Deborah Birx**

## PEPFAR has set ambitious targets for TPT acceleration

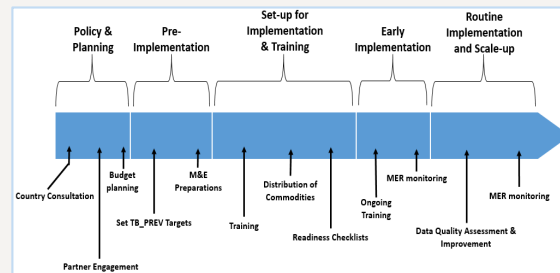


\*No data reported for Botswana, Cameroon, Cote d'Ivoire, Malawi, Rwanda, South Sudan, and Ukraine

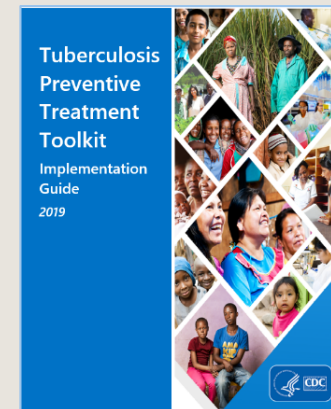


# CDC Strategy for Scale up

## 1 Baseline Country Assessment



## 2 TPT Implementation Toolkit and Operational Guide



## 3 Raising Awareness



## 4 Technical Assistance



**SOUTH-TO-SOUTH TPT MENTORSHIP VISIT  
KENYA — MAY 20-23, 2019  
(UGANDA, ZAMBIA, ZIMBABWE)**

## 5 Partnerships

### HIV Differentiated Service Delivery *Opportunities and Challenges for TB Prevention and Care*

#### MEETING REPORT

**March 26-29, 2019  
Lusaka, Zambia**

*Hosted by the HIV Coverage, Quality, and Impact Network (CQUIN) and the World Health Organization*



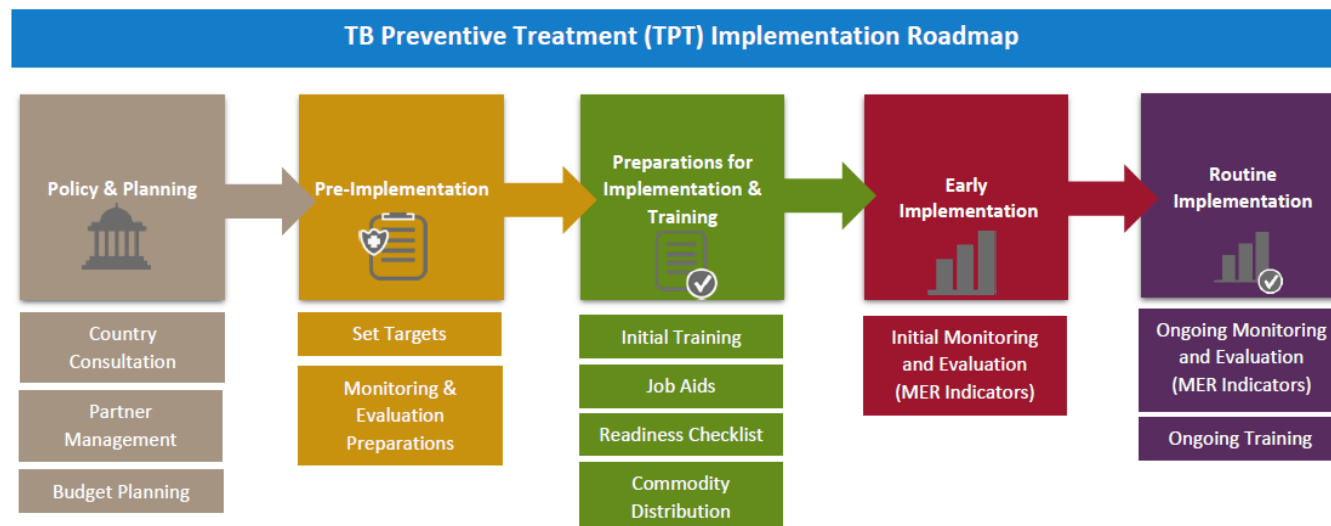
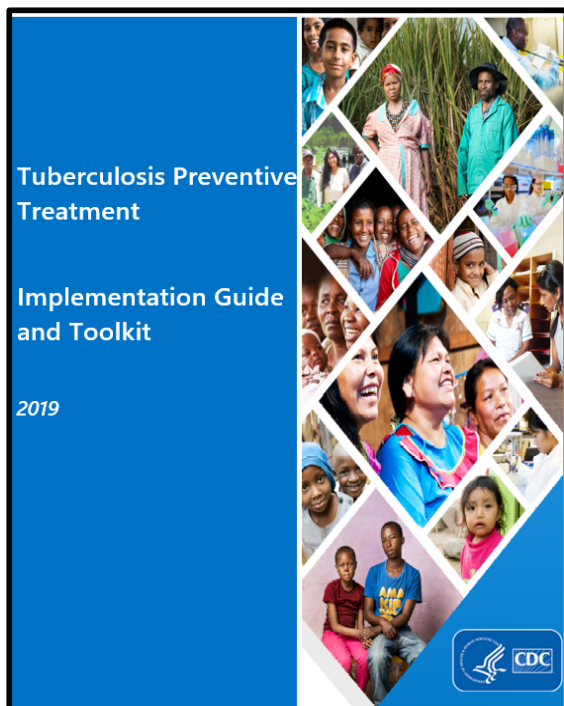
**JUNE 20, 2019 | CQUIN**

**Uganda and Zambia Receive Funding to Adapt TB Preventive Treatment for Differentiated ART Models**



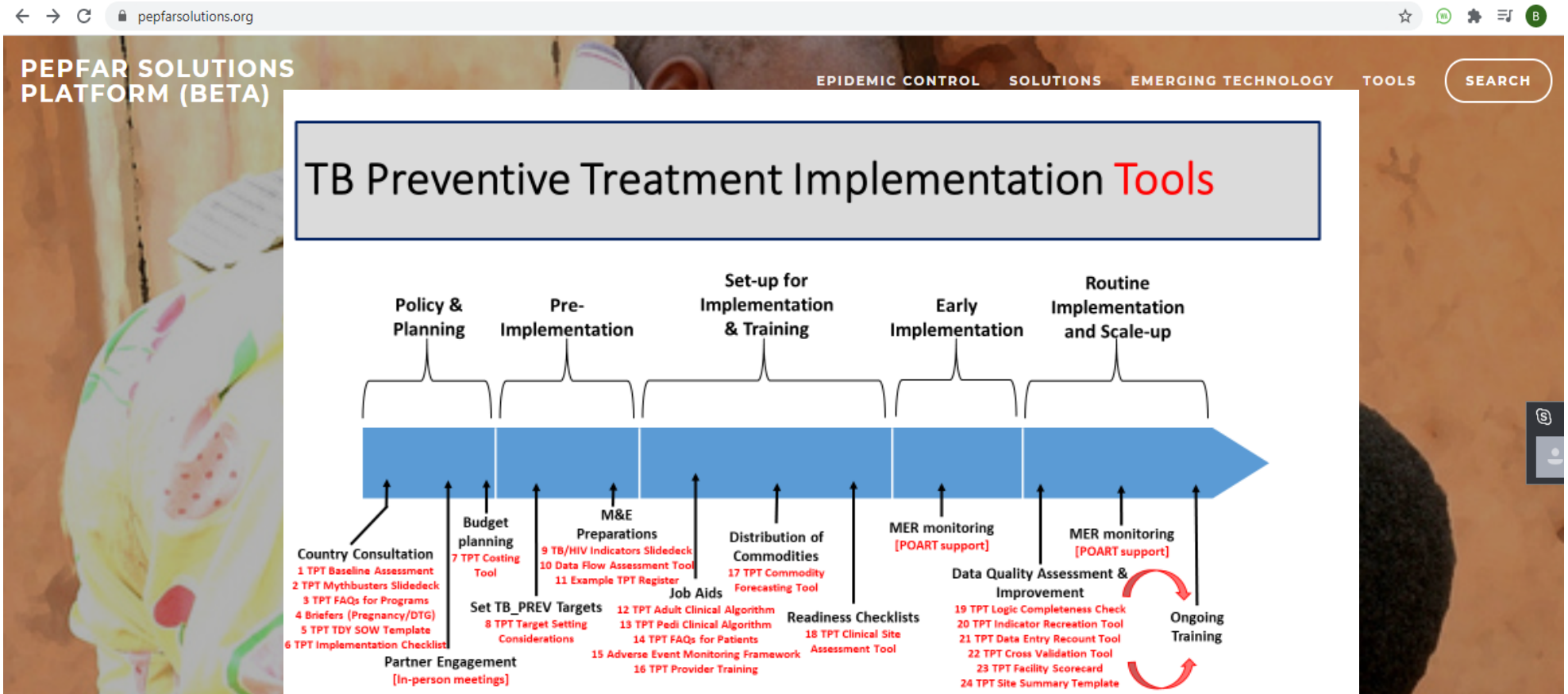
**UNITED NATIONS  
HIGH-LEVEL MEETING ON THE  
FIGHT TO END TUBERCULOSIS  
26 SEPTEMBER 2018, UNHQ, NEW YORK**

# TPT Implementation Guide & Toolkit



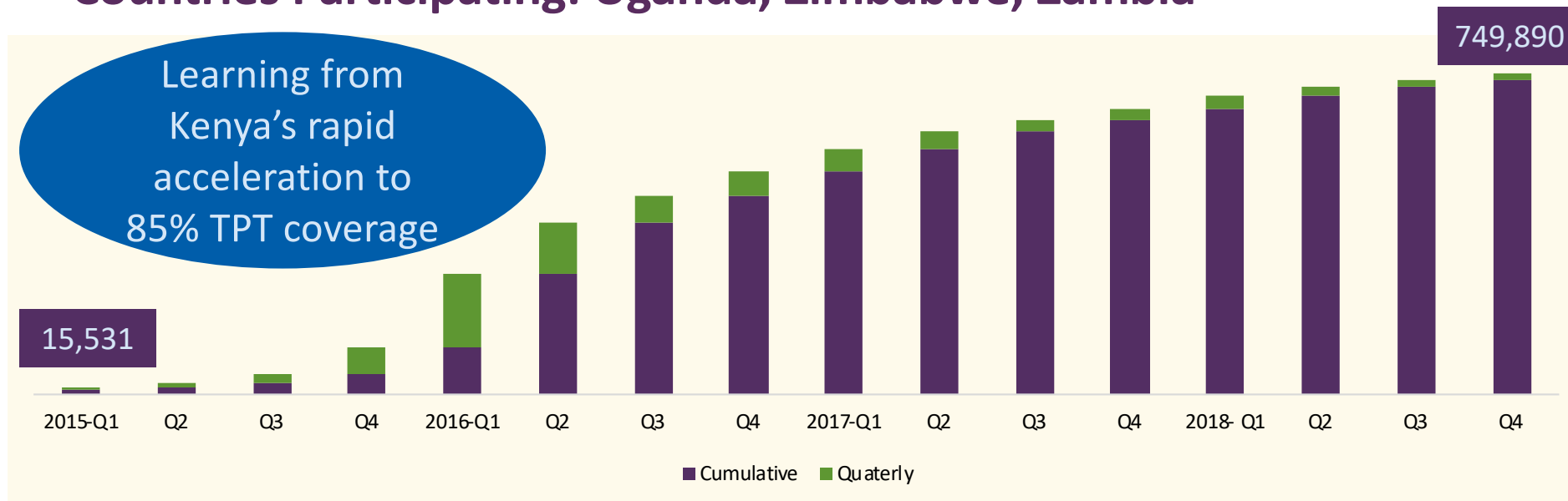
Available on PEPFAR Solutions website:  
<https://www.pepfarsolutions.org/imtest?rq=TPT>

# Tools available via PEPFAR Solutions Website

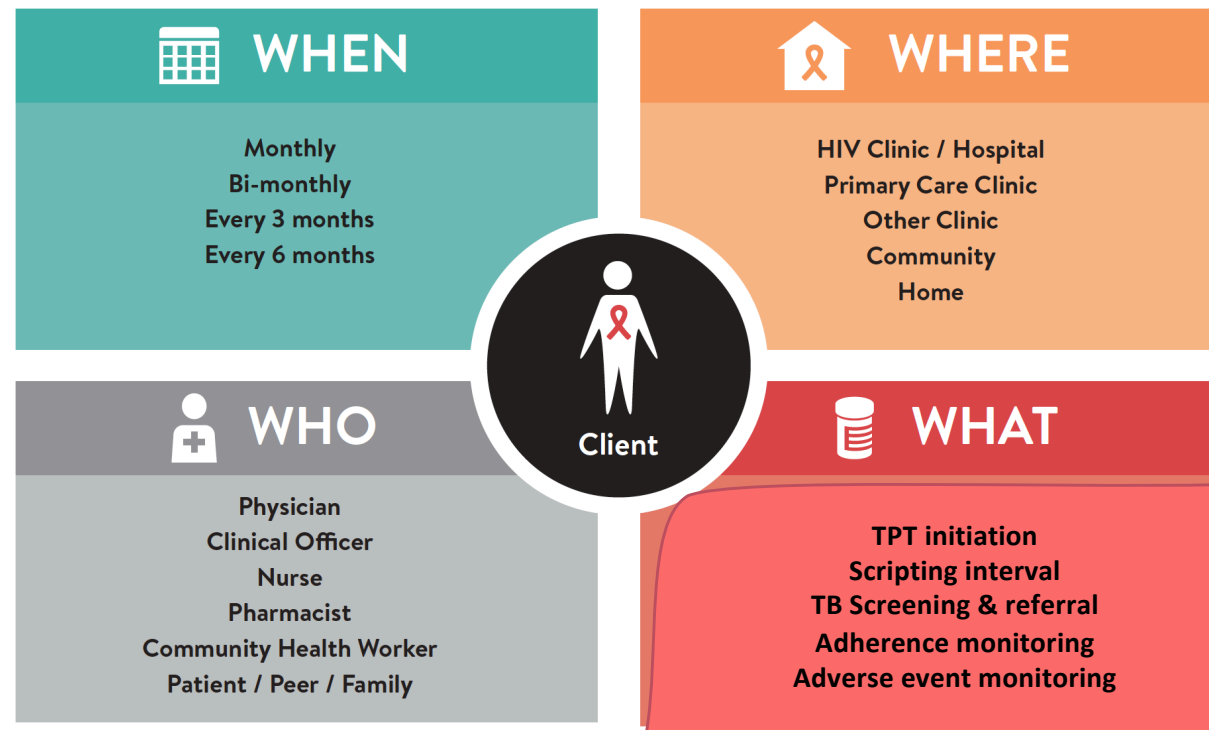


# South to South Mentorship – Kenya, May 2019

Countries Participating: Uganda, Zimbabwe, Zambia



# TPT within Differentiated Service Delivery (DSD) Models: Considerations



Graphic adapted from IAS Decision Framework for ART Delivery, 2016 ([www.differentiatedcare.org/Guidance](http://www.differentiatedcare.org/Guidance))



# DSD Models

## Health care worker-managed groups



Clients receive their ART refills in a group and either a professional or a lay health care staff member manages this group. The groups meet within and/or outside of health care facilities.

**Examples: facility-based adherence clubs, distribution points or treatment clubs, club refills**

## Facility-based individual models



ART refill visits are separated from clinical consultations. When clients have an ART refill visit, they bypass any clinical staff or adherence support and proceed directly to receive their medication.

**Examples: fast-track, multi-month scripting/dispensing, facility-based care with monthly refills**

## Client-managed groups



Clients receive their ART refills in a group but this group is managed and run by clients themselves. Generally, client-managed groups meet outside of health care facilities.

**Examples: community adherence groups, community client-led ART delivery**

## Out-of-facility individual models



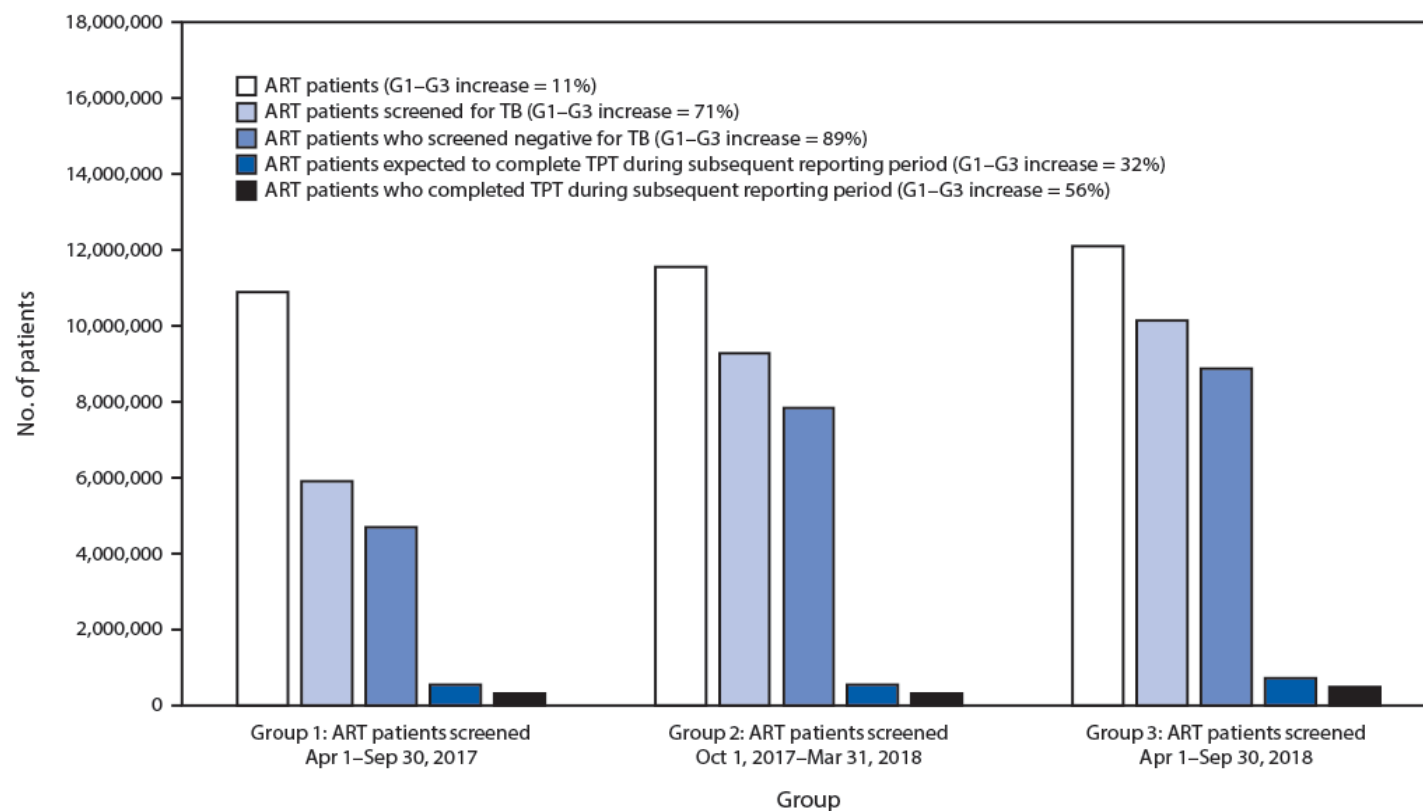
ART refills and, in some cases, clinical consultations are provided to individuals outside of health care facilities.

**Examples: mobile outreach, community drug distribution points, central chronic disease distribution**

Graphic adapted from International AIDS Society (IAS) ([www.differentiatedcare.org](http://www.differentiatedcare.org))

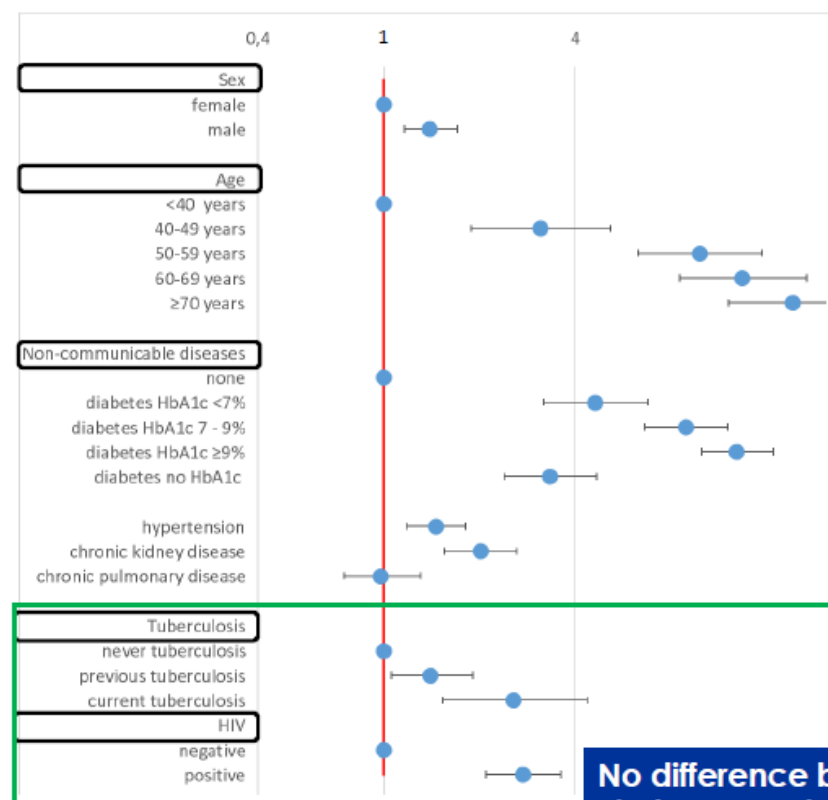
# TB Screening and TPT in PEPFAR-supported Countries

**FIGURE 1. Tuberculosis (TB) screening and TB preventive treatment (TPT) indicators\*<sup>†,§</sup> for persons living with human immunodeficiency virus (HIV) infection receiving antiretroviral therapy (ART patients) — 16 PEPFAR-supported countries,<sup>¶</sup> 2017–2019**



## What are the chances of dying from COVID-19 for different risk factors?

| Patient characteristics                   | Hazard ratio | 95% Confidence Interval |
|---|--------------|-------------------------|
| <b>Sex</b>                                |              |                         |
| female                                    |              |                         |
| male                                      | 1,40         | 1,16; 1,70              |
| <b>Age</b>                                |              |                         |
| <40 years                                 |              |                         |
| 40-49 years                               | 3,12         | 1,88; 5,17              |
| 50-59 years                               | 9,92         | 6,34; 15,54             |
| 60-69 years                               | 13,55        | 8,55; 21,48             |
| ≥70 years                                 | 19,53        | 12,20; 31,26            |
| <b>Non-communicable diseases</b>          |              |                         |
| none                                      |              |                         |
| diabetes well controlled (HbA1c <7%)      | 4,65         | 3,19; 6,79              |
| diabetes poorly controlled (HbA1c 7 - 9%) | 8,99         | 6,65; 12,14             |
| diabetes uncontrolled (HbA1c ≥9%)         | 13,02        | 10,06; 16,87            |
| diabetes – no measure of control          | 3,34         | 2,39; 4,68              |
| hypertension                              | 1,46         | 1,18; 1,81              |
| chronic kidney disease                    | 2,02         | 1,55; 2,62              |
| chronic pulmonary disease                 | 0,98         | 0,75; 1,30              |
| <b>Tuberculosis</b>                       |              |                         |
| never tuberculosis                        |              |                         |
| previous tuberculosis                     | 1,41         | 1,05; 1,90              |
| current tuberculosis                      | 2,58         | 1,53; 4,37              |
| <b>HIV</b>                                |              |                         |
| negative                                  |              |                         |
| positive                                  | 2,75         | 2,09; 3,61              |



No difference by viral suppression



## Guiding principles for PEPFAR service provision during COVID-19

- Protect the gains in the HIV response.
- The safety of PEPFAR-supported staff must be assured. If client services cannot be adapted to be performed safely, they should not be performed.
- Reduce risk of transmission of COVID-19 among clients served by PEPFAR and PEPFAR-supported staff
- In consultation with host governments, PEPFAR Operating Units (OUs) have flexibility to determine how best to continue to serve clients with HIV prevention and treatment services in areas affected by COVID-19 using the FAQs as a guide.

# PEPFAR guidance: Maintaining essential services

- TB screening, diagnosis and treatment remain priority public health activities.
- TPT is “essential.”
- Screening programs for Covid-19 should incorporate screening for TB and vice-versa.
- Community-based screening, monitoring and drug delivery
- Protecting HCWs and clients: Triage, early identification, and separation of persons with TB and/or Covid-19 symptoms.
- Multi-month Scripting/Month Dispensing (MMS/MMD):
  - Dispense enough anti-TB drugs to complete the course of treatment in order to minimize facility visits (TB treatment as well as TPT).
  - Align MMD of TPT with that of ART
  - Updating supply plans to take into account accelerated MMD and coordination with suppliers
- Understand cross-cutting impacts: Human resources and supply chain
- Address triple stigma, discrimination and isolation related to TB, HIV and Covid-19
- Proposed: Supplemental funding related to IPC and continuity of services

# Opportunities and Way Forward

## Opportunities

- Consensus that TPT be maintained as 'essential' service
- Differentiated service delivery: MMS/MMS
  - Accelerated uptake in ART & TPT

## Way Forward

- Close monitoring of PEPFAR M&E data by country and district to understand impacts
- Adapting technical support to virtual methodologies to continue to support scale-up TPT among PLHIV, using every opportunity to expand impact
- Integration of TB screening, diagnosis, treatment and prevention in Covid-19 efforts
- Collaborating with partners to develop on-the-ground tools needed to screen for TB and ensure initiation and completion of TPT
- Developing the systems and tools to evaluate impact and improve performance



# Thank you.

# Questions?

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**THANK YOU**

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