



Considerations for an Evolving TB Prevention Toolkit

2026

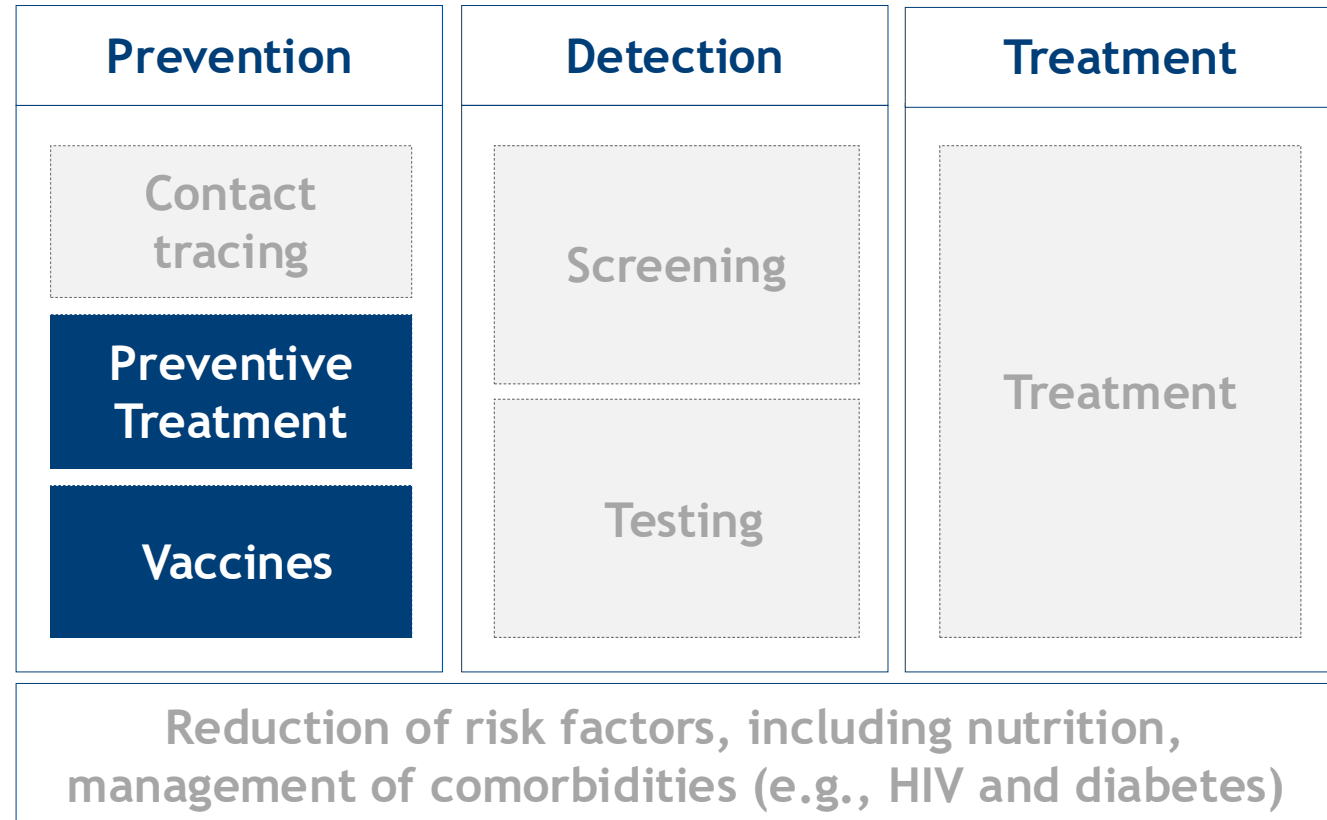
Contents

- **Context**
- TB prevention tools & their characteristics
- Considerations for TB prevention portfolio

Overview

- **Current pharmaceutical prevention options** for TB disease have limited use cases
 - **BCG vaccine:** efficacy wanes after age five
 - **Oral TB preventive treatment (TPT):** only indicated for several high-risk groups and close contacts of TB patients, and does not protect against future TB exposure
 - A promising **pipeline of new options** is expected over the next decade
 - **Long-acting injectables:** single-dose formulation for extended protection
 - **Ultra-short-course TPT:** shorter, more tolerable oral regimens
 - **Novel TB vaccines:** targeted at adolescents and adults after BCG wanes
 - As these pharmaceutical prevention options get licensed and come to market, countries will need to decide how to **deploy them within their TB prevention portfolios.**
 - These materials present an **overview of existing and pipeline TB prevention products**, grounded in WHO guidelines and target product profiles.
 - The aim is to build **shared understanding of the evolving TB prevention landscape** and help stakeholders consider how these tools may **fit within future TB prevention portfolios.**
-  **This work is not meant to provide recommendations or guidelines on the use cases for TB prevention tools**

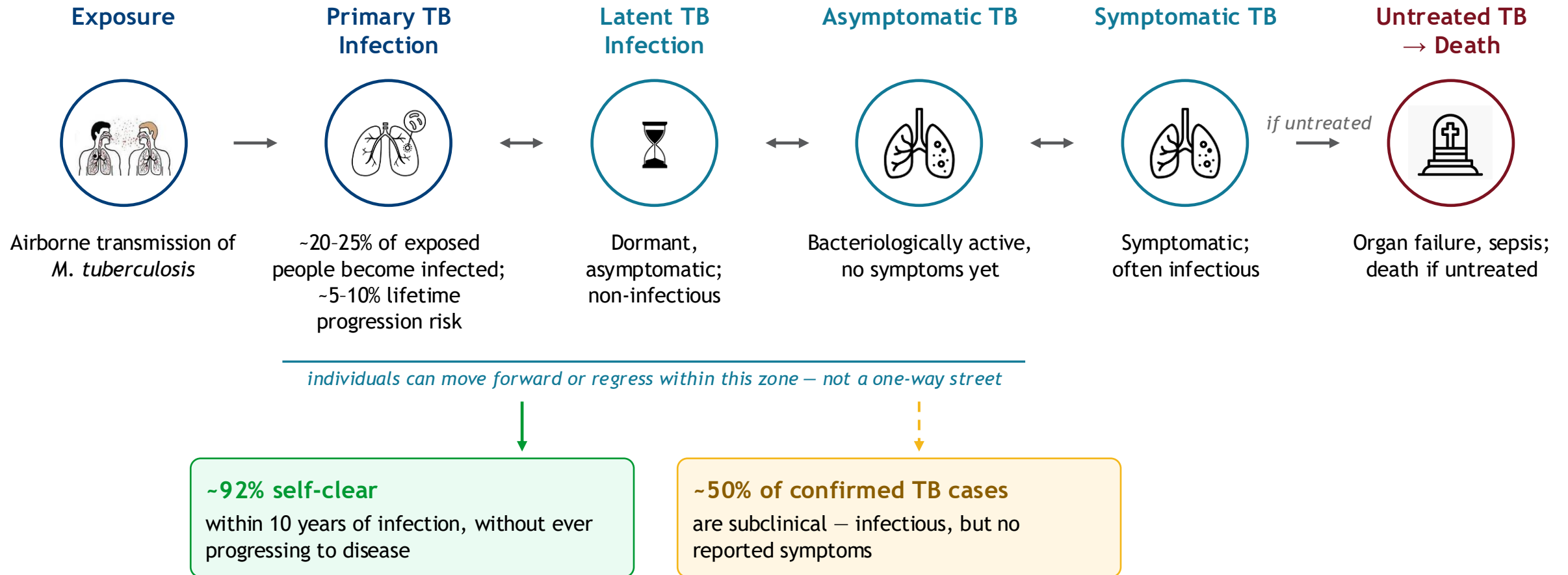
This document
focuses on
pharmaceutical
TB prevention
products



 In-scope

Current and pipeline TB preventive treatment and vaccines aim to prevent progression from TB infection to active TB disease

TB progression is a dynamic, non-linear spectrum — not a fixed sequence of stages



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The TB prevention toolkit is expanding, with several promising innovations in the pipeline



Existing products

BCG vaccine

Vaccine given to infants at birth. Vaccine prevents severe TB in children, but protection declines with age

Existing oral TPT

Long & short course regimens for preventing TB disease in high-risk groups (HRGs); adherence issues for long courses & no protection from future exposure

Pipeline products

Long-acting injectables

Single-dose injectable TPT aiming to improve adherence & extend duration of protection in high-risk groups

Pipeline oral TPT

Shorter-course regimens for prevention of drug-susceptible and drug-resistant TB in HRGs, incl. fluoroquinolone-resistant TB; aim to reduce treatment burden and improve adherence

Novel TB vaccines¹

Vaccine targeting adolescents & adults; leading pipeline candidates are for prevention of disease

1. Focus is on novel TB vaccines targeting adolescents and adults, while acknowledging ongoing infant vaccine trials e.g., MTBVAC infant vaccine candidate in Phase 3 trial

Existing Oral TPT | Currently, WHO recommends 7 TPT regimens to prevent TB disease in high-risk groups



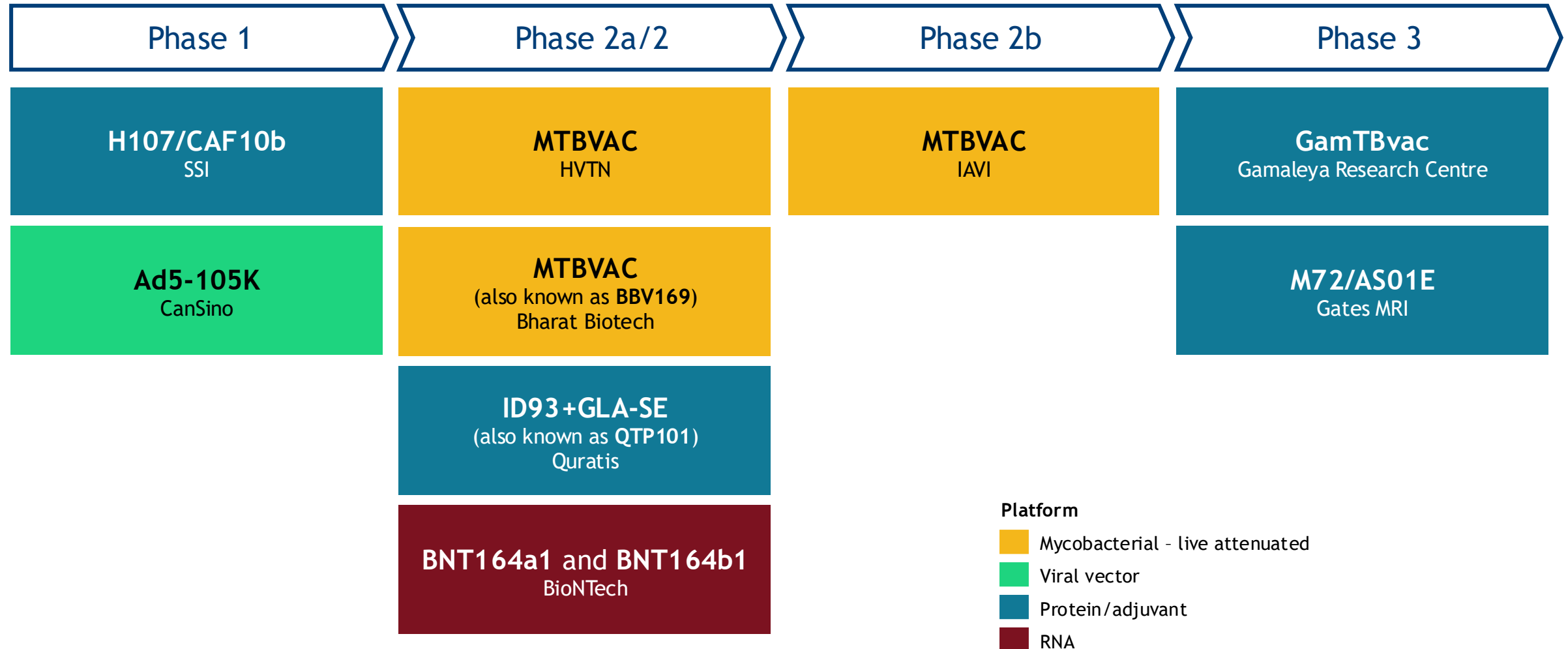
Characteristic	6H/ 9H	3HP	3HR	4R	1HP	6Lfx
Drug(s)	Isoniazid (H)	Isoniazid (H) + Rifapentine (P)	Isoniazid (H) + Rifampicin (R)	Rifampicin (R)	Isoniazid (H) + Rifapentine (P)	Levofloxacin (Lfx)
Treatment duration	6 or 9 months	3 months	3 months	4 months	1 month	6 months
Frequency	Daily	Weekly	Daily	Daily	Daily	Daily
Notes on usage	Cheap and widely available but adherence is challenging. Historically, the mainstay of TPT programs; gradually being replaced by 3HP	Being prioritized by countries recently, with increasing adoption in LMICs	Common in pediatric TB prevention and for some adults	Used in some settings where isoniazid resistance risk is high	Newer regimen; promising for adherence, but limited rollout in LMICs so far due to higher cost than other TPT options and lack of fixed dose combination	Targeted for contacts of people with multidrug resistant or rifampicin-resistant TB

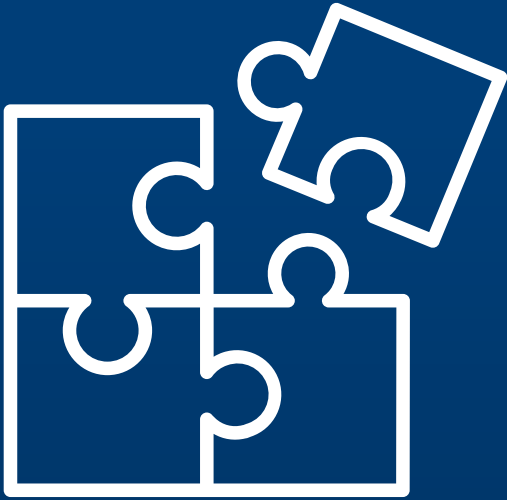
Pipeline Injectable/Oral TPT | Several new TPT innovations including oral and injectable products are in active clinical development



Characteristic	Long-acting injectables	Pipeline oral TPT					
	BDQ LAI <i>Bedaquiline-based</i> ¹	2R20 <i>Rifampicin-based</i> ²	1LP <i>Levofloxacin & rifapentine-based</i> ²	1BDQ <i>Bedaquiline-based</i> ³	6wP <i>Rifapentine-based</i> ⁴	1H ₃ P ₃ <i>Isoniazid & rifapentine-based</i> ⁵	DLM <i>Delamanid-based</i> ⁶
Dosing Schedule	One-off injection	Daily pills	Daily pills	Daily pills	Daily pills	Thrice weekly pills	Daily pills
Treatment duration	Single encounter	2 months	1 month	1 month	6 weeks	1 month	6 months
Duration of protection	TBD	Duration of treatment	Duration of treatment	Duration of treatment	Duration of treatment	Duration of treatment	Duration of treatment
Trial status	Phase I completed; moving to phase III	Phase II/III	Phase II/III	Phase II/III	Phase III	Phase III	Phase III
Reference for safety & efficacy	Non-inferior to existing oral TPT (3HP)	Non-inferior to existing oral TPT (4R)	Non-inferior to existing oral TPT (4R)	Non-inferior to existing oral TPT (6Lfx or 3HP)	Non-inferior to existing oral TPT (3HP, 4R, or 3HR)	Non-inferior to existing oral TPT (3HR)	Non-inferior to existing oral TPT for DS/DR-TB exposure (6H)

Novel TB Vaccines | Several TB vaccine candidates targeting adolescents and adults are currently in active clinical trials





These pipeline **TB prevention tools will coexist in the future**, creating a need to consider their positioning within comprehensive TB prevention portfolios.

When considering portfolio mix for TB prevention, several factors are expected to drive country use-cases and scale of adoption



1



Target population

Which population groups could potentially benefit from this product?

2



Market entry timeline

When is the product likely to become available assuming clinical trials and regulatory outcomes are positive?

3



Clinical performance

Does the product deliver meaningful protection and for how long?

4



Public health impact

Can this product meaningfully expand health impact?

Details on following pages based on publicly available/ early research



Acceptability

Will the product be readily adopted by the target population?



Cost-effectiveness & affordability

Is the product cost-effective compared to existing options and can the government sustainably afford it over the long-term?



Supply adequacy

Can supply meet national demand reliably?



Ease of delivery

Can the product be implemented within the existing health system?

Yet to be determined for the pipeline products

1 Target Population | Per WHO guidelines & TPPs, TPT is indicated for HRGs and vaccines could protect both HRGs & the broader population



Existing products
 Pipeline products
 Optimal target population per WHO Guideline, TPP/ TRP
(In the case of pipeline products, the optimal target populations reflect the intended use case; not all population groups are necessarily represented in current clinical trials)
 Not indicated

		BCG vaccine	Existing oral TPT	Long-acting injectables	Pipeline oral TPT	Novel TB vaccines
TB high-risk groups	PLHIV on ART	0-4				
		5-14				
		15+				
	Household contacts (HHC)	0-4				
		5-14				
		15+				
Unknown TB risk	Pregnant/lactating women (HHCs)					
	Other high-risk groups ¹					
	General population ²	0-4				
		5-14				
		15+				

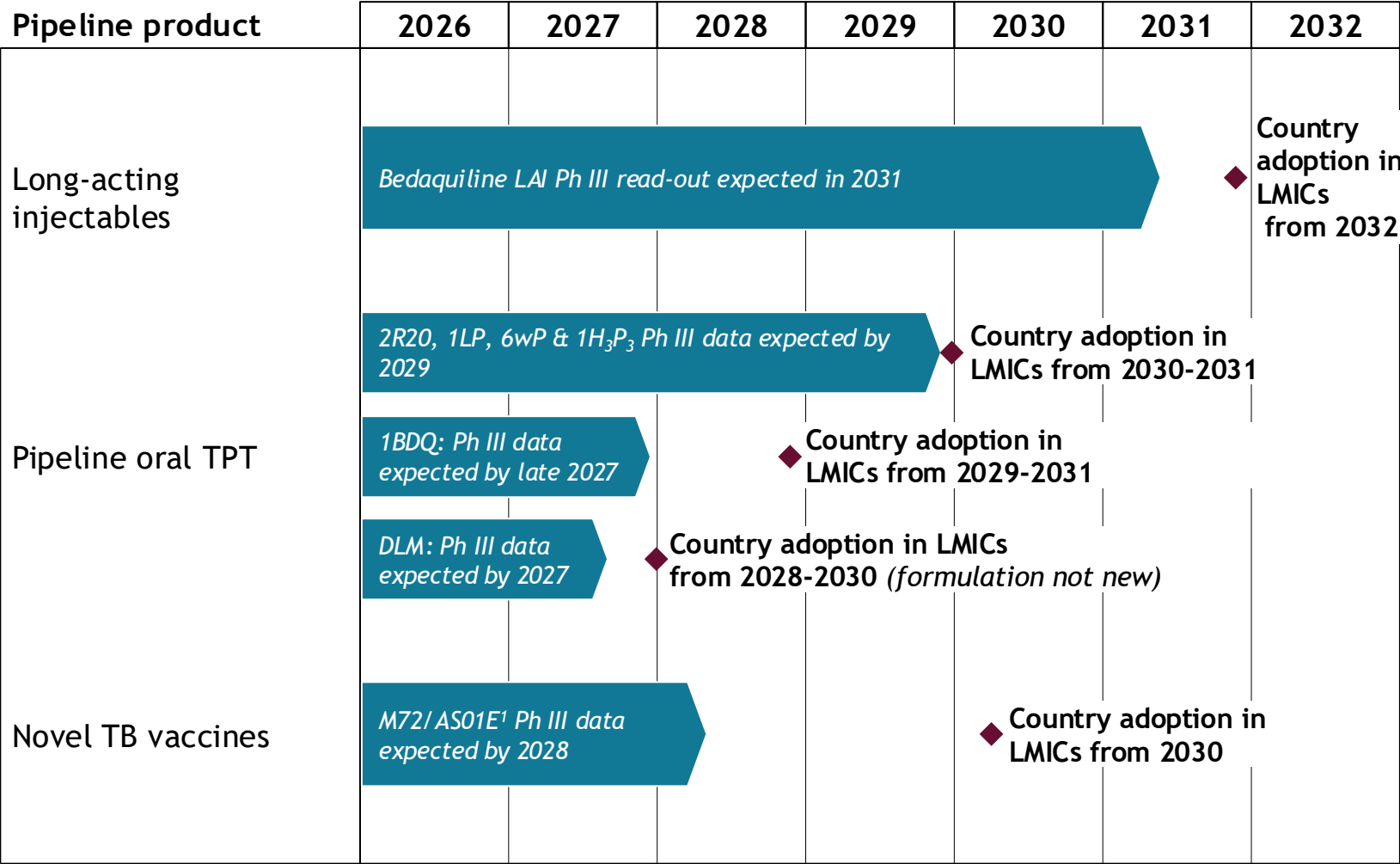
Note: Figure above illustrative, row heights do not suggest relative pop. sizes

1. Other occupational & biological TB high-risk groups - prisoners, miners, malnourished, people who smoke, people w/ alcohol & drug use disorders, other immunocompromised/ suppressed people, people w/ diabetes, homeless; 2. Includes PLHIV who may not have been tested or tested but not on ART

Sources: [WHO position paper on BCG vx 2018](#), [WHO guidelines on oral TPT 2020](#), [TRP for rifampicin 2016](#), [Target Product Profile \(TPP\) for ultra short course TPT 2022](#), [TPP for LAI 2022](#), [WHO preferred product characteristics for novel TB vaccines](#)

Market Entry Timeline | Pipeline regimens expected to be adopted in LMICs from 2028

Timelines are uncertain and will depend on the clinical trial, regulatory, policy recommendation outcomes



1. Vaccine candidate assumed to first reach licensure
Sources: [Medicines & Patent Pool LAPaL 2026](#), [SSTARLET Trial 2026](#), [Breach-TB 2025](#), [ASTERoid 2026](#), [TB-YOUTH](#), [PHOENIX MDR-TB 2025](#); [Gates MRI 2026](#)

③ Clinical Performance | Pipeline products aim to address limitations of existing prevention tools, to improve adherence and effectiveness



Existing products Pipeline products

	Based on real-world evidence		Expectation based on target product profiles or trial design		
	BCG vaccines	Existing oral TPT	Long-acting injectables	Pipeline oral TPT	Novel TB vaccines
Dosing Schedule	Single dose at birth or soon after	Daily or weekly pills	1 injection	Daily or thrice weekly pills	≤3 doses. No booster before 10 years
Vaccination/treatment duration	One-off	1-9 months depending on regimen	Several months expected but exact duration of protection is yet to be determined	≤2 months (<i>could be as short as 1-2 weeks</i>)	Based on number of doses
Duration of protection	Waning effectiveness from 5 years	Treatment duration ¹	Up to 6 months	Treatment duration; potential for follow-on course if reinfected	10+ years
(Target) Efficacy	60-80% against severe childhood TB	60-80% depending on regimen	Non-inferior to existing oral TPT (3HP)	Non-inferior to existing oral TPT (3HP, 3HR, 4R, 6Lfx)	At least 50%

1. TPT treats existing TB infection but does not provide ongoing protection; reinfection may require repeat TPT (e.g., every two years for PLHIV).

Sources: [WHO TB Knowledge '99](#); [Stop TB TPT](#); [WHO TPP for TPT '23](#); [WHO Preferred Product Characteristics for New TB Vaccines '18](#); [WHO Target Regimen Profile for TPT LAI '26](#);

④ Public Health Impact | Early modeling suggests pipeline tools will have significant impact when implemented within an integrated portfolio



Modeling work to date is limited, but three disparate studies provide context for some pipeline interventions:

Short-course oral TPT (modelled based on 3HP)

In 29 countries¹ for PLHIV:

21% reduction

Incidence of TB

22% reduction

Mortality from TB

Cumulative totals for 2023-2050

Delamanid-based TPT

In India for MDR/ RR-TB:

72% reduction

Incidence of MDR/ RR-TB over 2 yrs

51% reduction

Incidence of MDR/ RR-TB over 16 yrs

Cumulative totals for 2023-2040

Novel TB vaccine

Globally for a 50% efficacious vaccine:

37M - 76M

TB cases averted

4.6M - 8.5M

TB deaths averted

Cumulative totals for 2025-2050

Preliminary insights from ongoing modeling work suggest **integrated implementation of TPT, TB case finding, screening, diagnosis & treatment and TB vaccination** results in **significant reduction in TB incidence & mortality**

1. Study countries include Burundi, Bangladesh, Brazil, DR Congo, Ethiopia, Ghana, Haiti, Indonesia, India, Kenya, Cambodia, Liberia, Lesotho, Mongolia, Mozambique, Malawi, Namibia, Pakistan, Rwanda, Somalia, Eswatini, Thailand, Tajikistan, Timor-Leste, Tanzania, Uganda, South Africa, Zambia, Zimbabwe
Sources: [WHO Short-Course TPT for PLHIV 2023](#), [NIAID MDR/RR-TB Estimates 2024](#), [WHO TB Vx 2022](#); WHO TB Team Modelling

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Per WHO TPPs, Pipeline products will create new TB prevention access for some populations & expand/ improve prevention options for others



		Current TB prevention option		Potential future TB prevention option(s) ¹
First access	 Adolescents/adults (≥15 years) in general population	None available		Novel TB vaccine
Expanded TB prevention options	 Adolescents/adults in TB high-risk groups incl. pregnant and lactating women	Existing oral TPT		Existing oral TPT Ultra-short-course TPT Long-acting injectables Delamanid-based TPT Novel TB vaccine
	 Children under-5 in TB high-risk groups	Existing oral TPT		Existing oral TPT Ultra-short-course TPT Long-acting injectables Delamanid-based TPT
	 Children under-5 in the general population	BCG vaccine		BCG vaccine
No change	 Older children aged 5-14 years in the general population	None available		None available

1. Potential target population based on WHO target product/regimen profiles

Several questions remain on new prevention access for previously unprotected populations, especially around the breadth of indications



Emerging evidence

Open questions (select)



**Adolescents & adults
(≥15 years) in general
population**

- Modeling suggests **large-scale adolescent/adult TB vaccination** would be **impactful and cost-effective** in LMICs.¹
- Phase 3 clinical trial for leading TB vaccine candidate will **generate efficacy data for IGRA-positive**, but not IGRA-negative populations (only safety and immunogenicity).²

- Will TB vaccines be **licensed and recommended** for use in **IGRA-negative** populations?
- How should post-implementation studies be set up to generate **evidence of TB vaccine effectiveness** in **IGRA-negative** populations?

As TB prevention options expand, the optimal mix of tools to effectively protect target groups is still to be determined



Emerging evidence

Open questions (select)



Adolescents/adults who are TB high-risk groups

- High-risk groups including household contacts are **eligible for existing & pipeline TPT regimens**.
- In LMIC contexts, household contacts are hard to reach due to contact-tracing, latent TB infection testing (*recommended*), and follow-up to monitor adherence, as these are challenging and resource-intensive. So, they **could benefit from TB vaccination** in addition to TPT.
- Ongoing phase 3 clinical trial for leading TB vaccine candidate will **generate safety data for PLHIV, but not efficacy data**.¹

- **How effective are current TPT delivery approaches** in reaching challenging high-risk groups such as **household contacts**, and where do the gaps remain?
- For household contacts, could **TPT** continue to offer protection during recent/ongoing **TB exposure** (post-exposure prophylaxis), in addition to **vaccination for longer-term protection**?
- Will non-live attenuated TB **vaccines be recommended for immunocompromised persons** (e.g., PLHIV)?



Pregnant and lactating women who are TB high-risk groups

- Reachable through existing maternal & child health & contact tracing efforts. **TPT will remain an important preventive option for this group**.
- **Pregnant and lactating women are excluded** from leading TB vaccine trials, so unlikely to receive recommendation for vaccination in the early years.^{1,2}

- **Longer-term**, if TB vaccine trials generate evidence supporting use during pregnancy/lactation, **could non-live attenuated vaccines offer an alternative prevention option** for this group, avoiding toxicity associated with some TPT regimens?



Children under-5 in the general population

- **Infant BCG vaccination is well-established** via EPI programs with high coverage of 88% globally.³
- This group will **continue to benefit from BCG vaccination** and potentially a new infant vaccine.

- Are there opportunities to **improve BCG coverage** rates in sub-national geographies lagging in coverage?
- How can novel TB vaccines, be rolled-out and communicated to the public in a manner that **does not undermine the gains from BCG vaccination**?

With no TB prevention option for children aged 5-14 in the general population, need for innovations targeting this group to be determined



Emerging evidence



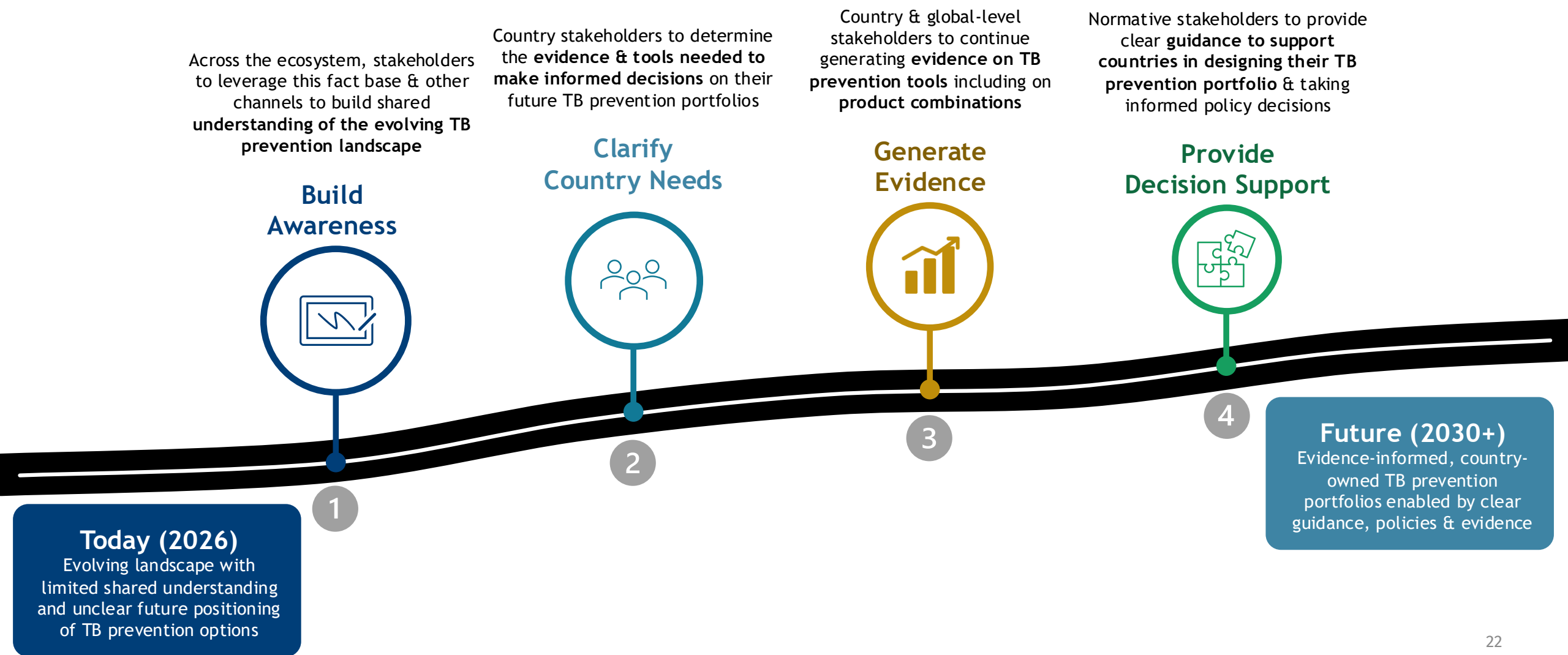
Older children aged 5-14 years in the general population

- Older children aged 5-14 years in the **general population** are **ineligible for all current and pipeline TB prevention options**, with only residual (if any) protection from BCG vaccination.

Open questions (select)

- To what extent do older children **contribute to the TB burden**, and could there be a need for next-generation TB prevention tools targeting this group?

As the landscape evolves, 4 ecosystem-wide actions are required to enable countries to build effective TB prevention portfolios





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