Webinar

Breaking the Chain:

Clinical Diagnosis and TB Preventive Therapy for Contacts in South Africa

Date: 19 June 2025

Time: 13h00 – 14h00

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

END TB BREATHE EASY

2030 NDP

30 YEARS OF FREEDOM
South Africa 1994 - 2024

Thank you for your interest in this webinar

- The chat has been disabled for the attendees.
- **Please use the Q&A box to post questions for our panel of experts.**
- The session is recorded and will be shared with all the presentations on the Knowledge Hub – **www.knowledgehub.health.gov.za/webinars**
- **E-mail** knowledgehub@health.gov.za
- Register in advance for the webinars (24 hours before)

Prof Norbert Ndjeka

Prof Ndjeka serves as the Chief Director TB Control and Management, under the National Department of Health in South Africa.

Under his leadership, there has been a decline in the number of cases of DR - TB in South Africa and a remarkable improvement in proportion of patients successfully treated for DR- TB.

Webinar Programme

Time	Duration	Topic	Presented By:
13h00 - 13h05	5 min	Opening & Welcome	Prof. Norbert Ndjeka
13h05 - 13h15	10 min	Aims and objectives of webinar	Prof. Norbert Ndjeka
13h15 - 13h35	20 min	Clinical Diagnosis and TB Preventive Therapy for Contacts in South Africa	Prof. Gavin Churchyard
13h35 - 13h55	20 min	Discussion (Q&A)	All
13h55 - 14h00	5 min	Vote of Thanks	Prof. Norbert Ndjeka

Prof Gavin Churchyard

Prof Churchyard is an NRF A-rated scientist and a specialist physician, internationally renowned for his contributions in Tuberculosis (TB).

He is the founder and President Emeritus; of The Aurum Institute NPC, an independent, public benefit organisation that focuses on TB and HIV service delivery, management and research.

He is an Honorary Professor at the University of Witwatersrand, School of Public Health and an Honorary Professor at the London School of Hygiene and Tropical Medicine.

TB Preventive Treatment: a new era

19th June 2025

Gavin Churchyard

MBBCh, MMED, FCP (SA), FRCP (Edin), PhD

Honorary Professor, School of Public Health, University of Witwatersrand

Adjunt Professor, Department of Medicine, Vanderbilt University

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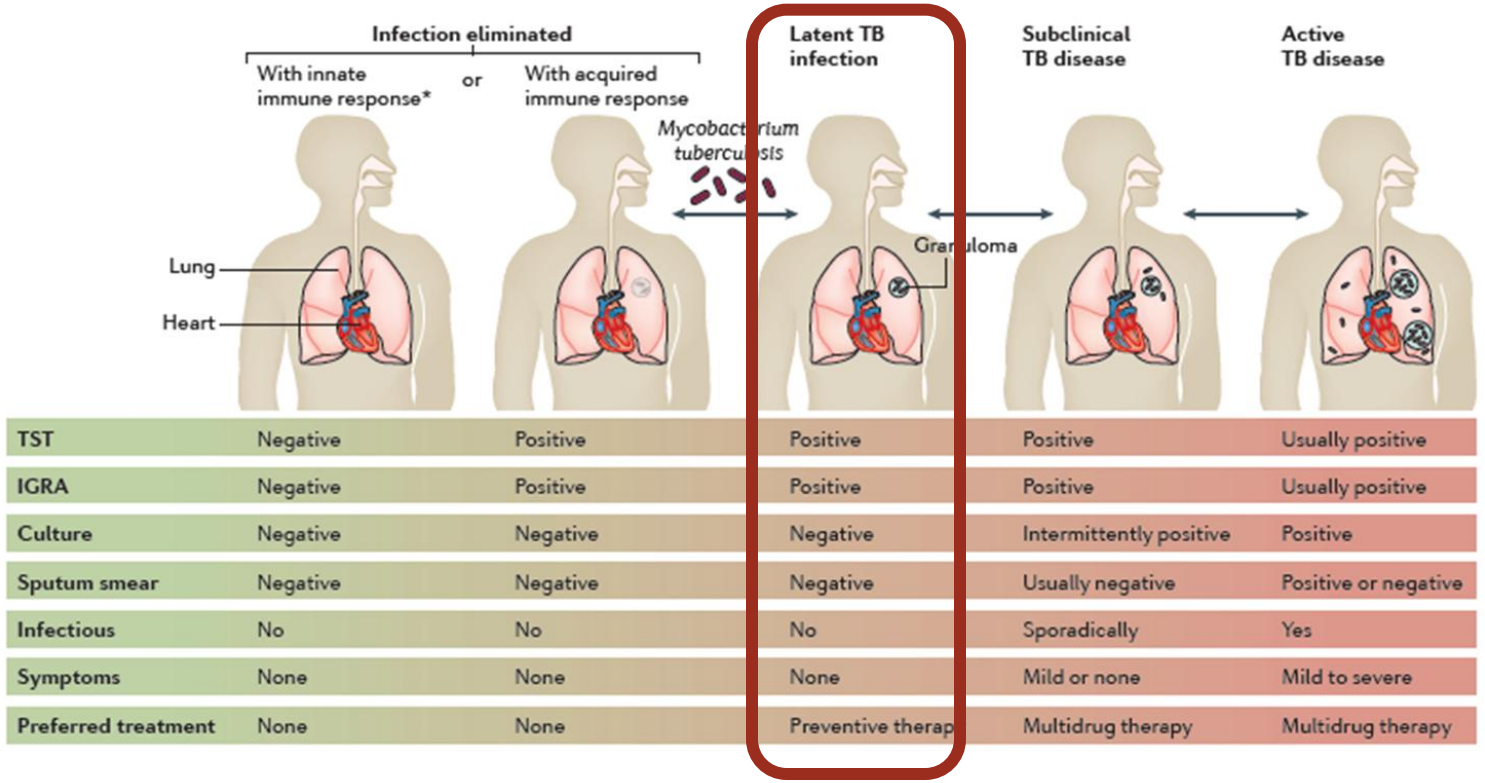
Overview

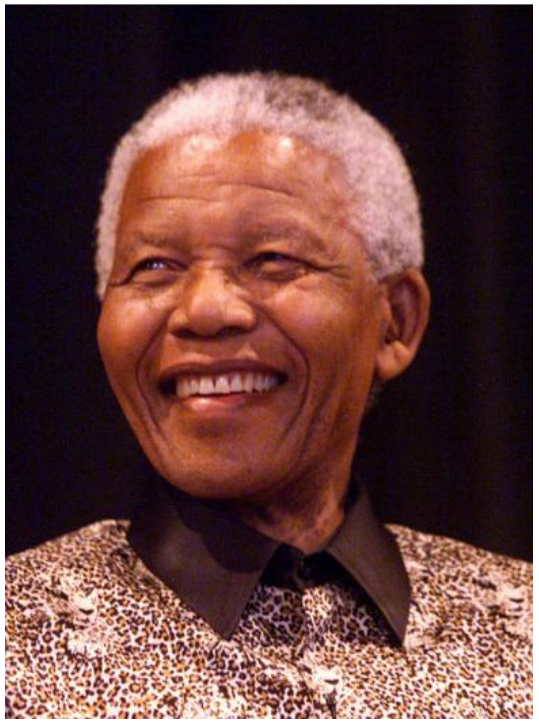
- Background
- TPT regimens
  - Short course
  - MDR TPT
  - Pan TPT
  - Long acting injectables
- Cascade of care
- Conclusion



TST	Negative	Positive	Positive	Positive	Usually positive
IGRA	Negative	Positive	Positive	Positive	Usually positive
Culture	Negative	Negative	Negative	Intermittently positive	Positive
Sputum smear	Negative	Negative	Negative	Usually negative	Positive or negative
Infectious	No	No	No	Sporadically	Yes
Symptoms	None	None	None	Mild or none	Mild to severe
Preferred treatment	None	None	Preventive therap	Multidrug therapy	Multidrug therapy

Pai. Nature Reviews | Disease Primers. 2016)

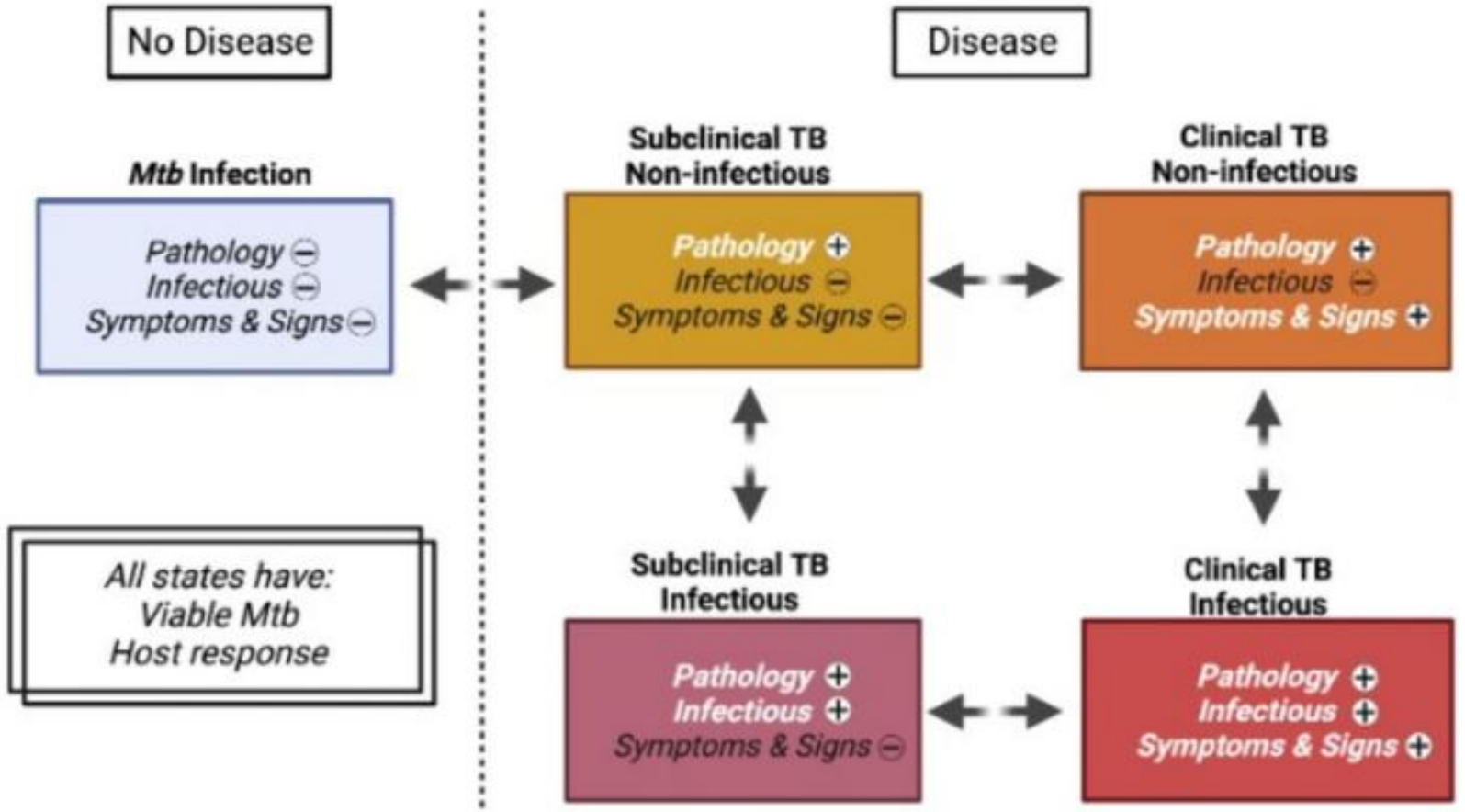
Background



"Today we are calling on the world to recognize that we can't fight AIDS unless we do much more to fight TB (*including preventingTB)* as well"

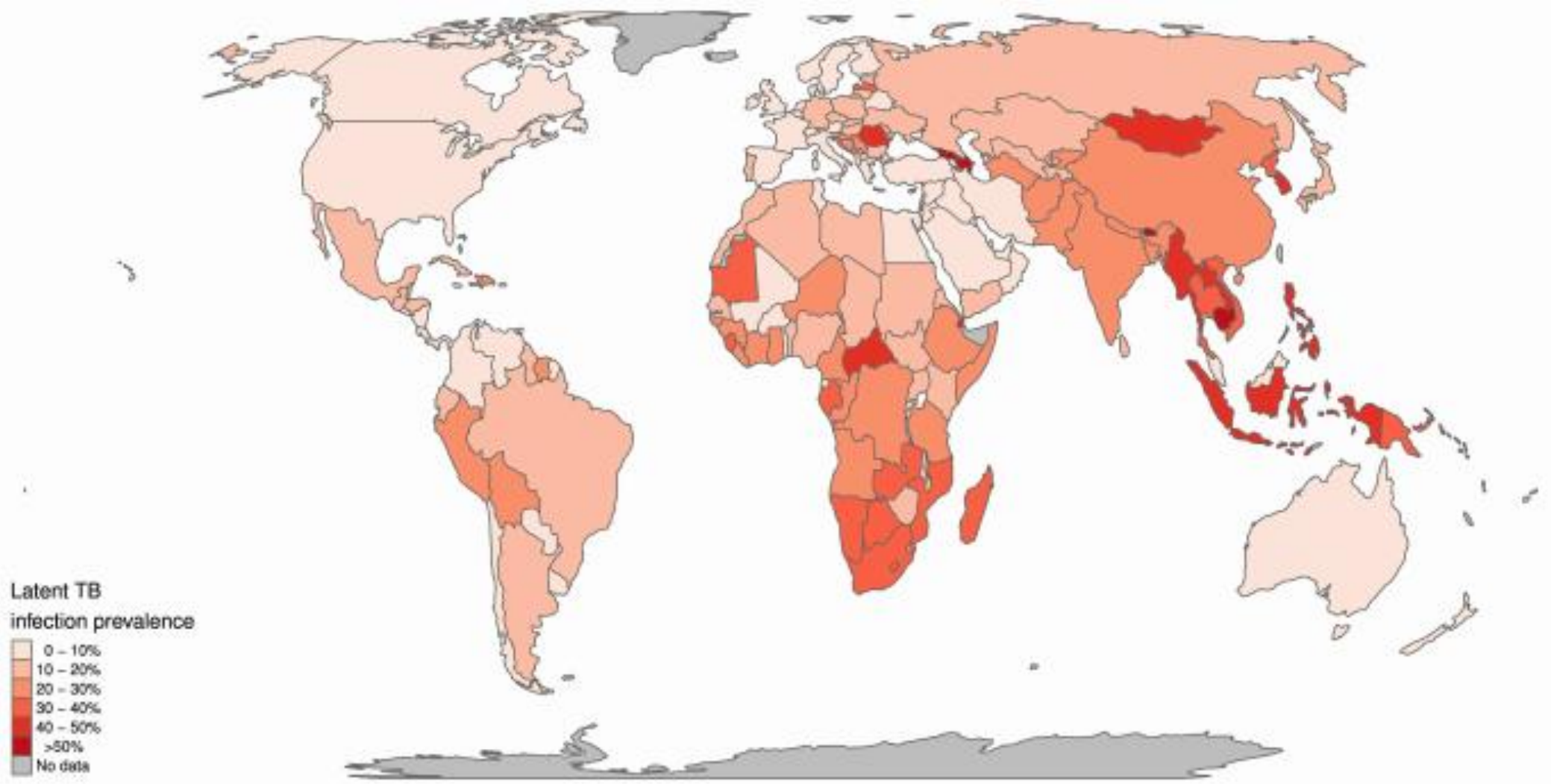
Nelson Mandela, 2004

International Consensus Classification of early TB infection and disease states



(Coussens et al. Lancet Respir Med. 2024)

Global prevalence of TB infection



(Houben. Plos Med, 2016)

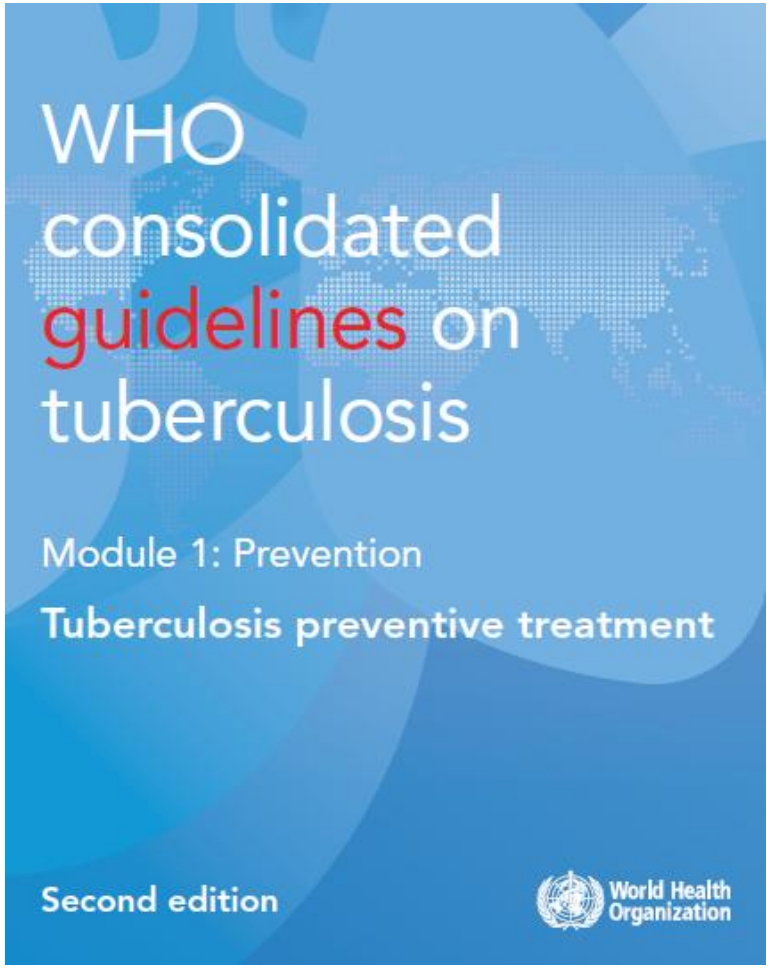
WHO Recommended TB preventive treatment regimens for PLWH

Recommended regimens

- 6 or 9 months of daily isoniazid
- 3 months of weekly high-dose isoniazid & rifapentine
- 3 months of daily isoniazid and rifampicin

Alternate regimens

- One month of daily isoniazid & rifapentine
- Four months of daily rifampicin



High risk groups

People living with HIV

Household contacts
<5 years

Household contacts
≥5 years

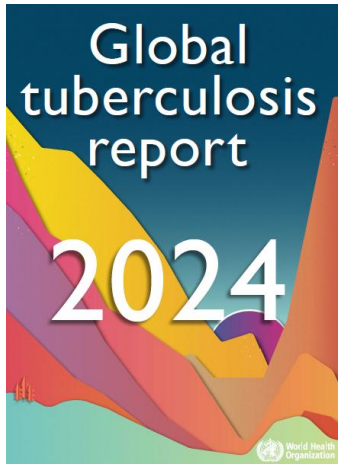
Other people at risk

(Oxlade et al. Int J Tuberc Lung Dis. 2021)

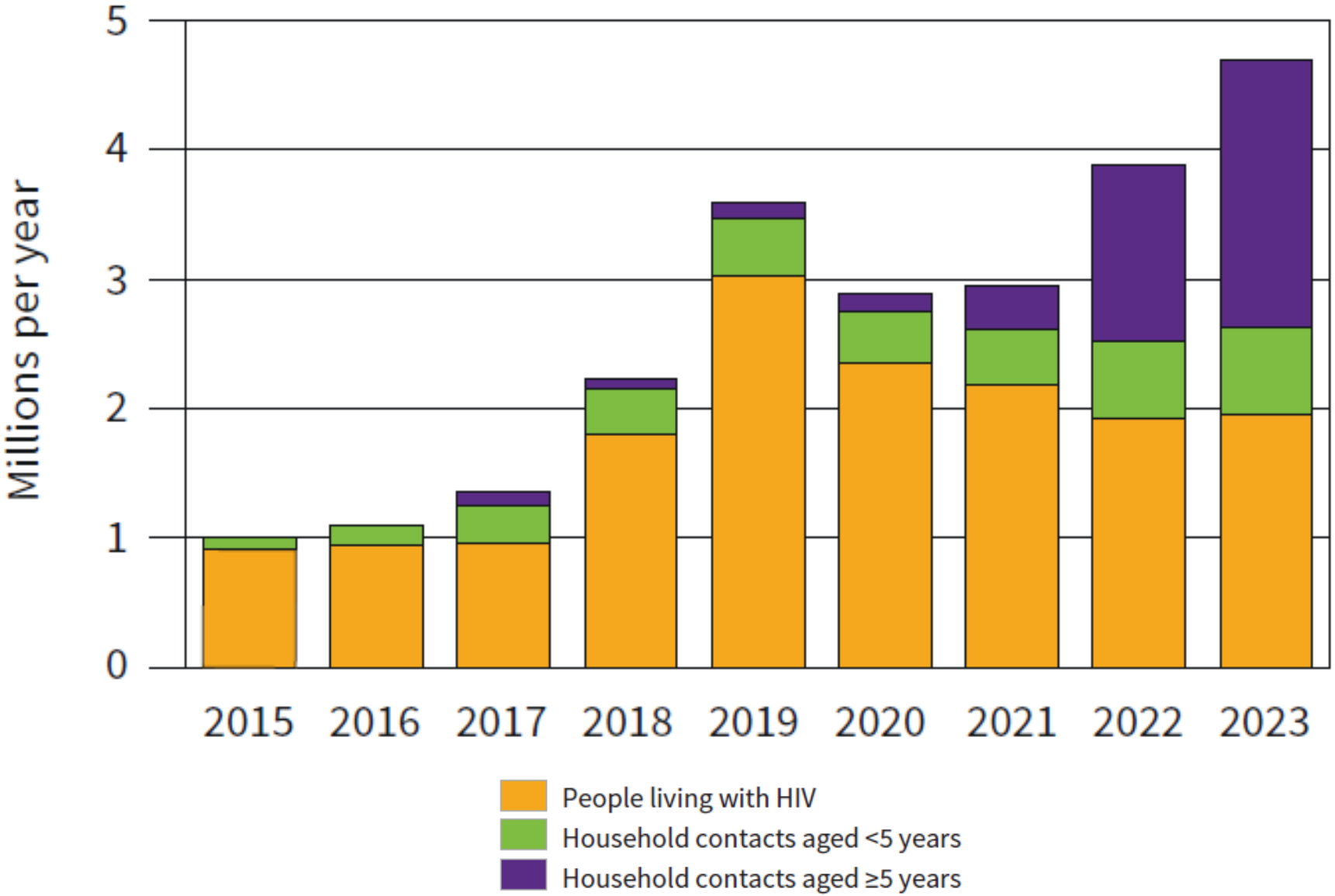
Efficacy of IPT vs placebo on TB among PLWH

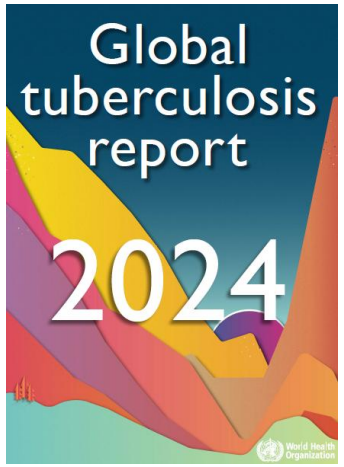
Meta-Analysis	Population	# of RCTs	Risk Reduction	Rate Ratio	95% CI
Akolo and colleagues	All participants	8	33%	0.67	0.51, 0.87
	TST+	4	64%	0.36	0.22, 0.61
	TST-	7	14%	0.86	0.59, 1.26
	TST unknown	2	14%	0.86	0.48, 1.52
Ayele and colleagues	All participants	10	35%	0.65	0.51, 0.84
	TST+	5	52%	0.48	0.29, 0.82
	TST-	9	21%	0.79	0.58, 1.08
	TST unknown	4	32%	0.68	0.42, 1.10

(Akolo, Cochrane Database Syst Rev. 2010, Ayele, PLoS ONE, 2015)

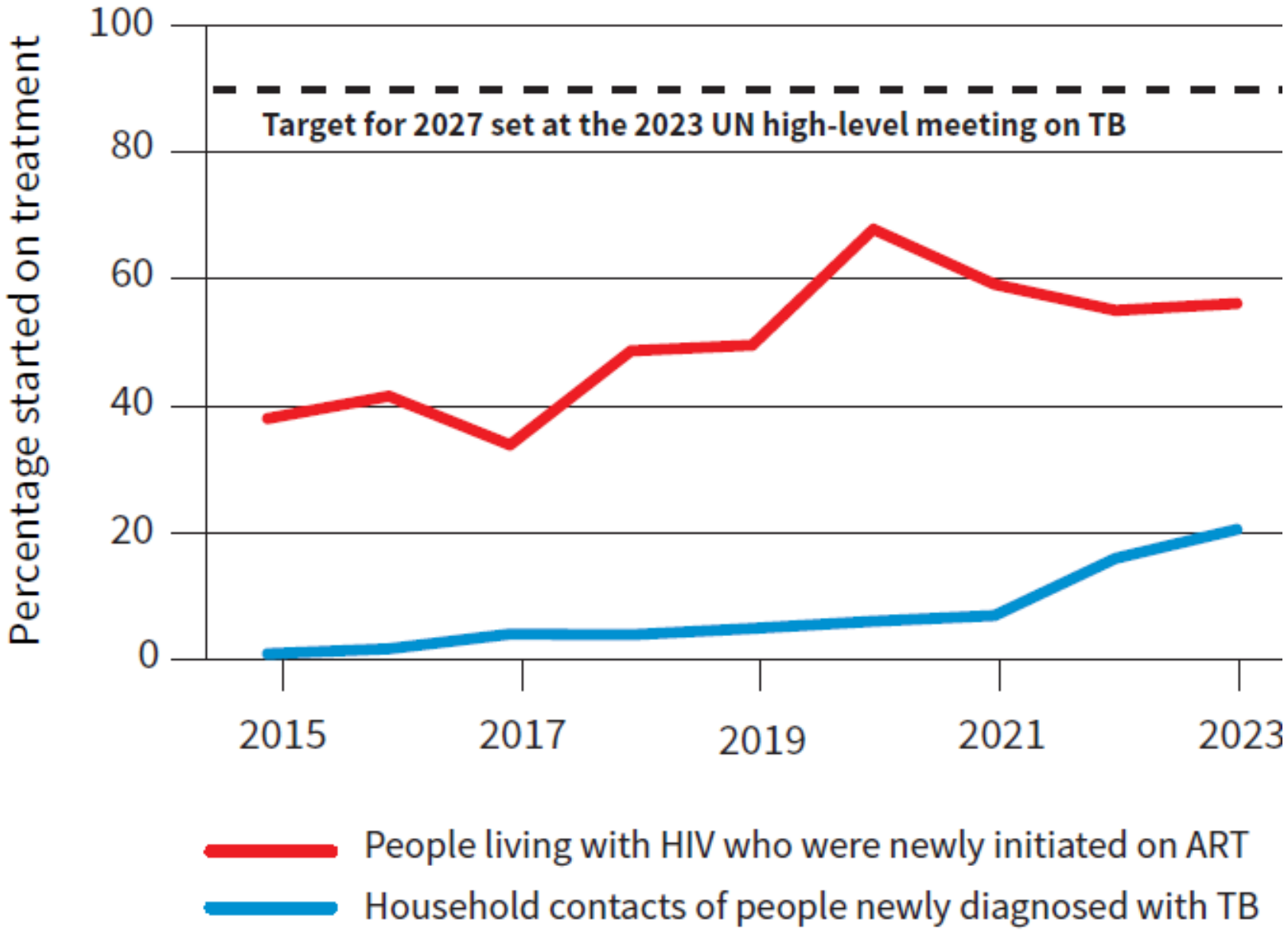


Number provided with TPT





Global coverage of TPT



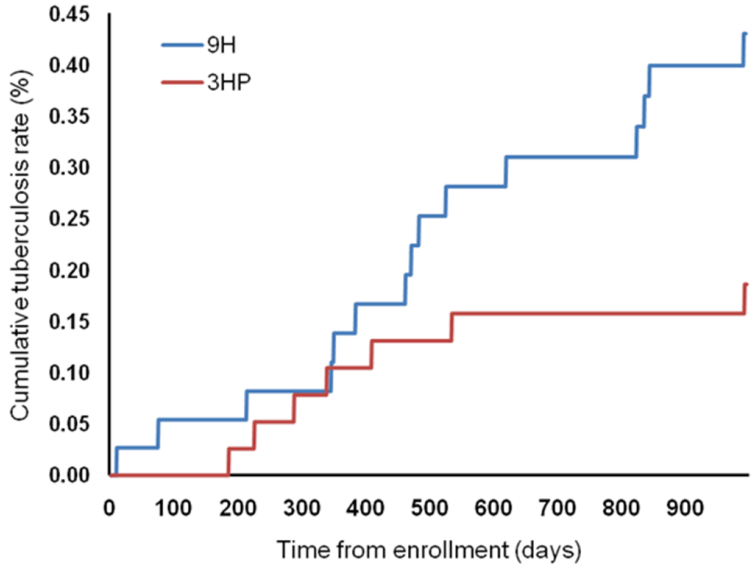
Short Course Regimens

Three months of weekly isoniazid & rifapentine: 3HP

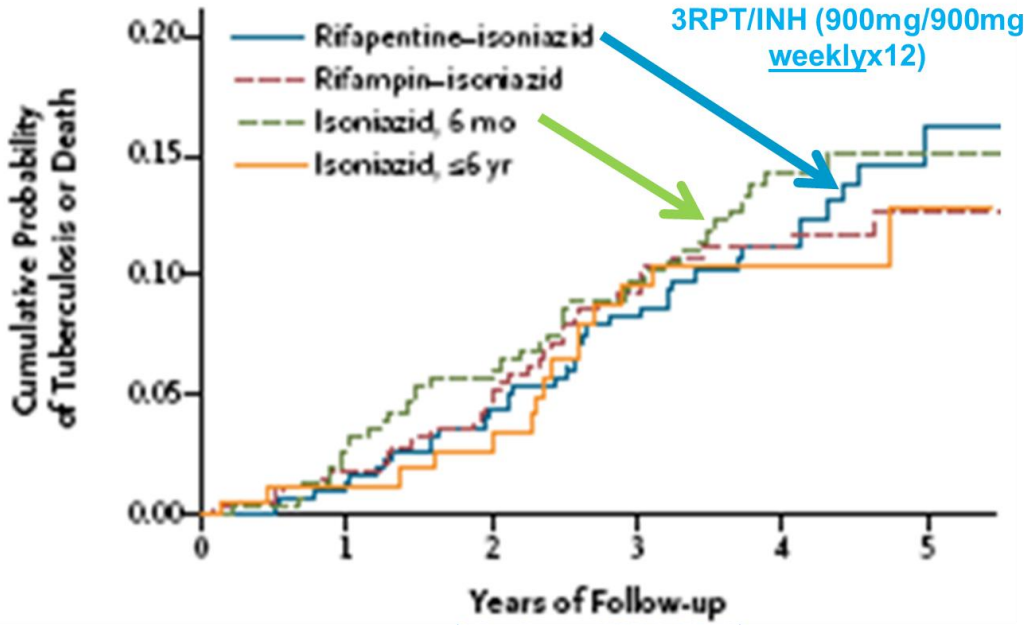
- Similar efficacy to 6/9H
- Shorter
- Less hepatotoxicity
- Better adherence

- Similar efficacy in persons living with or without HIV
- Higher barrier to resistance
- Less burden to health programmes

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



Sterling NEJM 2011;365:2155



(Martinson NEJM. 2011)

One month of daily isoniazid & rifapentine (1HP) *(Ultra short)*

1HP vs 9H

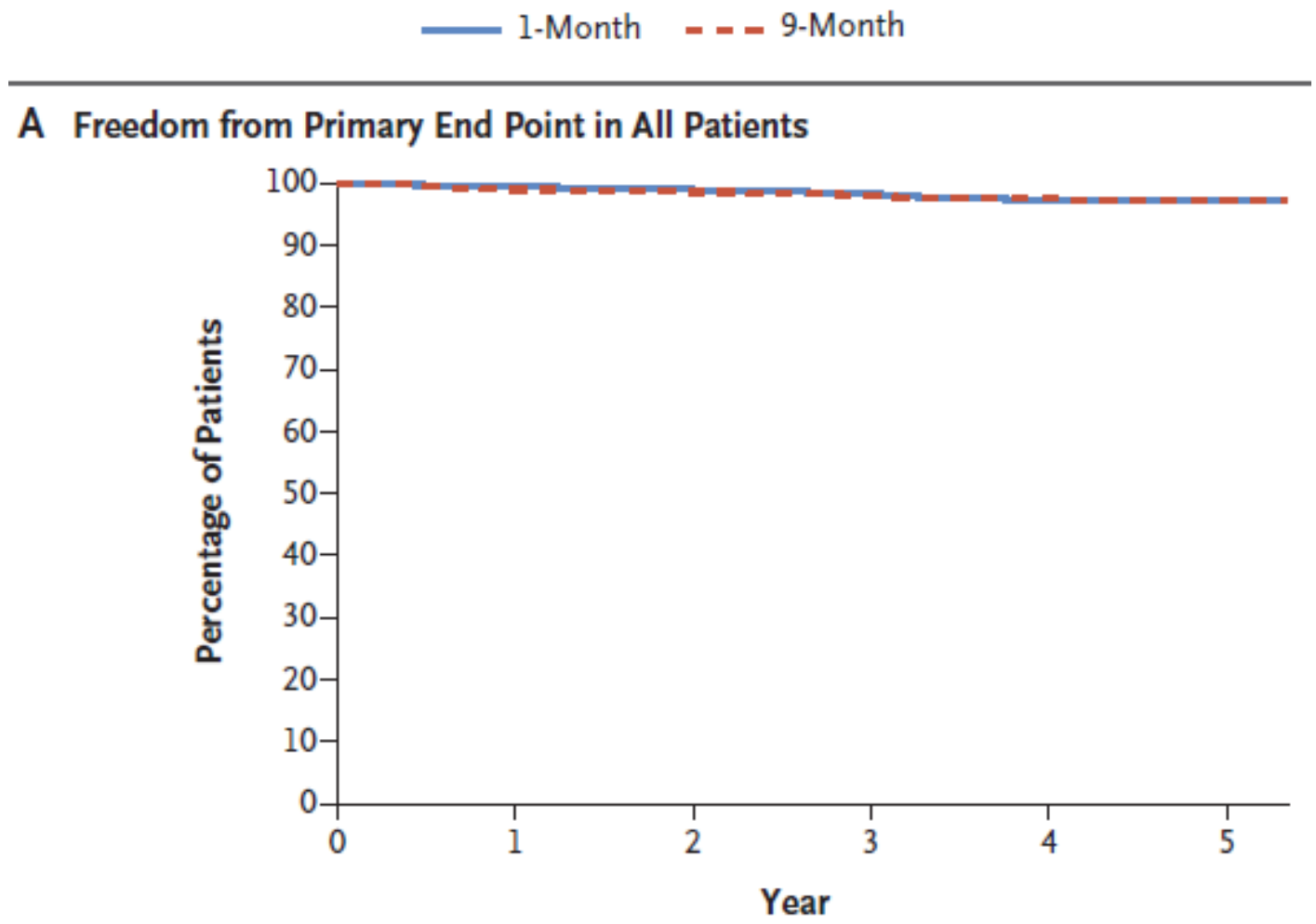
- 1HP non-inferior to 9H
- Better
  - Safety & tolerability
  - treatment completion

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. Nuermberger, and R.E. Chaisson, for the BRIEF TB/A5279 Study Team*



(Swindells. NEJM. 2019)

1HP vs 3HP: safety & treatment completion

- Among people living without HIV in Brazil exposed to TB in the household or workplace, treatment completion and treatment discontinuation was non-significantly higher in 1HP vs 3HP (Ultra Curto)
- The One-to-Three study is comparing safety & treatment completion of 1HP vs 3HP in household contacts and PLWH in South Africa, India, Indonesia, & Mozambique.

(Durovni, Union 2024, LB02-1210-13)

Drug-drug interactions between rifapentine based TPT & DTG

- Drug–drug interactions (DDIs) between the rifamycins, including rifampicin and rifapentine, and antiretrovirals are common
- Dolutegravir (DTG) with tenofovir disoproxil fumarate & lamivudine (or “TLD”), are the most used first line ART in high-burden settings for HIV & TB
- The INSPIRING trial, reported that DTG dose should be doubled with rifampicin based TPT
- The interaction between rifapentine and DTG is expected to decrease DTG concentrations, which may result in lack of viral control and emergence of drug resistance.

(Dooley, Lancet HIV, 2020)

DOLPHIN: 3HP with stable DTG based ART

- In the DOLPHIN trial
  - 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

(Dooley, Lancet HIV, 2020)

DOLPHIN TOO: Simultaneous initiation of DTG-based ART & 3HP in ART-naïve PLWH

Simultaneous initiation of 3HP TPT and DTG in ART-naïve individuals

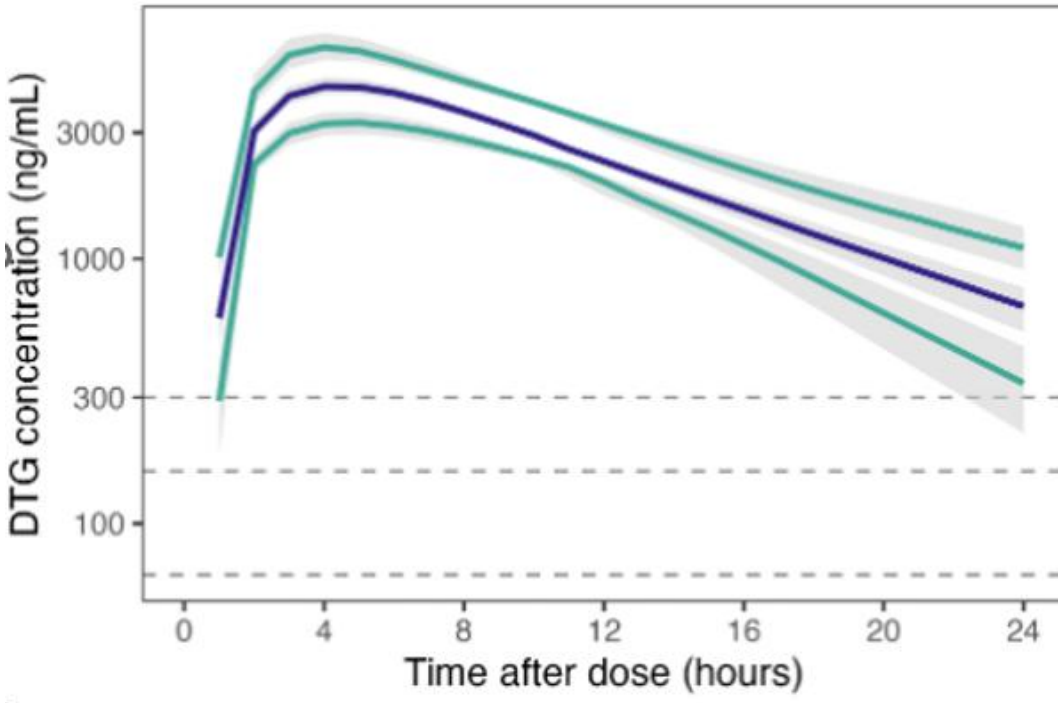
- Was safe and well tolerated
- Achieves and maintains rapid viral suppression with robust DTG trough concentrations
- Results support adopting a policy of simultaneously starting ART and 3HP in newly diagnosed people with HIV

(Weld, Lancet HIV, 2025, In press)

DOLPHIN KIDS: Once vs. twice daily DTG with 3HP in Children living with HIV

- Co-administration of 3HP with twice-daily DTG was safe and resulted in effective DTG exposures

- Modelled co-administration of 3HP with once-daily DTG predict effective DTG exposures



(Salazar-Austin, Union 2024)

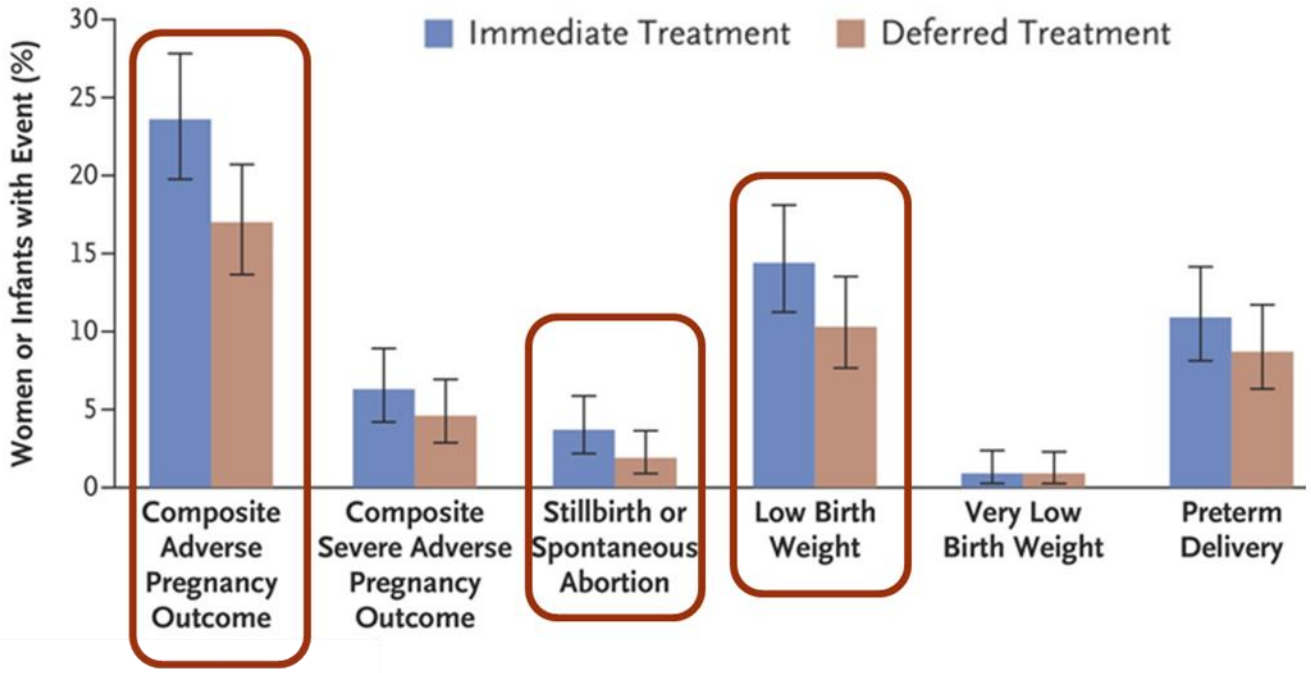
DTG dosing with 1HP

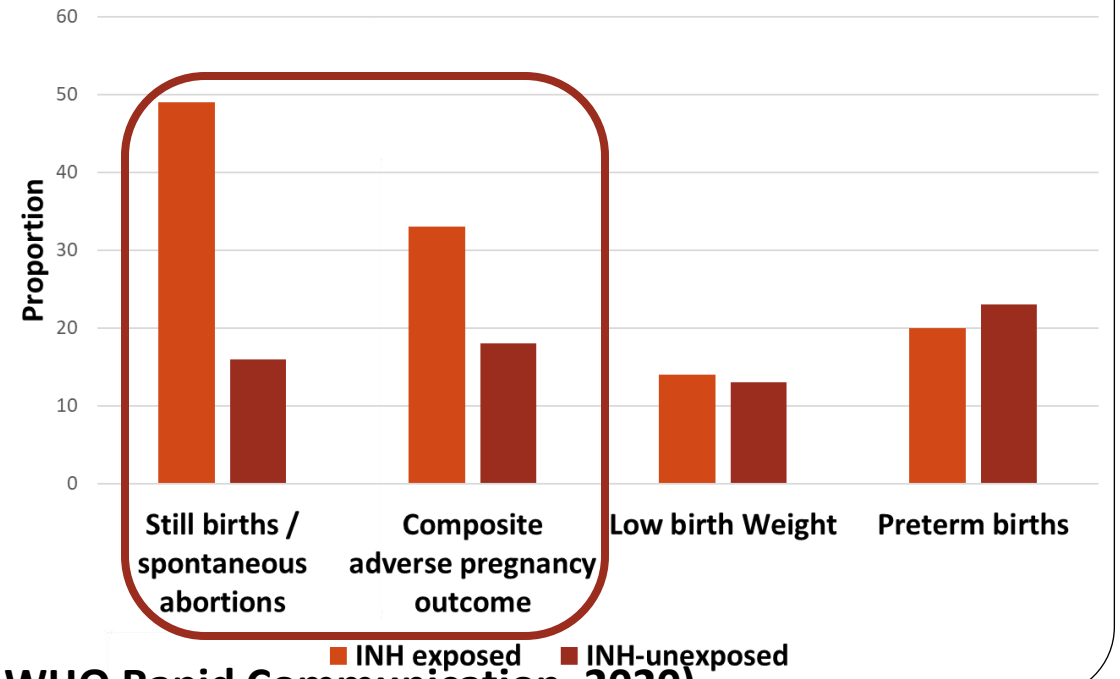
- The A5372 trial suggests that twice-daily DTG dosing is required in combination with 1HP for TB prevention
- Among Thai PLWH, co-administration of 1HP with standard dose of DTG was well tolerated, with high rates of HIV viral suppression

(Podany, Clin Infec Dis, 2924; Avihingsanson, AIDS 2024)

IPT in pregnant HIV-positive women

- TB APPRISE:IPT during pregnancy was associated low birth weight and fetal demise
- Brief TB: INH exposure starting in first trimester associated with increased adverse pregnancy outcomes
- WHO does not recommend deferring IPT to the postpartum period[2]





(Gupta, NEJM, 2019, Gupta, CROI, 2021, WHO Rapid Communication, 2020)

DOLPHIN MOMS

- In pregnant women living with HIV, 1HP or 3HP with BID DTG results in DTG troughs above 158 ng/mL and viral suppression, with BID DTG adherence
- 1HP must be given with BID DTG during pregnancy
- 3HP: may be given with once daily DTG during pregnancy.

TPT	BID DTG	Once daily DTG
1HP	✓	✗
3HP	✓	?

(Mathad, CROI2025)

Rifapentine formulations & pill count

= RPT 150 mg Single

INH Single 300mg

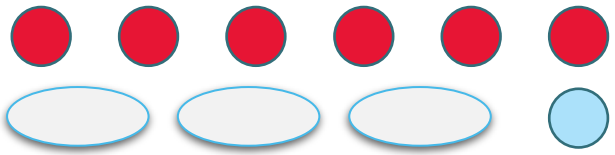
Vitamin B6

INH/RPT 300mg/300mg FDC

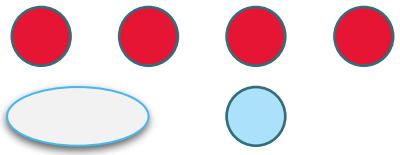
RPT 300mg Single

Pill count with single tables

3HP



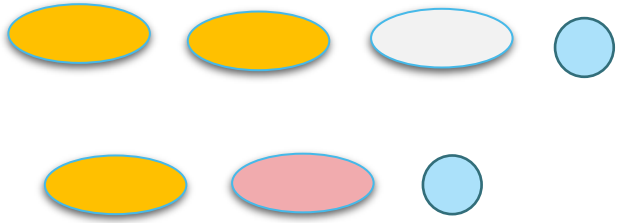
1HP



Pill count with FDCs

3HP

1HP



A dispersable, functionally scored, 150mg, child friendly, rifapentine tablet is now available

Price reduction of 3HP through IMPAACT4TB market shaping

- 13.3 million 3HP patient courses were procured across 104 countries

Cost effectiveness of 3HP vs IPT

Per 1000 individuals on ART, 3HP vs IPT estimated to

- Avert 9 cases of TB and 1 death
- Cost $9402 per DALY averted
- Cost-effectiveness depended on
  - The price of rifapentine
  - Completion of 3HP
  - Prevalence of latent TB
- At a willingness to pay of $1000 per DALY averted, 3HP is likely to be cost-effective relative to IPT only if
  - Price of RPT can be greatly reduced (to ~$20 per course)
  - High treatment completion (85%) can be achieved

IMPAACT4TB

PREVENTING TB TO END TB

(Johnson. CID. 2018)

Cost-Effectiveness of 1HP vs 3HP

A Comparison of TB Short-Course Preventive Regimens

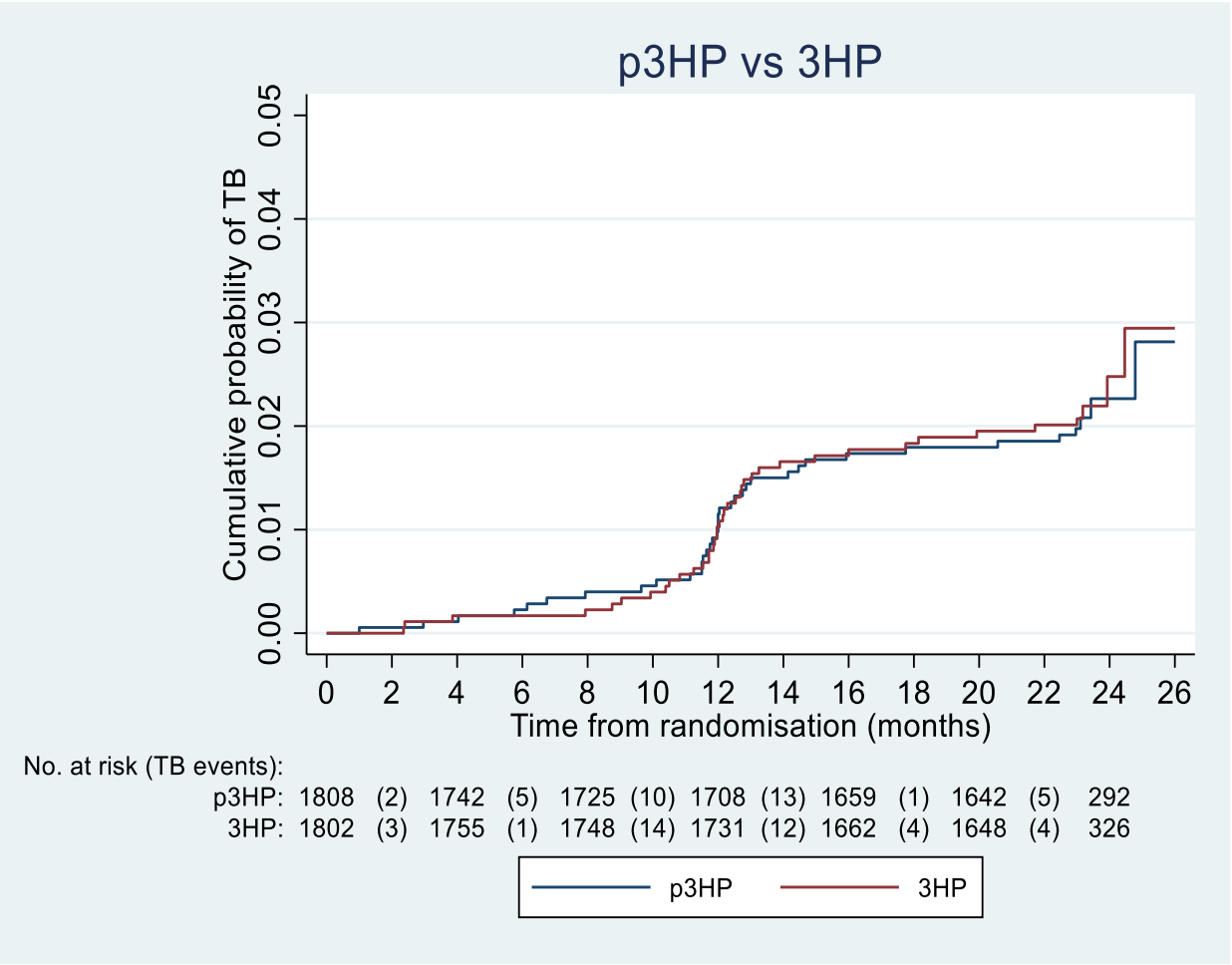
- Assuming 1HP is noninferior to 3HP, it would cost an additional $16 per patient to achieve the same outcomes at current prices
  - Falls to $0.70 if the price of rifapentine per 600mg can be reduced by 66% (corresponding to $15 per course of 3HP)
- Cost effectiveness of 1HP is driven by 1HP completion rates & efficacy relative to 3HP, cost of rifapentine, and TBI prevalence

IMPAACT4TB

PREVENTING TB TO END TB

Ferguson et al, Union 2019

Efficacy of 3HP in PLWH given annually vs once



- Treatment completion was higher with 3HP (90%) vs 6H (50%)
- In settings with high TB transmission, a second round of 3HP did not provide additional benefit to PLWH on ART

(Churchyard, Ann Intern Med, 2021)

TPT for household contacts

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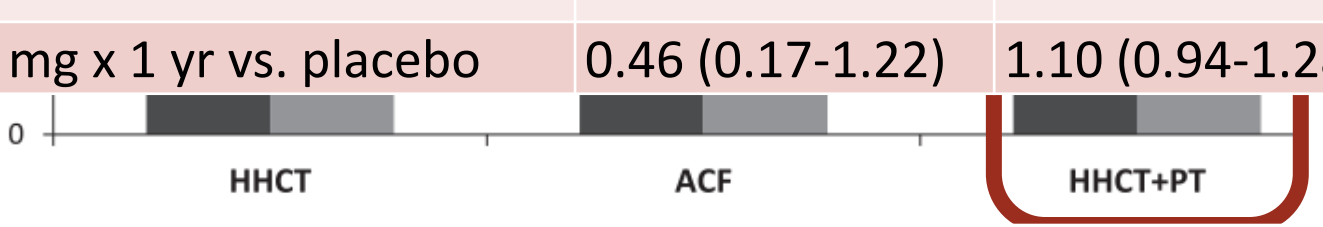
Household case-finding & IPT

Effectiveness & modelled impact of household case-finding & TPT

Author, Year	Location	Intervention	Effectiveness TB Incidence	Effectiveness All Deaths
Egsmose, 1965	Kenya	INH 300-500 mg x 1-2 yrs vs. placebo	0.36 (0.15-0.85)	0.93 (0.33-2.61)
Ferebee, 1962	US, Puerto Rico, Mexico	INH 300 mg x 1 yr vs. placebo	0.22 (0.1-0.47)	-
Mount, 1962	US	INH 300 mg x 1 yr vs. placebo	0.46 (0.17-1.22)	1.10 (0.94-1.28)

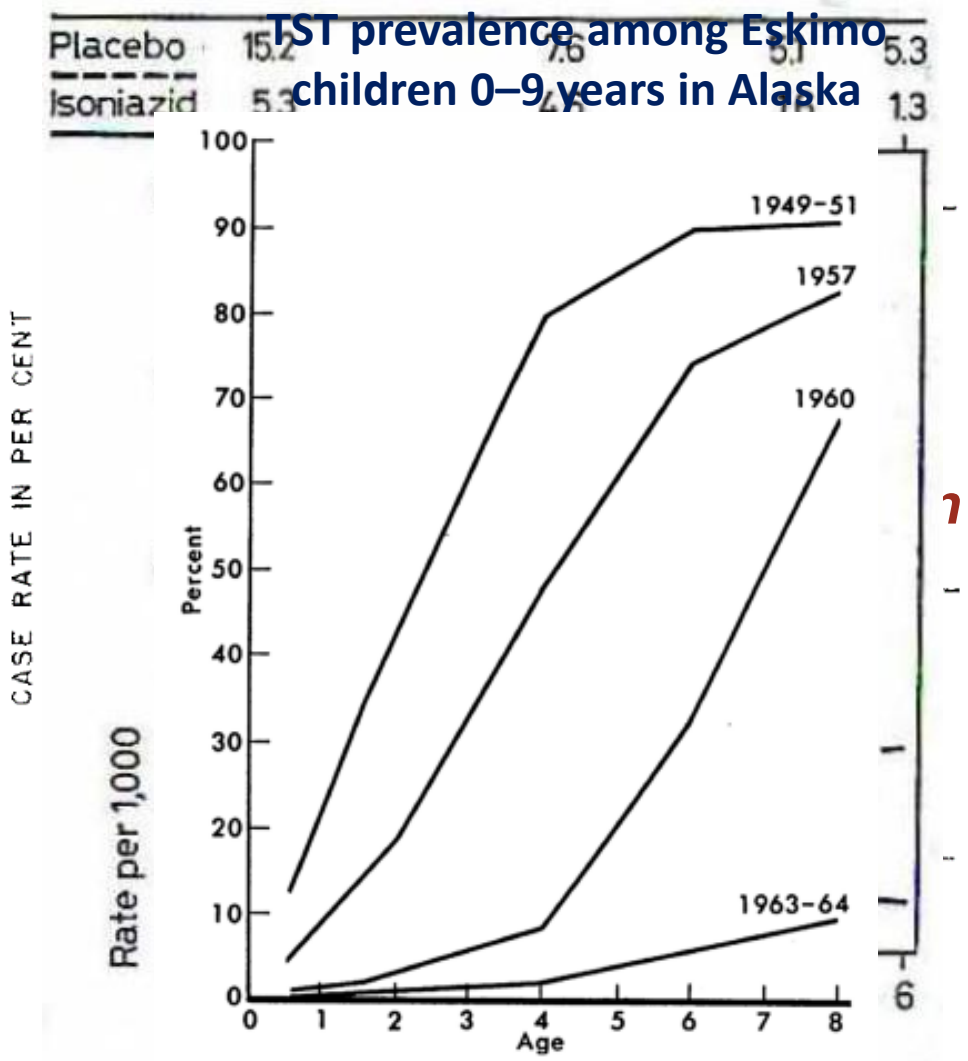


(Kasaie, et al. Am J Respir Crit Care Med. 2014)

Community-wide IPT: Alaska

- **Households randomised**
- Isoniazid 5mg/Kg daily
- Duration: 12 months
- High uptake
- 30% had calcified, inactive or possibly or probably active CXR lesions
- Third completed 80% treatment
- Other interventions
  - CXR screening
  - Hospitalised treatment

TST prevalence among Eskimo children 0–9 years in Alaska



(Comstock, AM Rev Resp Dis, 1967; Ferebee, Am Rev of Resp Dis, 1963; Hanson et al. Public Health Rep. 1967)

TPT for Drug-resistant TB infection

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PHOENIx Feasibility study

Objectives

- To describe the feasibility of identifying, recruiting, and characterizing adult MDR TB index cases and their adult and child household contacts

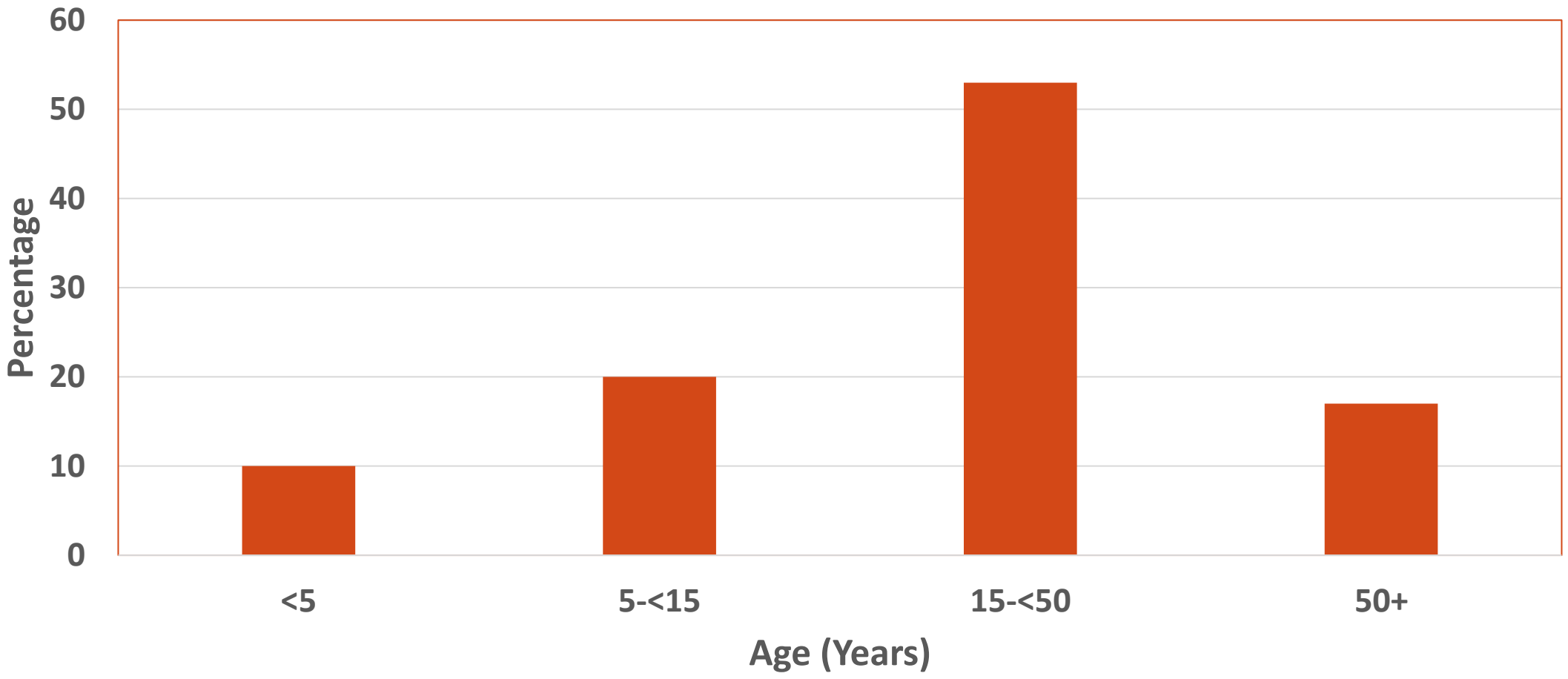
- To describe the prevalence of TBI, TB disease and HIV infection among adult and child household contacts

Participant Characteristics

Characteristic	Index (N=284)	HHC (N=1007)
Median age, years (IQR)	35.5 (26-45)	25 (12-43)
Female	120 (42%)	593 (59%)
Countries (# sites)		
Botswana (1)	10 (4%)	38 (4%)
Brazil (1)	10 (4%)	17 (2%)
Haiti (1)	14 (5%)	52 (5%)
India (2)	58 (20%)	205 (20%)
Kenya (1)	7 (3%)	12 (1%)
Peru (2)	54 (19%)	203 (20%)
South Africa (7)	121 (43%)	450 (45%)
Thailand (1)	10 (4%)	30 (3%)

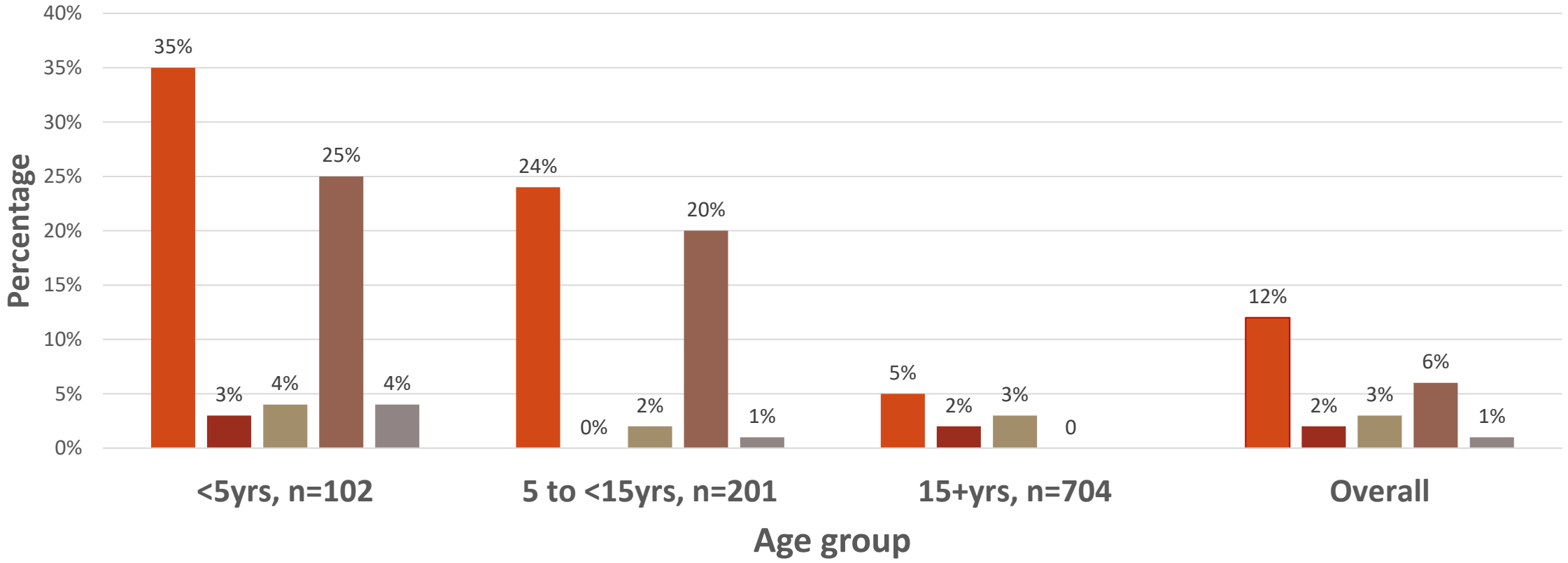
(Gupta, CID, 2019)

Age Distribution of Household Contacts



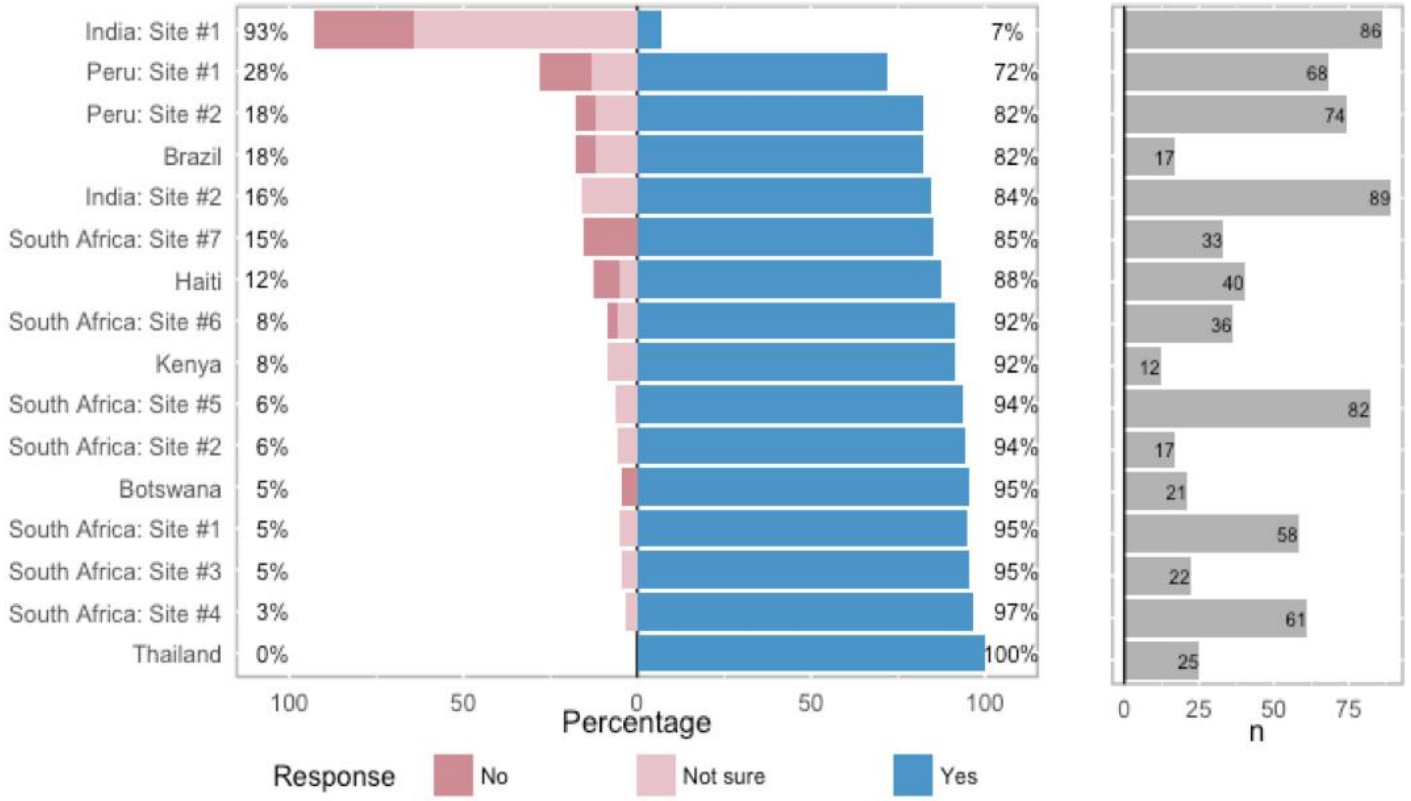
(Gupta, CID, 2019)

Prevalent TB by age group



(Gupta, CID, 2019)

Willingness to take TB preventive therapy



- HHC willingness to take TPT was high (79%) with significant site-level variation
- Willingness to take TPT associated with: current employment or schooling, appropriate TB-related knowledge ,confidence in taking TPT, comfortable telling others about taking TPT.

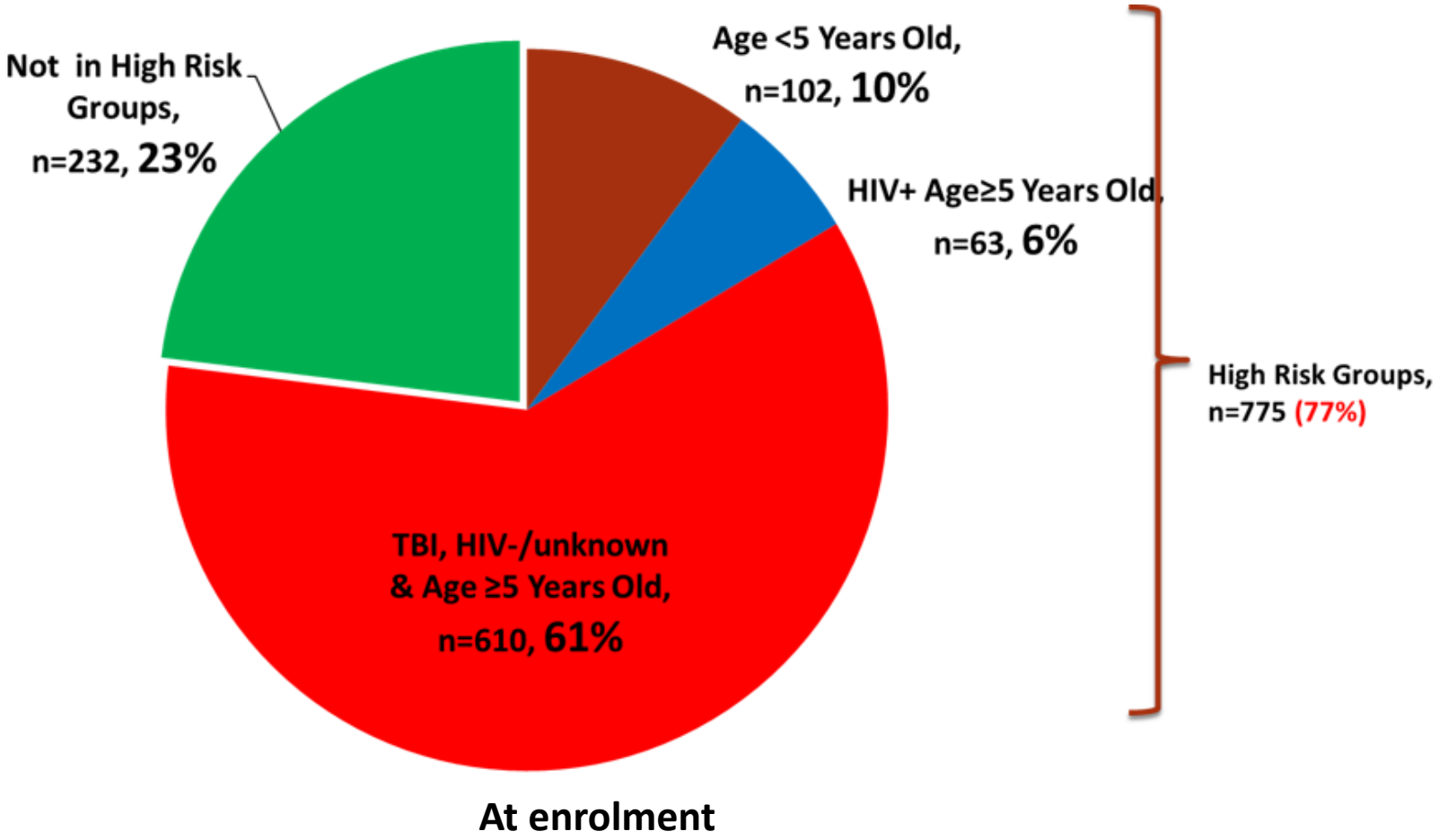
(Suryavanshi, Murrill CID, 2019)

Resource utilization

- 16 sites made 512 attempts to evaluate 308 households
  - up to 5 attempts per household
- Median HH size was 4 people plus index case
  - Range 1 – 19 persons
- Median time spent by site staff per attempt was 4 hours

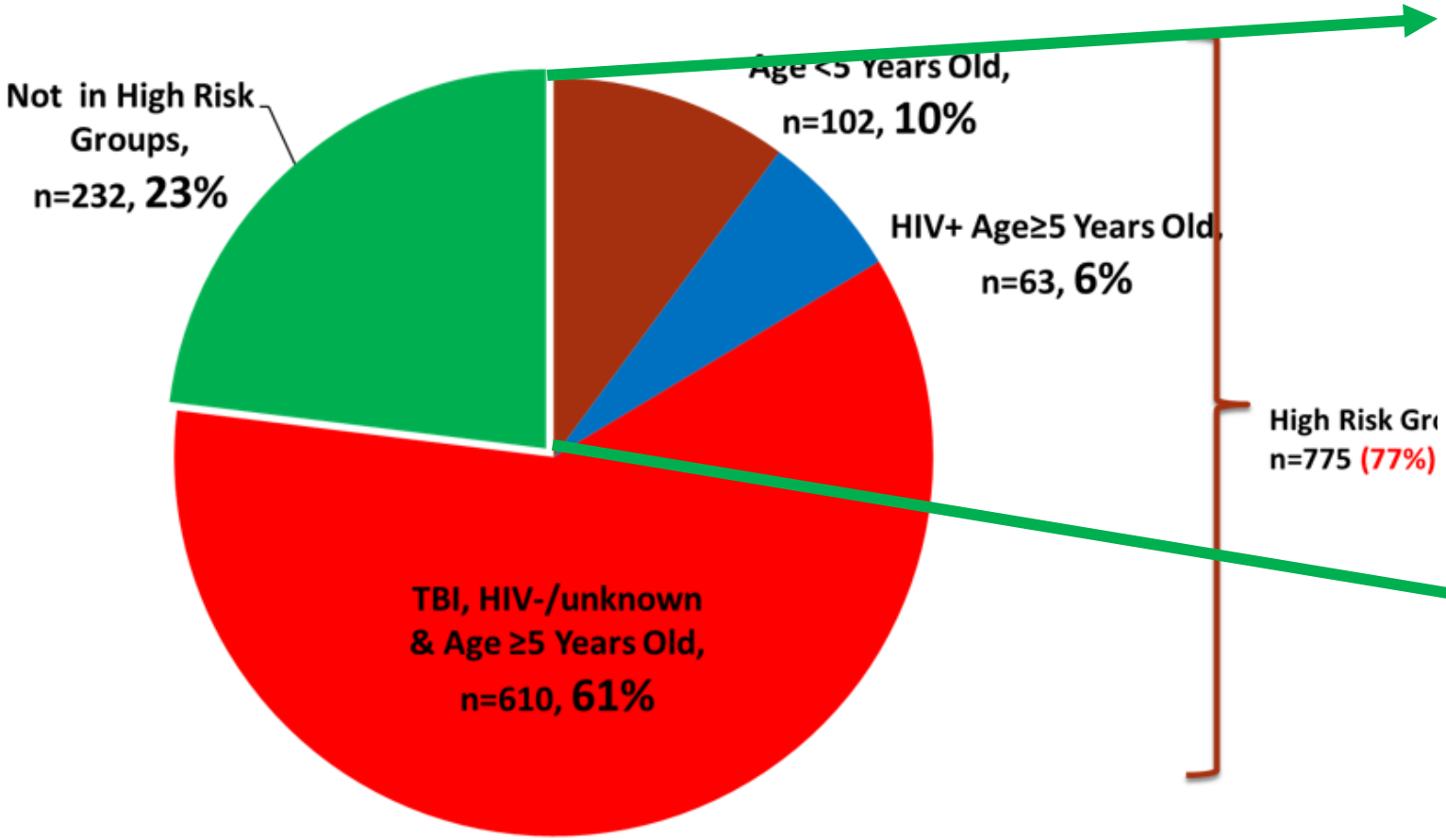
(Swindells. Int J Tuberc Lung Dis. 2018)

MDR TB exposed household contacts at high risk of developing TB

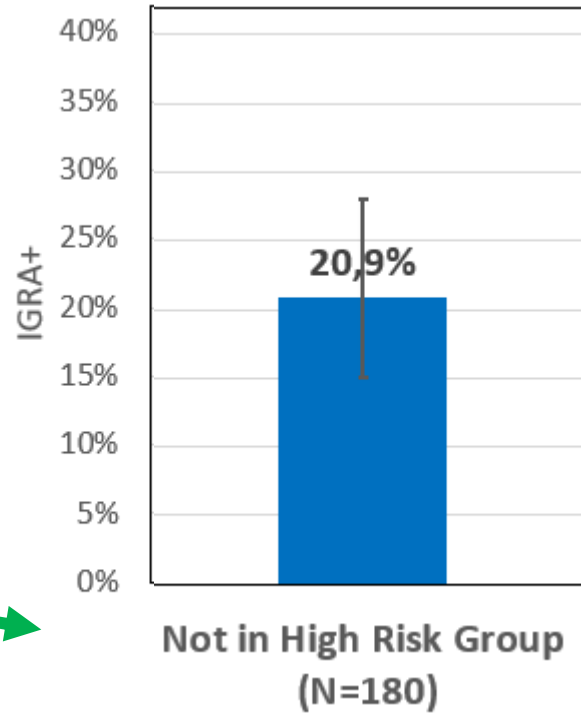


(Gupta. CID. 2019, Kim. CROI. 2020)

MDR TB exposed household contacts at high risk of developing TB



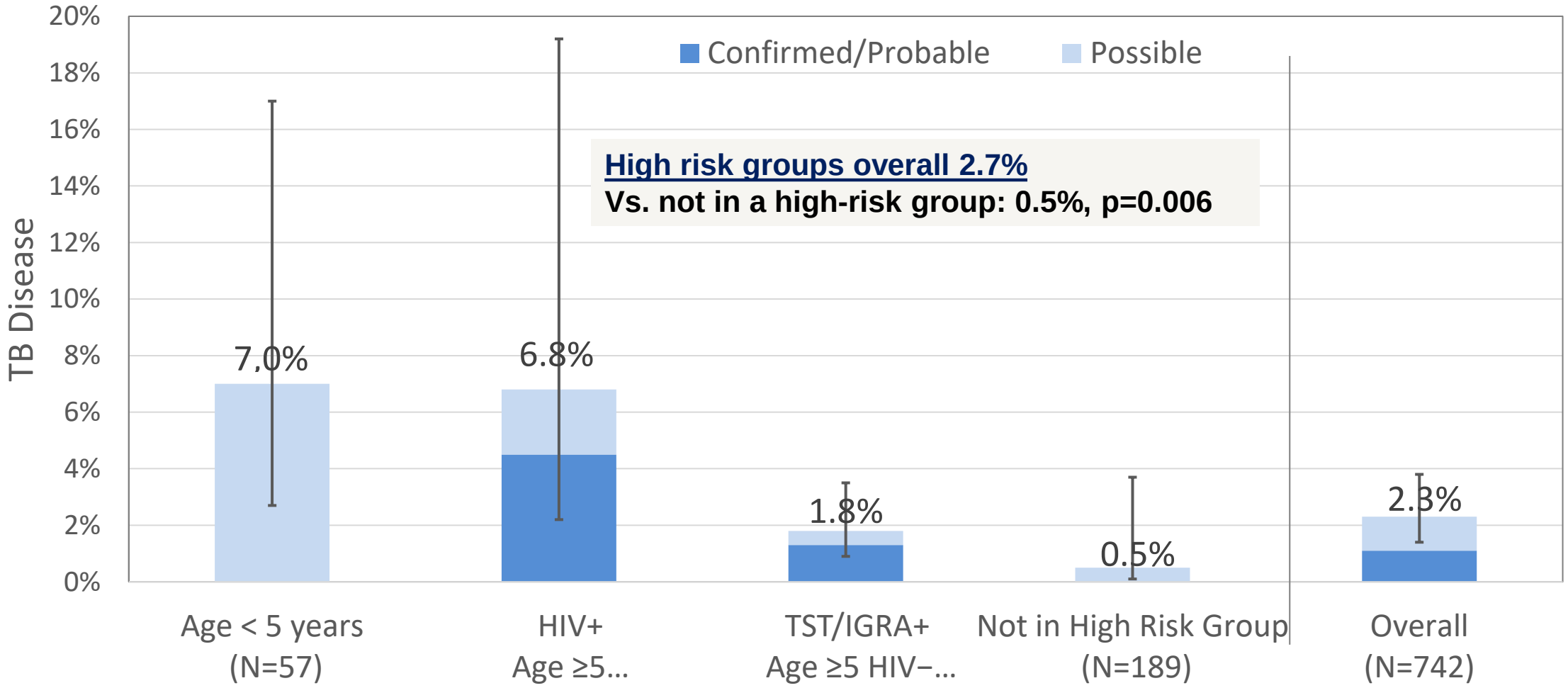
At enrolment



Proportion of HHCs≥5 years, HIV- that converted from IGRA negative at baseline to positive after one year

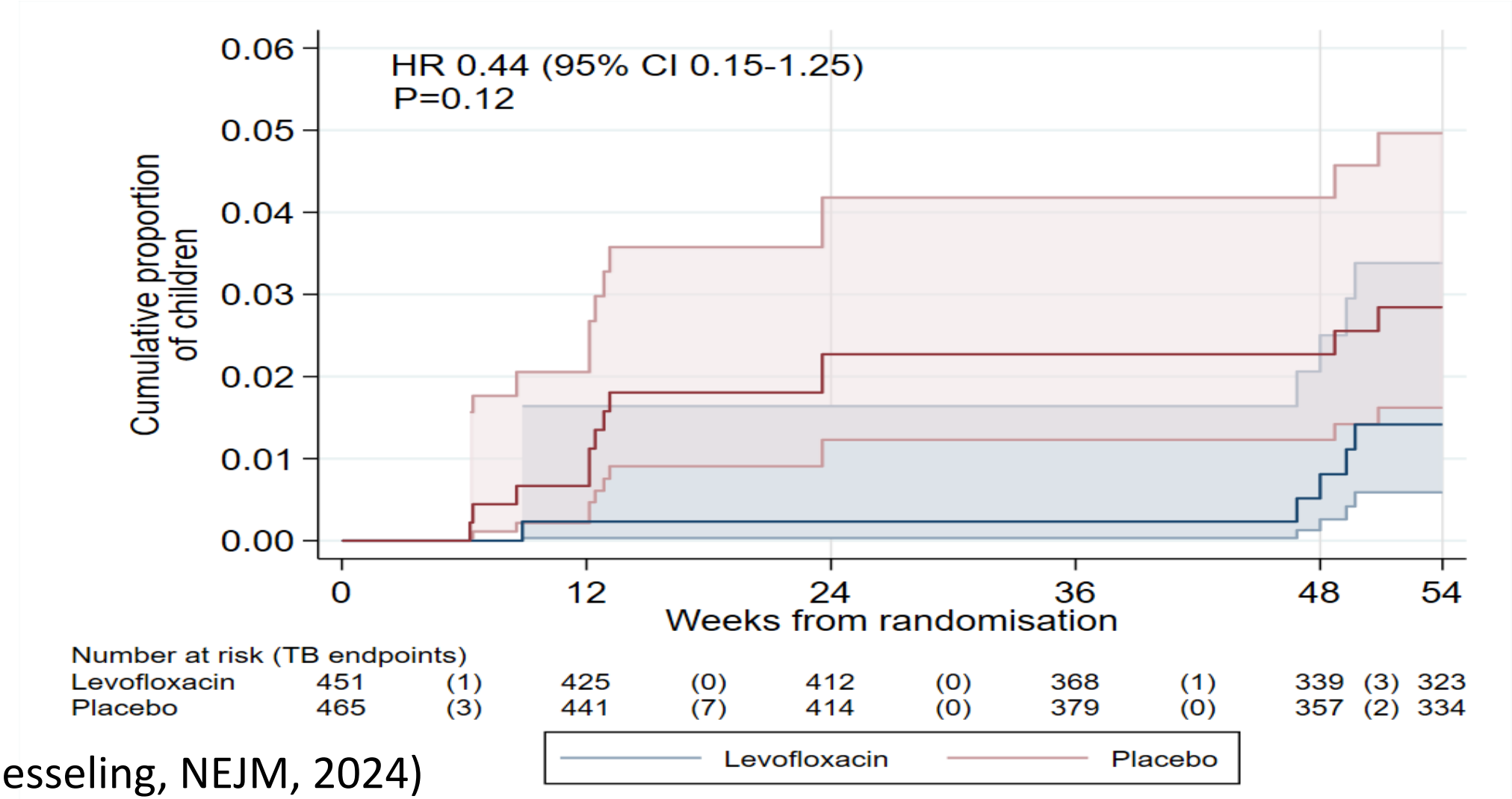
(Gupta. CID. 2019, Kim. CROI. 2020)

Incidence of TB Disease among high risk HHCs



(Gupta. AIDS. 2020)

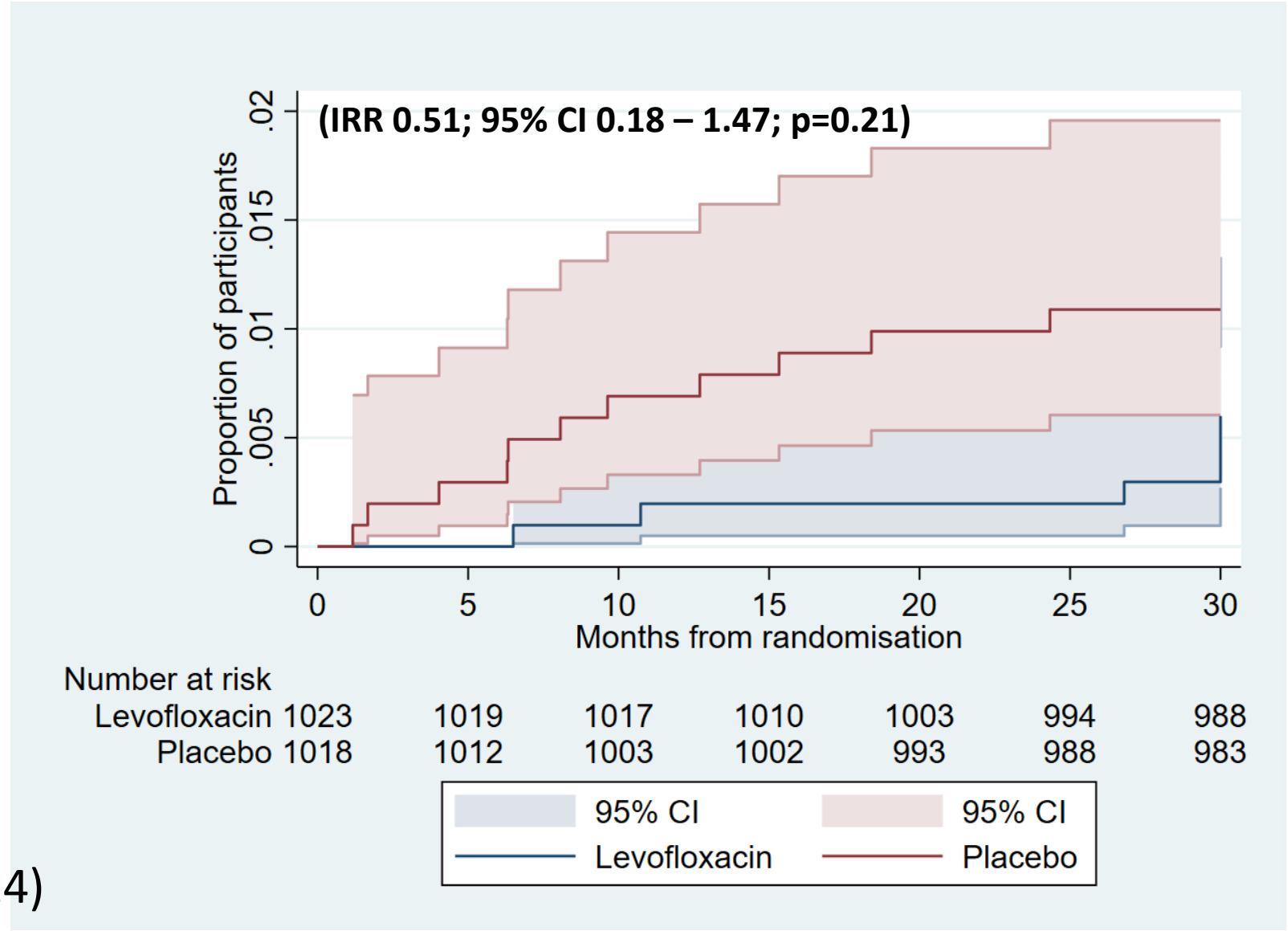
Levofloxacin efficacy in child contacts



(Hesseling, NEJM, 2024)

* Allowing for pre-defined ±6 weeks window at study visit at 48 weeks. + Test for non-proportional hazards p-value = 0.106

Levofloxacin efficacy in contacts

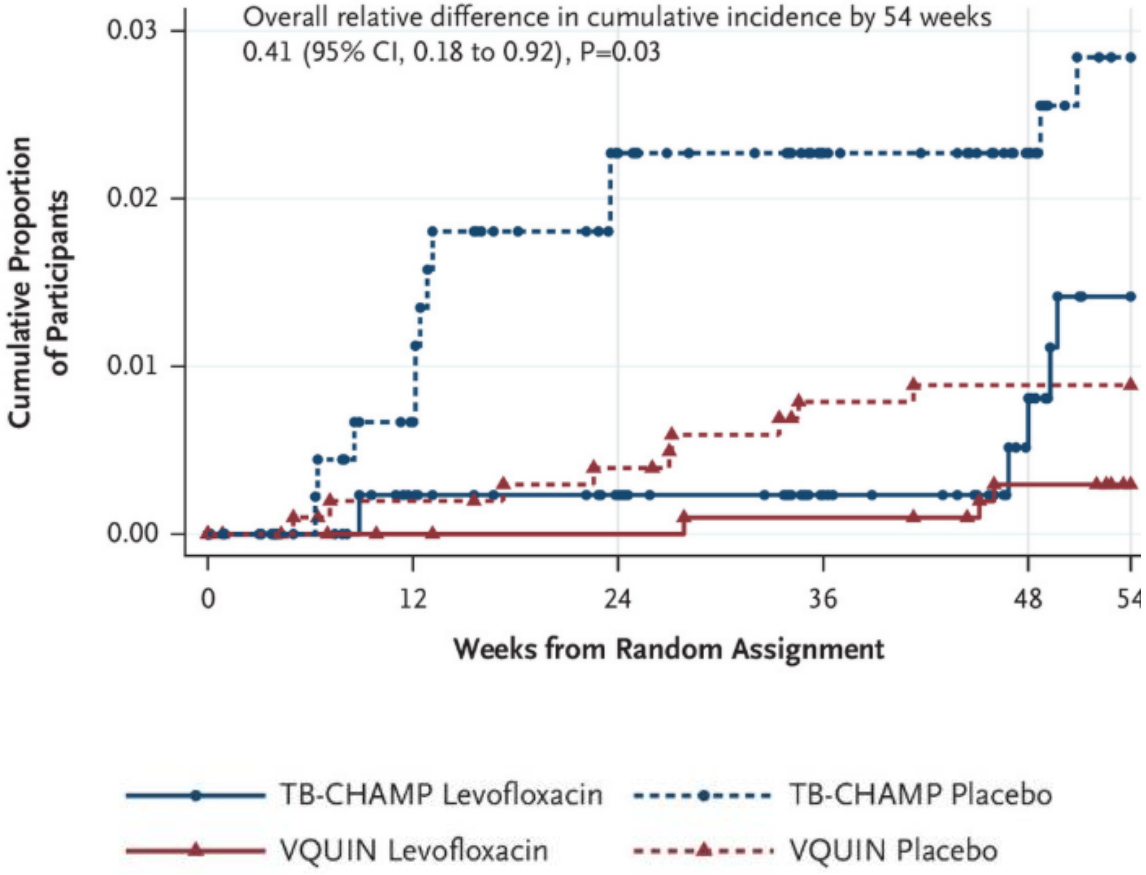


(Fox, NEJM, 2024)

TB CHAMP & VQUIN

Pre-planned Individual Patient Meta-analysis Using Data from Both Trials

- Levofloxacin significantly reduced the risk of TB by 60% over a year
  - HR 0.40 (95%CI: 0.17-0.90)
- Levofloxacin was safe
  - In children, there was no indication of tendinitis, arthralgia, & arthritis
  - In adults, there was a higher risk of tendinitis, arthralgia and arthritis & more treatment discontinuation due to levofloxacin



(Duong, NEJM Evid, 2024)

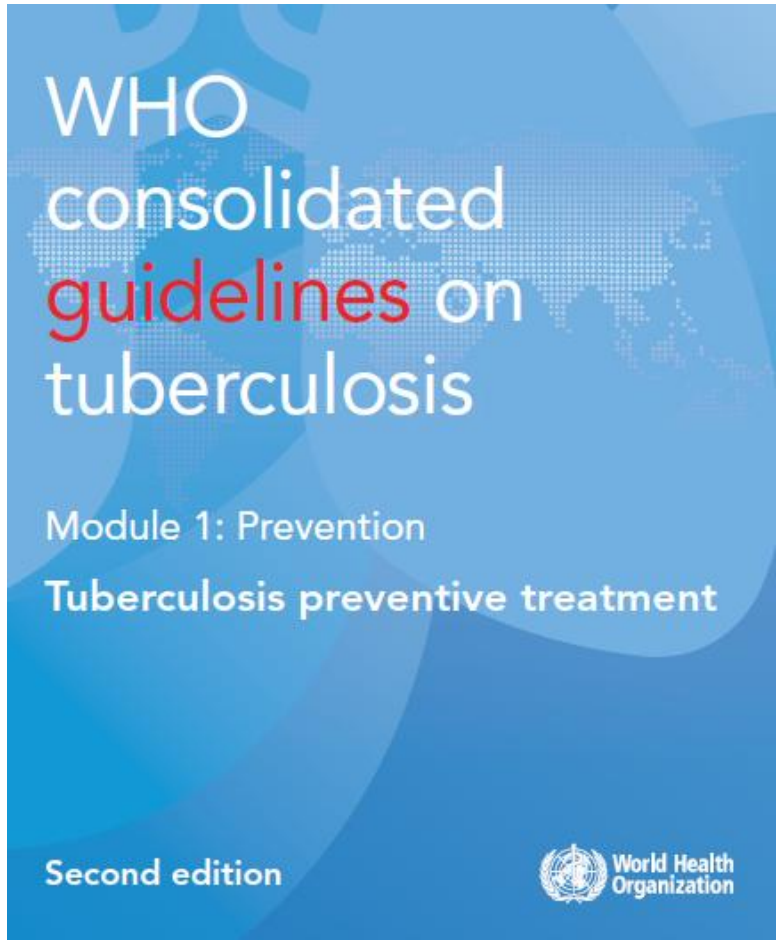
Updated WHO Guidelines

Prior WHO recommendation (2017)

- Conditional recommendation for MDR/RR-TPT
- No specific regimen recommended
- Uptake and implementation has been poor

Updated WHO guidelines (2024)

- 6 months of levofloxacin should be used as TPT for contacts of all ages exposed to persons with MDR/RR-TB

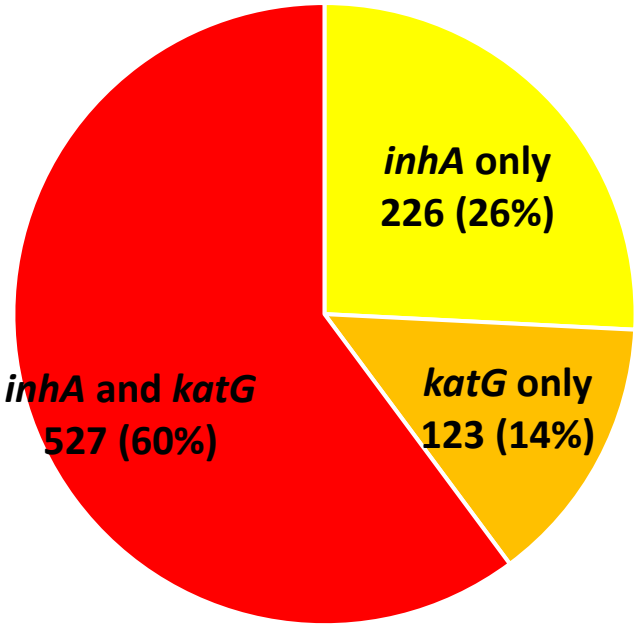


Resistance Profile of MDR TB* Index Cases

(N=1355)

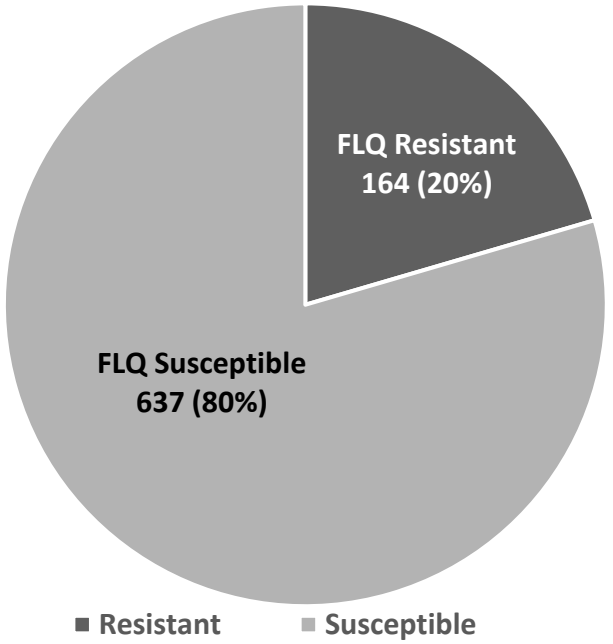
***inhA* promoter and *katG* mutations**

N=876



Fluoroquinolone Susceptibility

N=801



KIM, Union 2024

- 74% of index cases have high-level INH resistance due to katG mutations
- Documented fluoroquinolone resistance prevalence varied from 0% in Haiti (0/47) and Zimbabwe (0/6) to 86% (38/44) in Vietnam ($p<0.001$).

* Old definitions used: Pre-XDR=MDR plus FLQ resistance or SLID resistance but not both, XDR = MDR plus both FLQ and SLID resistance

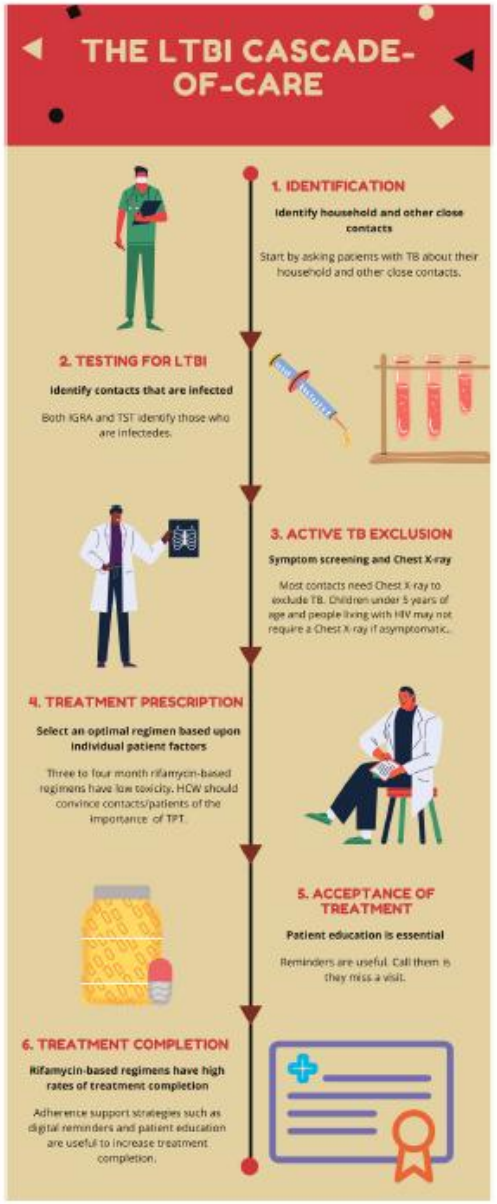
Levofloxacin TPT: programmatic considerations

- In adults, there is a higher risk of low-grade tendinitis, arthralgia and arthritis and more treatment discontinuation due to levofloxacin
- Resistance to fluoroquinolones is relatively high
- Levofloxacin not likely to be effective in preventing quinolone resistant TB
- Alternative MDR TPT regimens are needed

Protecting Households On Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients

	PHOENIx (A5300B/I2003B)
Intervention	DLM vs INH daily for 26 weeks
Design	Cluster randomized; superiority, Phase III trial
Target Population	Children 0-5 yrs, HIV +, TST/IGRA + over 5 year olds
Assumptions	DLM decreases incidence by 50% from 5% to 2.5%; 90% power
Sample size	1726 HH 3452 contacts

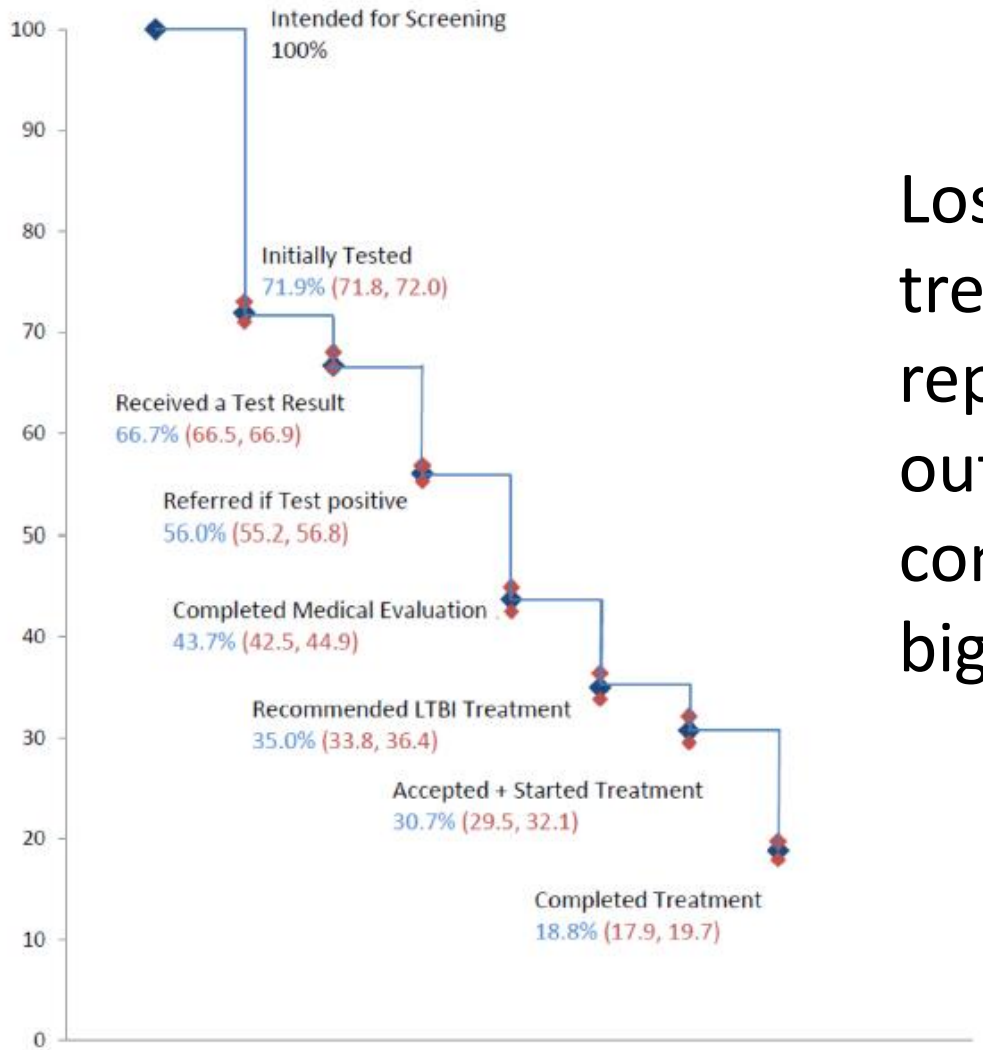
TPT cascade of care



- The ‘cascade-of-care’ provides a framework to strengthen TBI treatment by quantifying where attrition occurs, and monitoring the progress of interventions to strengthen each step
- The reasons for pre-treatment fall-out are numerous and context-specific
- Efforts to expand TPT should address barriers through use of the TPT cascade of care

(Fox. Int J Infect Dis. 2021)

TPT cascade for household contacts



Losses occurring before treatment commencement represent the biggest drop-out (occurring up to 70% of contacts) and presents the biggest barrier

Alsdurf H et al. Lancet Infect Dis 2016

A health system intervention for TPT management
ACT4

- **Aim**
  - To evaluate the effectiveness and cost-effectiveness of a health systems intervention to strengthen TPT management in HHCs
- **Methods**
  - The intervention focused on identifying, quantifying, and addressing barriers throughout the cascade up to the point of treatment initiation, as losses before treatment initiation is > numbers lost during TPT
  - Cluster-randomised trial in Benin, Canada, Ghana, Indonesia, & Vietnam
  - Sites randomly assigned to either a three-phase intervention (TBI programme evaluation, local decision making, and strengthening activities) or control (standard LTBI care).

Oxlade.Lancet Public Health. 2021

ACT4 intervention phases

Programme evaluation

Activities

- Cascade analysis
- Stakeholder questionnaire

Outcomes

- # Index patients, # HHC started on TPT in 6 mnths

Cost

- Resource use & implementation costs
- Micro-costing

Decision making

Activities

- Stakeholder meetings to review results of evaluation phase & select solutions

Outcomes

- Not measured

Cost

- Resource use & implementation costs

Strengthening

Activities

- Implementation of local solutions
- In-service training
- Repeat cascade analysis

Outcomes

- # Index patients, # HHC started on TPT in 6 mnths

Cost

- Resource use & implementation costs

Oxlade.Lancet Public Health. 2021

Examples of issues identified during the evaluation phase

- Highly entrenched community stigma
- Limited staff for TB control
- TPT not recognized as a priority
- Lack of
  - Knowledge about TBI by contacts and HCW
  - Training for health workers on TPT
  - Information to clients
  - Management of TBI in adults and children ≥5 years
  - Home visit to identify contacts, visit registry and TPT cards
  - Tests: X-ray, TST
  - Financial resources for patients to access to care

Oxlade.Lancet Public Health. 2021

Examples of solutions identified & implemented

Patient centred solutions

- Home visits
- Payment for transport, CXR, TST
- Educational materials
- Patient incentives
- SMS reminders
- Evening Clinics
- Community meetings
- Group education
- Treatment supervision

HCW solutions

- WhatsApp group for doctors to read CXRs
- Training on LTBI management
- Incentives
- Registry
- In service training
- Job aids (Flip charts, posters)

System solutions

- Re-structuring contact management to the LTBI management program
- Develop home visit book and LTBI card
- Develop Guidelines for LTBI prescribing

Oxlade.Lancet Public Health. 2021

"solutions" available at:

https://www.mcgill.ca/tb/projects/act4-training-materials

A health system intervention for TPT management
ACT4

Results

- A three-phased approach of programme evaluation, local decision making, and strengthening improved TPT initiation rates in health facilities in four LMICs, at relatively low cost
- Improvements were greatest, and cost per contact initiating TPT lowest, in LMICs where household contacts of all ages were identified, tested, and provided with TPT
- Repeat cascade analysis was essential to identify new barriers & identify solutions

Oxlade.Lancet Public Health. 2021

Cumulative proportion completing each step along TPT cascade of care (Vietnam)

	Estimated	Identified	Started screening	Completed Scr.	Med eva	Complet med eva	Indicated Tx	Started Tx
Baseline	100%	5.0%	1.6%	1.3%		0.8%		0.6%
Intervention	100%	100%	92%	76%	52%	52%	39%	38%

Hannah. J Clin Tuberc Other Mycobact Dis. 2020

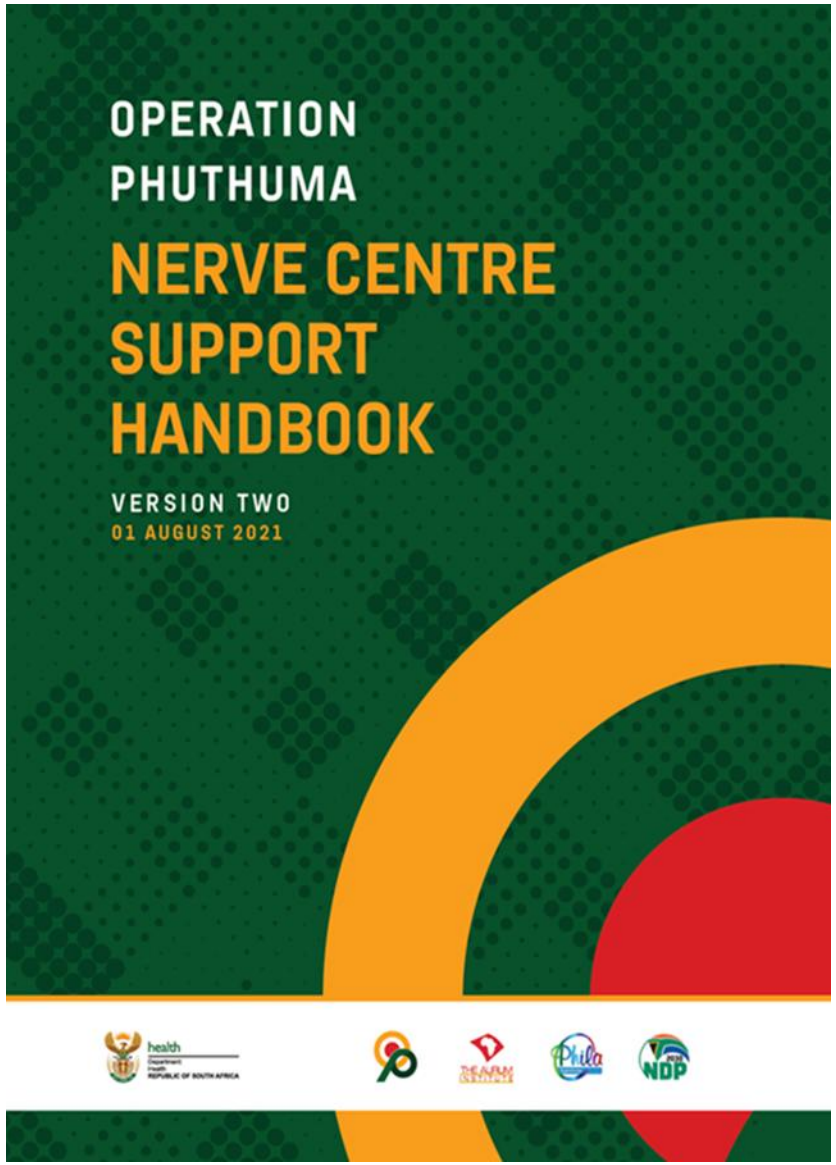
A health system intervention for TPT management
ACT4

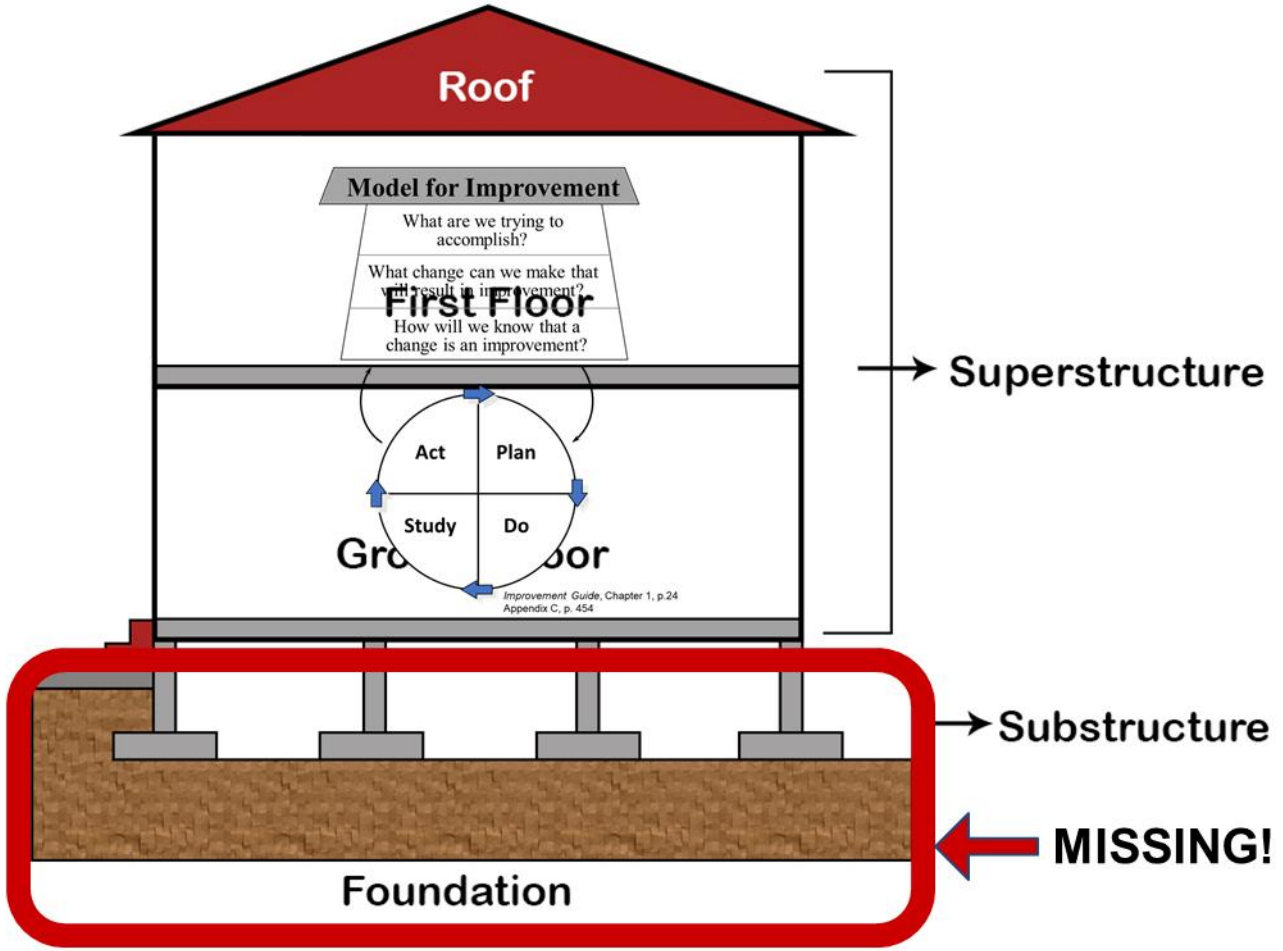
Implications

- The approach provides a framework for TBI programme scale-up that capitalises on local data, and involves key stake holders and feasible low-cost solutions
- Rather than a one-size-fits-all approach, understanding and resolving local barriers with ongoing support and training is needed for TBI programmes to expand successfully.
- Major funding is required to strengthen TBI programmes globally

Oxlade.Lancet Public Health. 2021

Improvement Approach developed for SA National Department of Health HIV/STI Programme



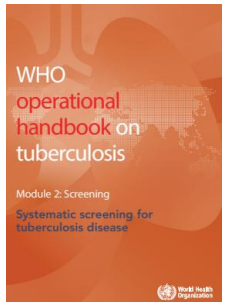


What is missing is the approach that address the foundations of how work is done

Patient choice & completion of 3HP in Uganda

- Patient choice improves self-efficacy and intention to complete TPT in a routine HIV program setting in Uganda[1]
- 3HP widely accepted by PLHIV in Uganda [2]
- Associated with very high levels of treatment completion (92.9%) under programmatic conditions [2]
- Results suggest that 3HP can enable effective scale-up of TPT in high-burden countries, particularly when delivery strategies (DOT, SAT, patient choice) are tailored to target known barriers to treatment completion [2]

1. Lim, PLOS ONE, 2021; 2. Semitala, PLOS Medicine, 2021)



W4SS in PWLH

Population	Sensitivity (%)	Specificity (%)
All people living with HIV	83	38
Inpatients	96	11
Outpatients on ART	53	70
Outpatients not on ART	84	37
≤ 200 CD4 cells/μL[a]	86	30
Pregnant women living with HIV	61	58

Targeted Universal Testing

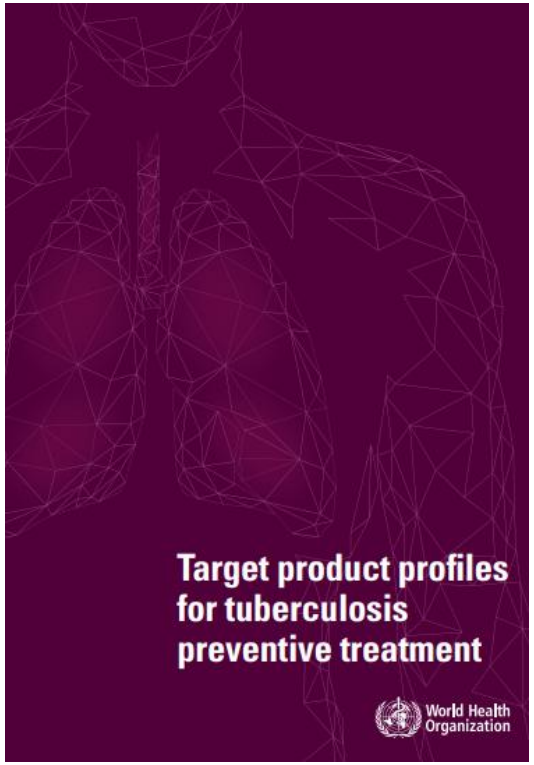
- Cluster randomized trial: routine testing of all high TB-risk individuals: HIV positive, Previous TB, TB contacts

Yield by risk factor	HIV+ n=21734	TB Contact n= 12492	Prior TB n=1573	Overall Yield n=30513	Overall Yield Excluding Prior TB N=28402	Overall yield in patients without symptoms N=21829
Positive Xpert Ultra (including trace)	6.9%	9.3%	15.7%	**7.8%**	7.3%	6.2%
Positive Xpert Ultra (excluding trace)	4.2%	6.7%	11.1%	**5.2%**	4.9%	3.7%

- TUTT demonstrated **17% increase in yield in TUTT** compared to SOC clinic

Lebina, CROI 2021

TPT Target Regimen profiles



WHO Target Product Profiles for TPT (2020)

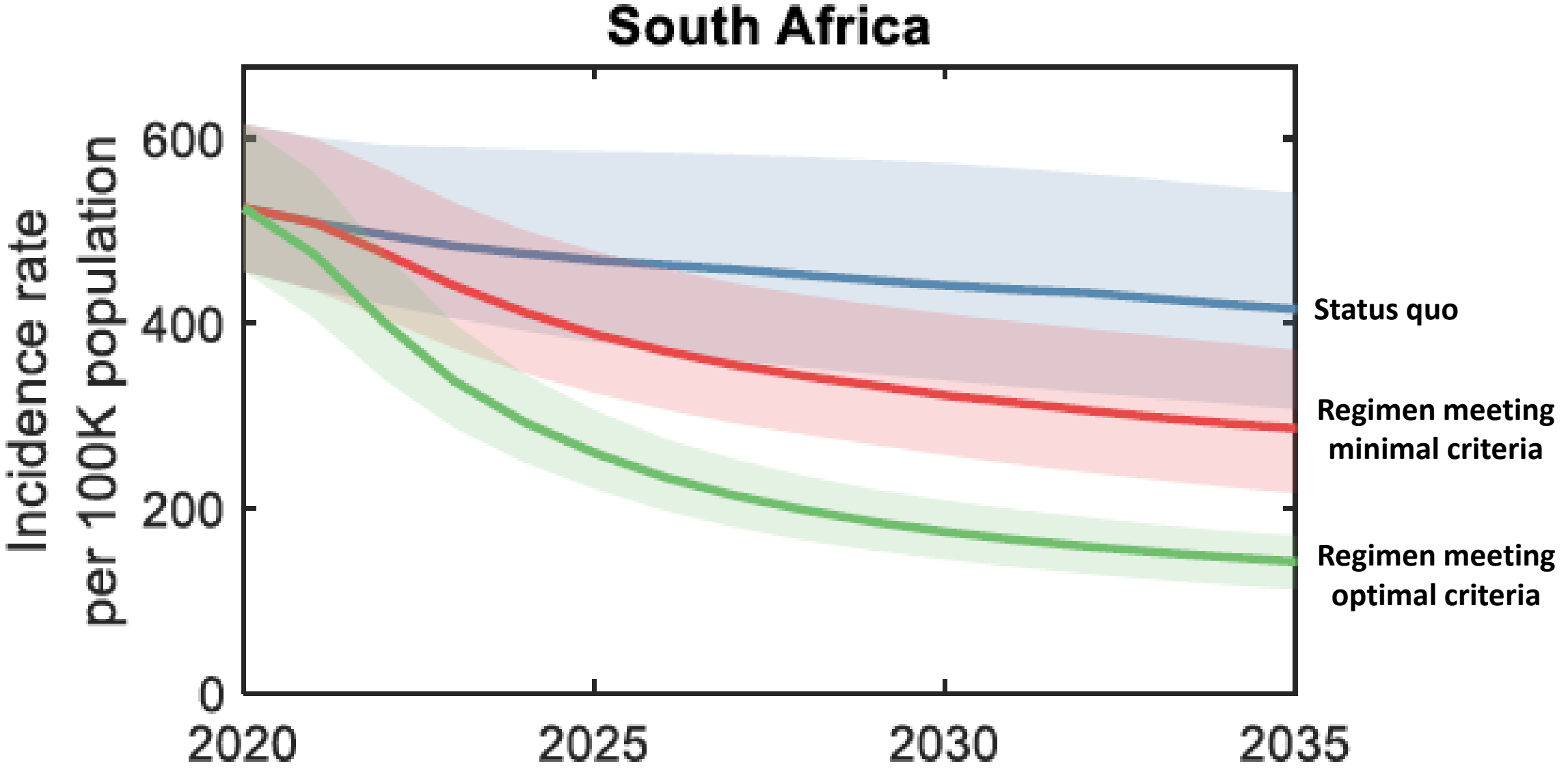
Priority attributes

- Regimen duration
- Efficacy
- Ease-of-adherence under programmatic conditions
- Forgiveness to non-completion
- Barrier to developing rifampicin resistance during treatment

Attribute characteristics

- *Minimum requirements* provides targets that improve on the current standard of care, and which represent an acceptable minimum for global health impact when developing candidate regimens
- *Optimal requirements* specify performance and use characteristics of an 'ideal' product for which the global health impact would be broader, deeper, and quicker

Modelled impact of future TPT regimens

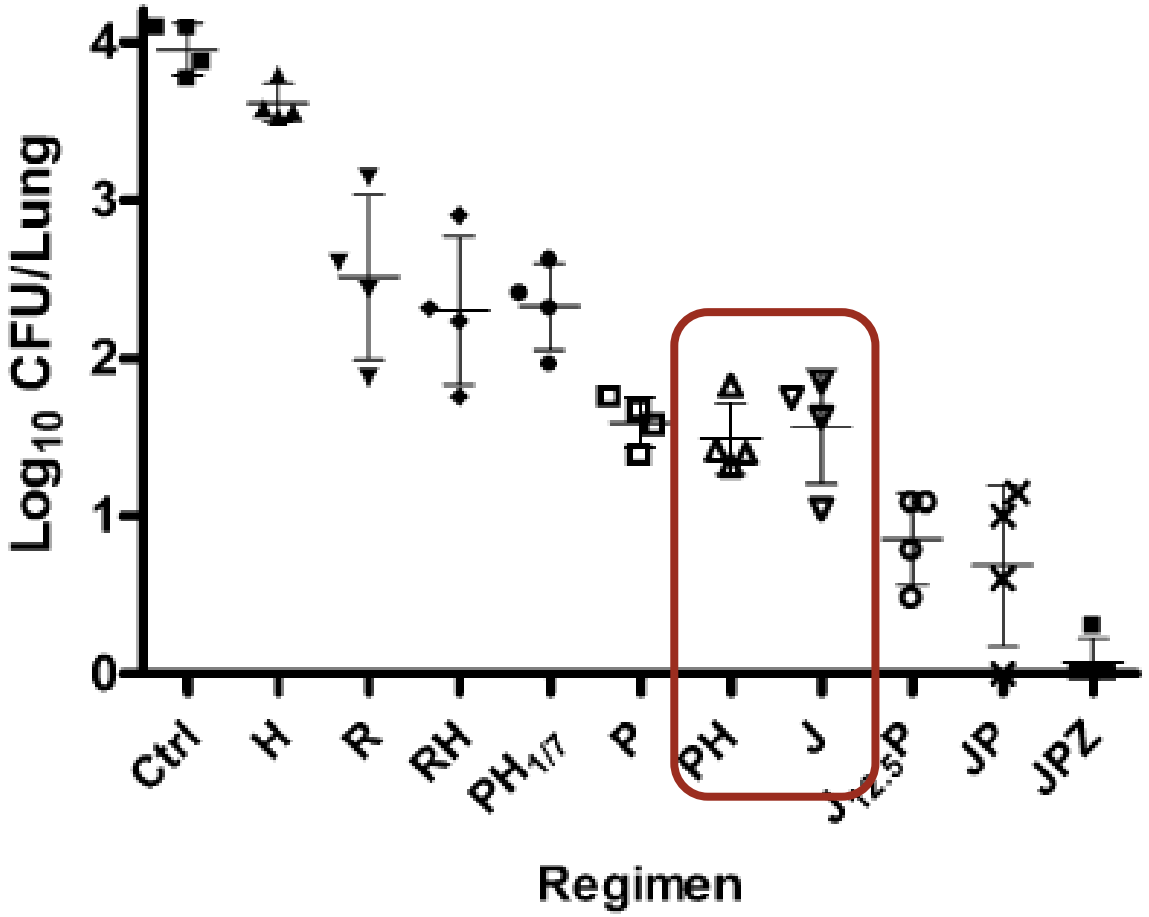


(Vesga. PLOS Medicine. 2021, In press)

Pan TPT regimens

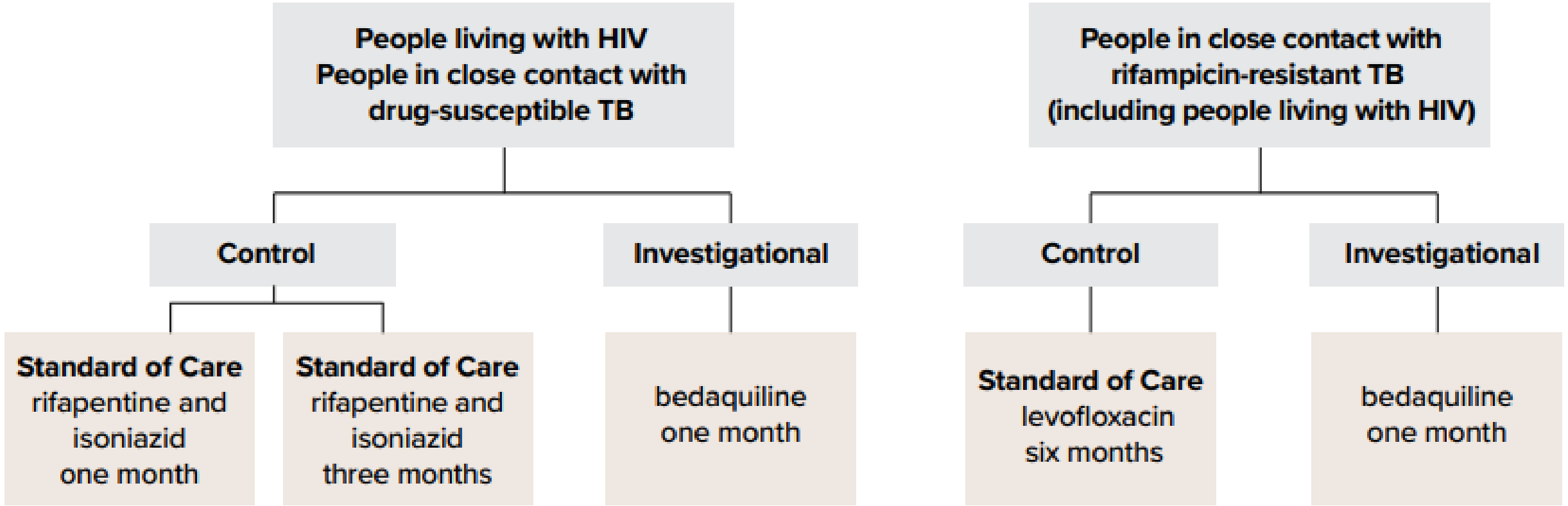
One-month oral bedaquline (BDQ) TPT

Potential shorter TPT regimens in the murine model Lung CFUs after 4 weeks of treatment



Zhang et al., Am J Respir Crit Care Med,184:732–737, 2011

One-month oral BDQ TPT for PLWH & close contacts: *Breach TB*



(NCT03568383)

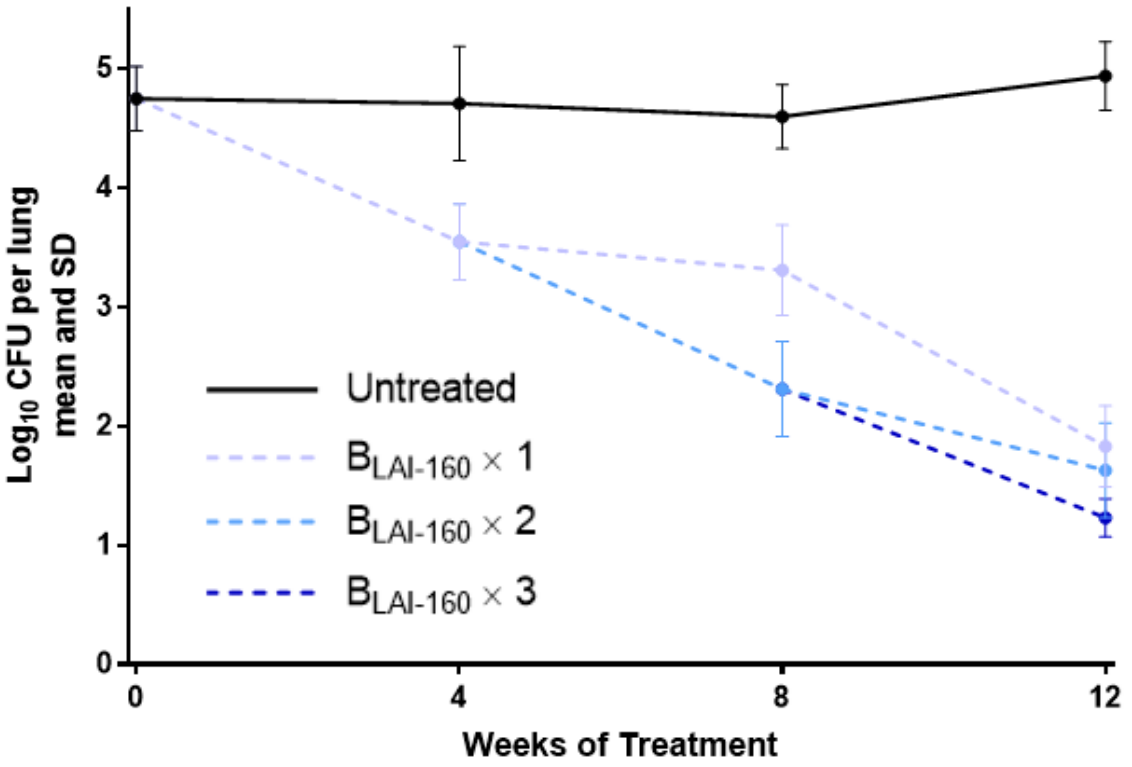
Long acting injectable TPT regimens

Long acting injectable TPT

- Certain drugs have physicochemical properties that enable the development of long-acting formulations that may allow less frequent dosing, thereby improving patient convenience, adherence, and treatment completion rates
- Long-acting formulations would simplify TPT regimens and reduce the burden on health programs

Bedaquiline (BDQ) long acting injectable TPT

- Diarylquinolines have physicochemical properties that allow them to be formulated as long-acting injectables
- BDQ is a potent sterilizing drug
- LAI formulation of bedaquiline has demonstrated activity for up to 12 weeks in a validated mouse model
- Phase I trial of a single dose LAI BDQ ongoing



(Kaushik. *Antimicrob Agents Chemother* 2019; pii: AAC.00007-19).

Next-generation Diarylquinolines (DARQ) LAI TPT

- TBAJ-876 is a next-generation DARQ with greater potency and lower potential to prolong the QTc interval than BDQ
- Long-acting injectable formulations for TBAJ-876 demonstrated encouraging exposure profiles and efficacy in a mouse model of TB preventive therapy
- These data provide proof-of-concept for a highly efficacious pan-TPT regimen comprised of a single IM dose of a TBAJ-876 LAI formulation

(Hobson, CROI 2024, 881)

Evolution of TPT regimens

Drug susceptible, dru resistant, & Pan TB regimens

New formulations: Dispersible, singles, FDCs, LAIs

Price RPT massively reduced

People living with HIV

Household contacts

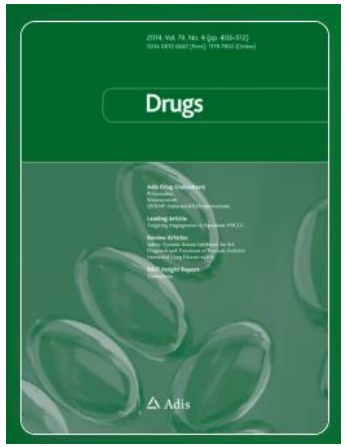
Other people at risk

Conclusion

- Managing the global burden of TB infection is essential to meeting the End TB targets
- Although global TPT uptake is increasing, gaps remain particularly among children<5 years
- Rifapentine based short-course TPT regimens are associated with better adherence & safety, & may be given with DTG based ART

Conclusion

- The price of rifapentine has been substantially reduced & new formulations are available that reduce pill burden of 3HP & 1HP
- A single round of short-course treatment is effective in high TB burden countries
- Six-months of Levofloxacin MDR TPT is now recommended
- Strengthening the TPT cascade of care improves programmatic outcomes
- Pan TPT & LAI formulations are in development



Resource

Tuberculosis Preventive Treatment in High TB-Burden Settings: A State-of-the-Art Review

Therapy in Practice | Open access | Published: 28 December 2024

Volume 85, pages 127–147, (2025) Cite this article

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