How tuberculosis modelling and health economics is used in National TB Strategic Planning

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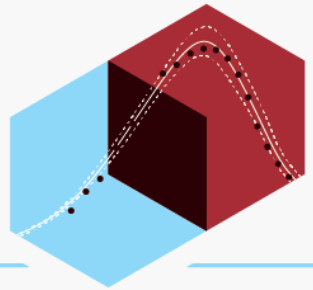

Linganisa

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Background: TB funding in South Africa

TB funding:

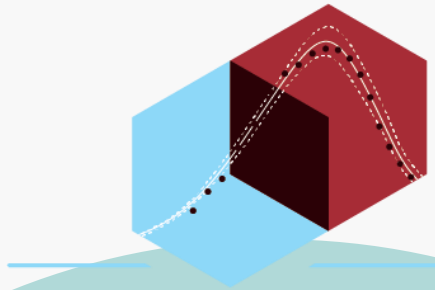
- mostly through provinces' general health budget ("equitable share", ES)
- HIV, TB, Malaria and Community Services Conditional Grant: MDR-TB hospitals, BDQ, Xpert tests
- complicates budget planning and expenditure tracking

Luckily, we know a lot more about TB expenditure right now then we ever did!

- NASA+: In 2019/20,
  - TB expenditure from all (most) sources was 4.4B ZAR
  - 66% of this was publicly funded (48% from general health budget, ES)
  - 60% was spent on treatment (of which 66% DR-TB), 18% on screening, 3% on prevention
  - 37% of all TB expenditure on staff, 23% on medical products and supplies

https://sanac.org.za/reports/sa-nasa/

Project Linganisa



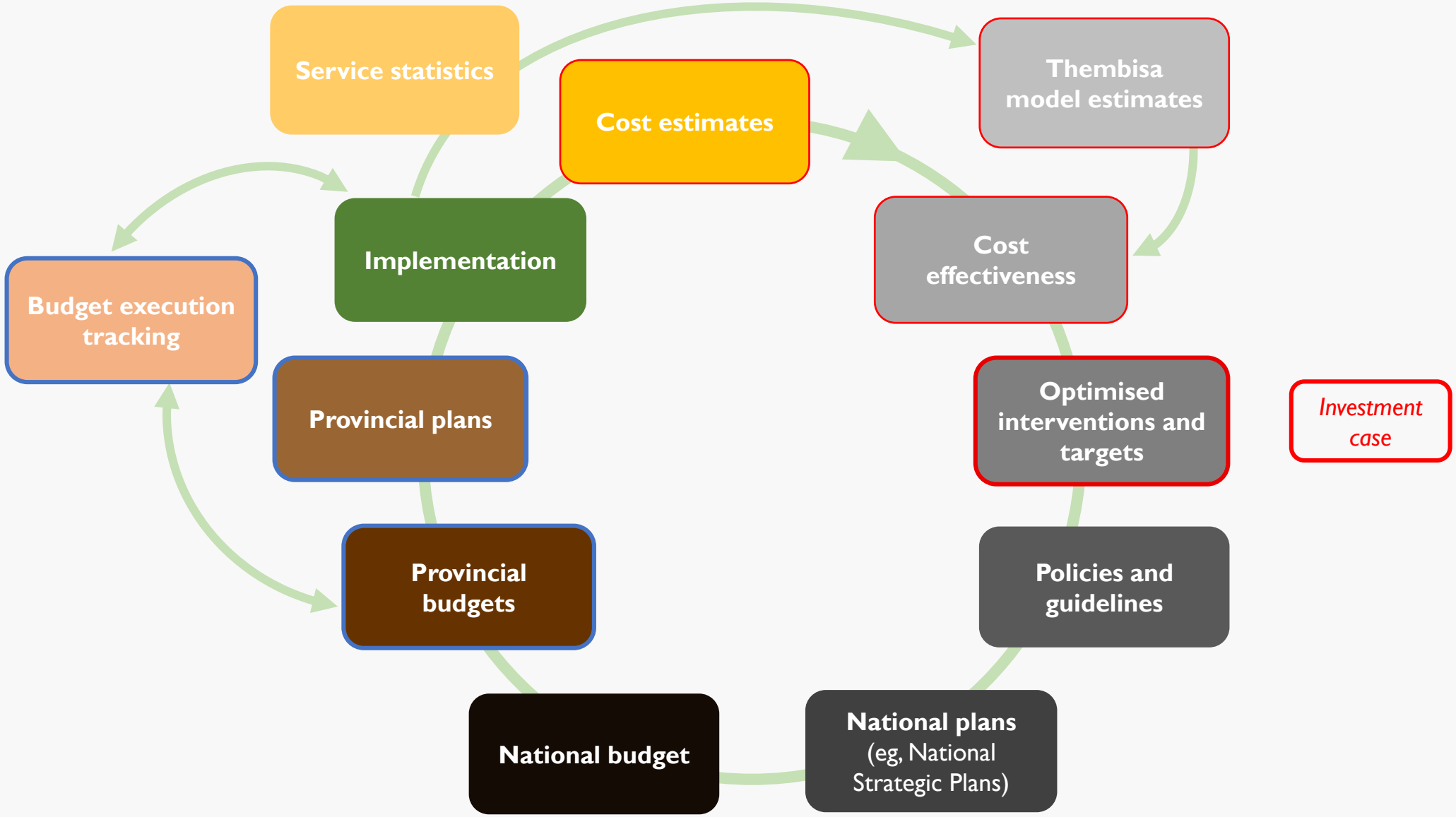
Linganisa

- BMGF-funded project (2020-2023)
- PI: Leigh Johnson, UCT
- Epi estimates, economic analyses and budgets for HIV and TB in South Africa
- Stakeholder engagement

→ New TB interventions to focus on:

- New TB screening strategies (digital chest X-ray, TUTT)
- Active TB case finding
- IPT for individuals who were previously treated for TB

An optimal health decision making - planning - budgeting cycle

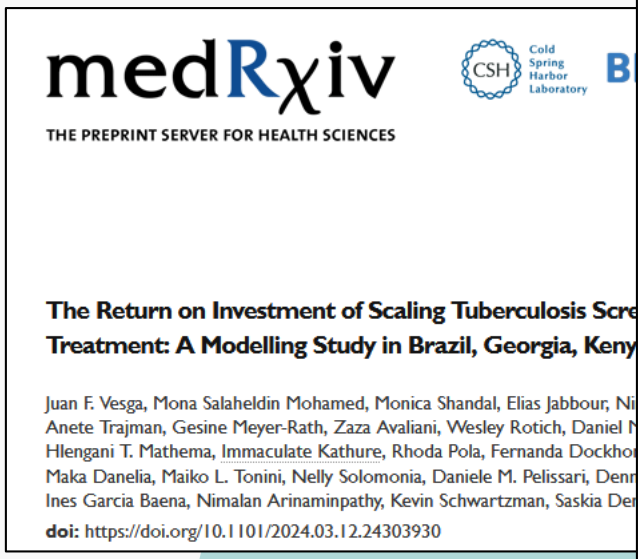


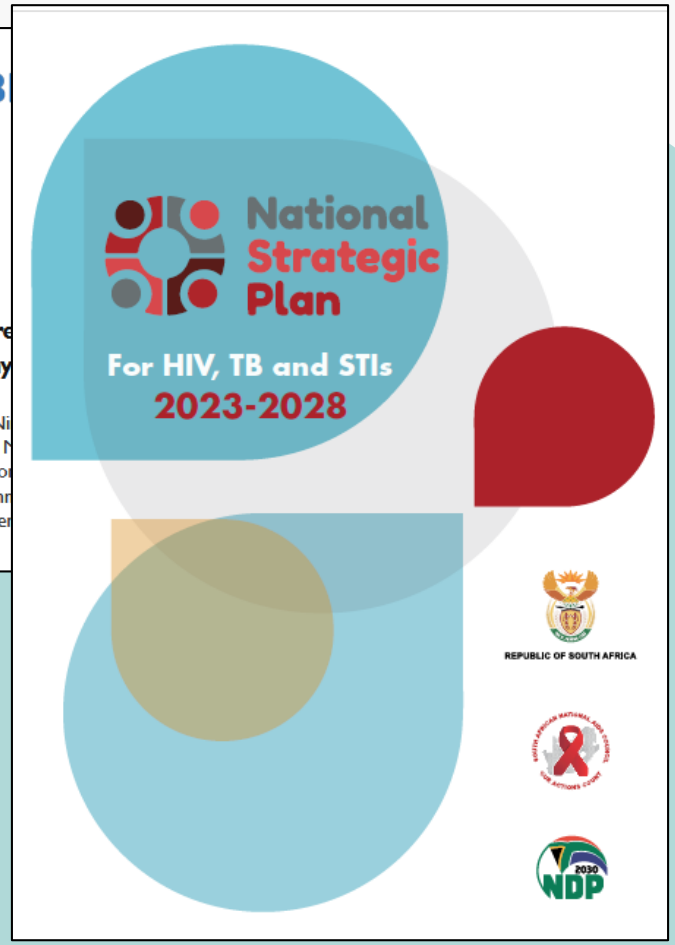
A new TB Investment Case

- **Model**: Thembisa TB
- **Average cost** of a number of existing and novel TB interventions
  - Literature review
  - Cost analysis of recently trialled interventions
- **Output**: Total cost, total budget required for NSP and NTP SP, and incremental cost effectiveness of each intervention at different coverage levels
- **Scenarios**:
  - ***NSP scenario***: Targets agreed to by NTP and NSP working groups
  - ***Max scenarios***: Trying to get to WHO TB targets by 2030 (80% reduction in incidence, 90% in mortality, over 2015 levels)
- **Outstanding: Optimisation** under a) budget envelope, b) available HCW, c) other factors

Uses of TB Investment Case

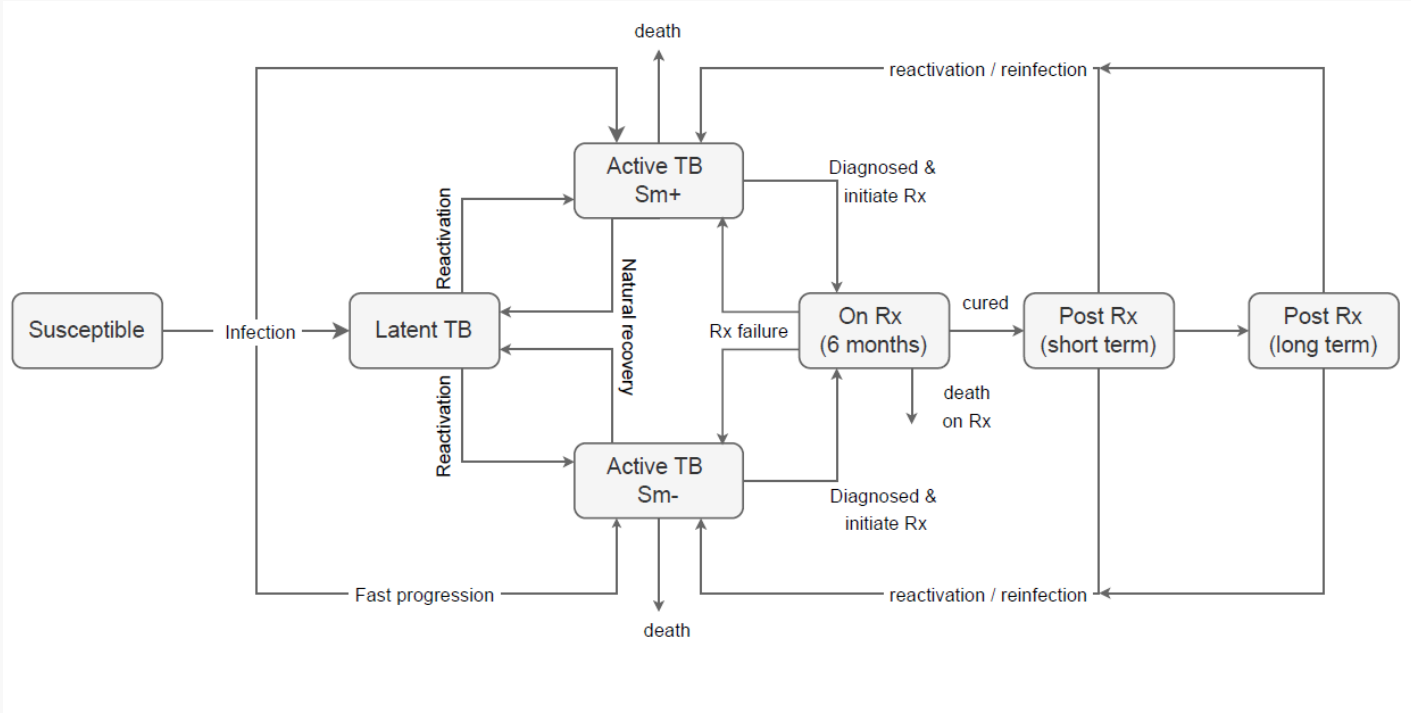
- **Cost estimates:**
  - Own publications
  - International collaborations
- **Budget estimates:**
  - **SANAC**: NSP 2023-2028
  - **NTP**: National TB Programme Strategic Plan
  - **Global Fund** proposal
- **Expenditure estimates:**
  - NTP
- **Other engagements:**
  - National TB Think
  - Rural Health Advocacy Project
  - Global Fund
  - BMGF
  - USAID
  - FIND





Thembisa TB transmission model

- Integrated a TB transmission model within the Thembisa HIV model
- The South African population simulated over time, from 1985
- Population stratified into:
  - Demographic: Age, sex,…
  - HIV-related: HIV testing history, HIV status, CD4 count levels, ART status & duration
  - TB: natural history states



Kubjane et al. IJID. 2022

Estimating TB programme cost

1. Use Thembisa TB model to generate **target populations** based on coverage levels deemed feasible by NTP-SP and NSP stakeholders
2. **Average service cost** of existing and novel TB interventions informed by the HE^{2}RO National TB cost model
3. Total cost = **average service cost** x **target population**
4. Cost are from providers' perspective
5. Costs are 2021/2022 ZAR and undiscounted

Interventions and populations

Intervention	Parameters changed	Description of populations
Isoniazid Preventive Therapy (IPT) for PLHIV	Monthly rates of TPT initiations	# of PLHIV on ART initiated on IPT
IPT / 3HP for household (HH) contacts	% of HH screened % of 3HP provided Rate of monthly TPT initiations	# of HH contacts initiated on TPT (IPT/3HP)
3HP for PLHIV	Rate of monthly TPT initiations; % of 3HP provided	# of PLHIV initiated on 3HP
Symptom screening (PLHIV)	Relative rates of health facility attendance in PLHIV (3x compared to HIV-)	*# of screenings* in PLHIV
Symptom screening (General PHC)	% of symptomatic TB patients screened microbiologically	*# of screenings at* general PHCs
Symptom screening (HH contacts)	% of HH contacts screened	# of symptom screening in HH contacts
Symptom screening (Door-to-door)	Rate of D2D screening the adult population	# of symptom screenings in everybody regardless of contact with cases; symptomatic get an Xpert test

Interventions and populations

Intervention	Parameters changed	Description of populations
Mobile digital chest radiography	Rate of D2D screening the adult population; % screened with dCXR	# of dCXR tests in asymptomatic individuals following D2D symptom screens; positive dCXR get an Xpert test
Xpert MTB/RIF Ultra	% of Xpert tests	of Xpert performed as an initial test
Culture in liquid medium (Xpert neg PLHIV)	% of culture tests in PLHIV	# of culture tests in PLHIV with initial neg Xpert
TUTT for PLHIV	Rate of TB screening/testing in PLHIV on ART; % of PLHIV on ART patients tested without symptom screen	# of PLHIV tested (Xpert)
TUTT for previous TB	Rate of TB screening/testing in individuals with previous TB % of persons with previous TB tested without symptom screen	# of previous TB individuals tested (Xpert)
TUTT for household contacts	Rate of TB screening/testing in HH % of HH contacts tested without symptom screen	# of HH contacts tested (Xpert)
Linkage to care	% of initial loss to follow-up (linkage to TB treatment following diagnosis)	# of people initiated on DS-TB treatment

Average service costs I [2021/22 ZAR]

Intervention	Average service cost	Source
Isoniazid Preventive Therapy (IPT) for PLHIV	R 173.91	Own calculations
Isoniazid Preventive Therapy (IPT) for HH contacts	R 173.91	Own calculations
3HP	R 370.85	Own calculations
Symptom screening (PLHIV)	R 11.58	Aurum
Symptom screening (General PHC)	R 11.58	Own calculations
Symptom screening (HH contacts)	R 23.29	Aurum
Symptom screening (Door-to-door)	R 26.47	Aurum
Mobile chest radiography	R 758.78	TBHIVCare
Xpert MTB/RIF Ultra	R 266.56	Own calculations
Culture in liquid medium (Xpert neg PLHIV)	R 92.15	Own calculations
Smear microscopy	R 77.74	Own calculations

Average service costs II [2021/22 ZAR]

Intervention	Average service cost	Source
TUTT for PLHIV	R 303.49	PHRU
TUTT for previous TB	R 303.49	PHRU
Outpatient treatment (DS-TB), adults	R 2,098.92	HE2RO (TB SEQUEL)
Inpatient treatment (DS-TB), adults	R 4,786.56	HE2RO (TB SEQUEL)
Treatment (DR-TB), adults	R 95,586.93	LSTM (STREAM)
Outpatient treatment (DS-TB), children	R 1,545.73	HE2RO

Overview of scenarios

Baseline scenario

Current trajectory of TB epidemic and programme interventions (no changes)

NSP scenario

Informed by stakeholders: NSP, NTP-SP/ TB Think Tank, etc

Max scenario 1

Max scenario 2

Aggressive efforts to reduce TB incidence and mortality to meet WHO's End TB targets

NSP scenario: Coverage targets

Intervention category	Description/population	Coverage	Numbers reached	Unit
Prevention	IPT or 3HP for household contacts	55%	269,555	clients initiated TPT
	IPT for people living with HIV (PLHIV)	3%	38,122	clients initiated TPT
	3HP for PLHIV	28%	+ 323,576	clients initiated TPT
Symptom screening	For PHCs	100%	35,992,794	screenings
	For PLHIV on ART	81%	14,475,258	screenings
	For household (HH) contacts	87%	429,158	clients screened
	Door-to-door (D2D)	11%	5,343,903	clients screened
	Digital chest X-ray following D2D screening	8%	429,848	clients screened
TUTT	For household contacts	74%	361,454	clients tested
	For PLHIV	51%	3,061,506	clients tested
	For individuals with history of TB	12%	317,553	clients tested
Testing	Xpert Ultra	100%	3,330,904	clients tested
	Culture (PLHIV with Xpert neg)	30%	717,981	clients tested
Linkage to treatment	Reduce initial loss to follow up (ILTFU)	7%	7%	% ILTFU

Max scenario 1: Interventions

- Testing aggressive intervention strategies to reduce TB incidence and mortality
- Focus on: preventative therapy, screening, and linkage to treatment

Prevention	Screening and testing	Treatment
Doubled baseline monthly rates of TPT initiations for PLHIV	Door-to-door x4 (symptom screen SA adults 4 times/year)	Assume no loss to follow-up between diagnosis and treatment: ILTFU=0%

Max scenario 2: Interventions

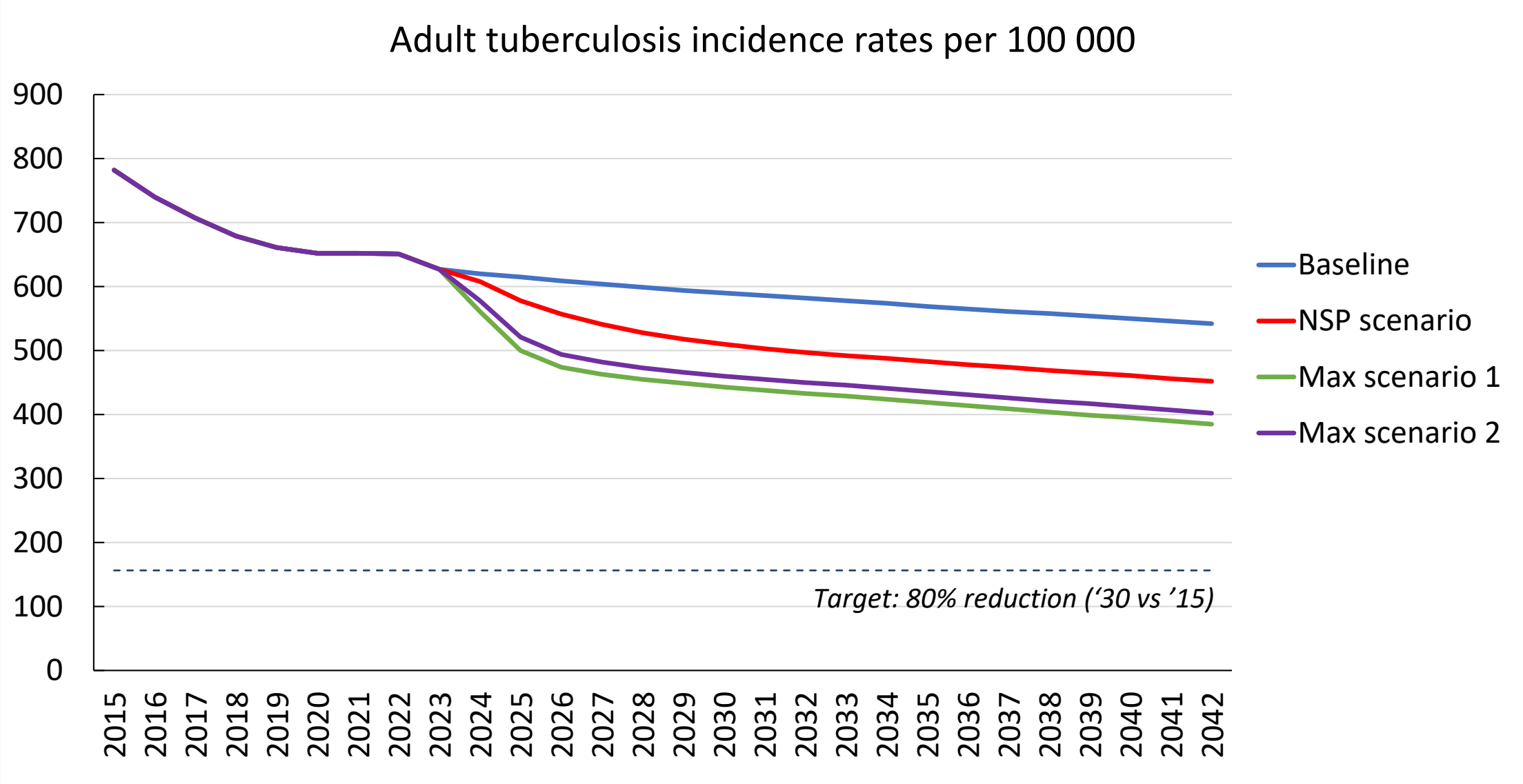
- Testing aggressive intervention strategies to reduce TB incidence and mortality
- Focus on: preventative therapy, screening and testing, and linkage to treatment

Prevention	Screening and testing	Treatment
Doubled baseline monthly rates of TPT initiations rates (PLHIV, household contacts)	Door-to-door x2 (symptom screen SA adults 2 times/year) Targeted universal testing (TUTT) for household contacts	Assume no loss to follow-up between diagnosis and treatment: ILTFU=0%

Outcomes

- Impact of interventions: % reduction in TB incidence and mortality compared to baseline.
- Budget required over 5 years (2023–2027) under different scenarios.
- Cost-effectiveness per life years saved over 20 years (2023–2042).

Incidence


Adult tuberculosis incidence rates per 100 000
900
800
700
600
500
400
300
200
100
0
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
2025
2026
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2028
2029
2030
2031
2032
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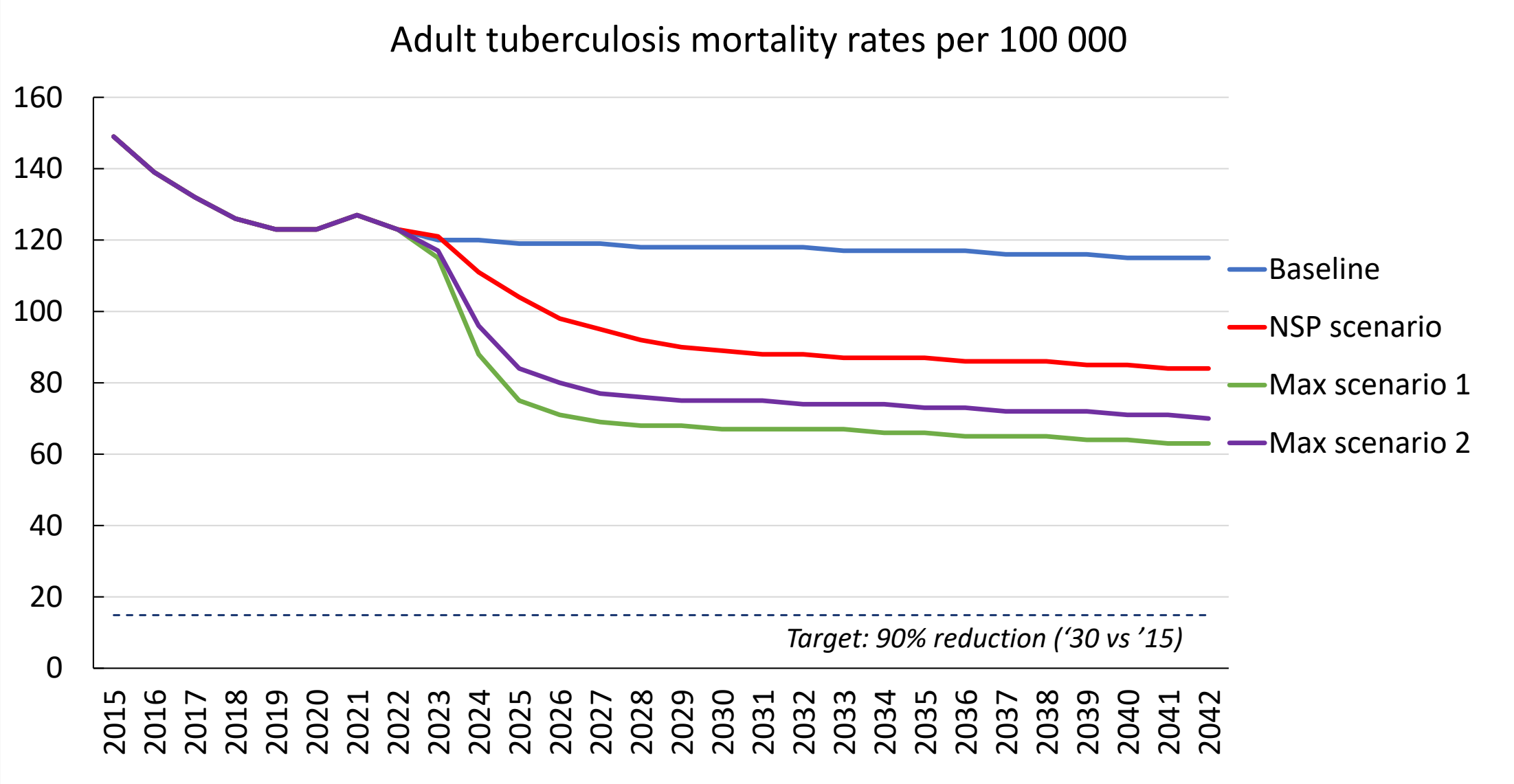
2034
2035
2036
2037
2038
2039
2040
2041
2042
Target: 80% reduction ('30 vs '15)
Baseline
NSP scenario
Max scenario 1
Max scenario 2

Mortality


Adult tuberculosis mortality rates per 100 000
160
140
120
100
80
60
40
20
0
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
2025
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2028
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2030
2031
2032
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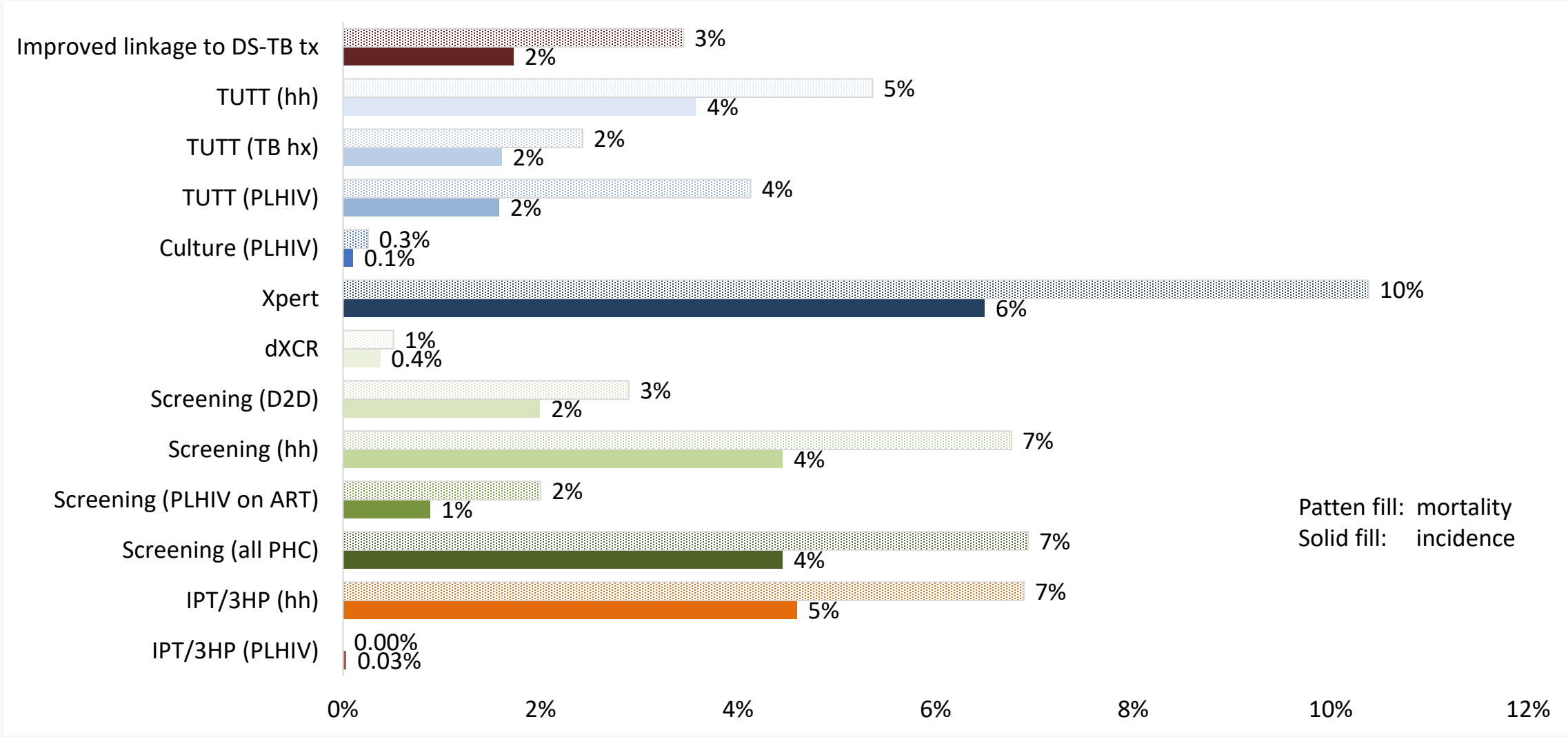
2035
2036
2037
2038
2039
2040
2041
2042
Target: 90% reduction ('30 vs '15)
Baseline
NSP scenario
Max scenario 1
Max scenario 2

TB incidence and mortality reductions by 2030

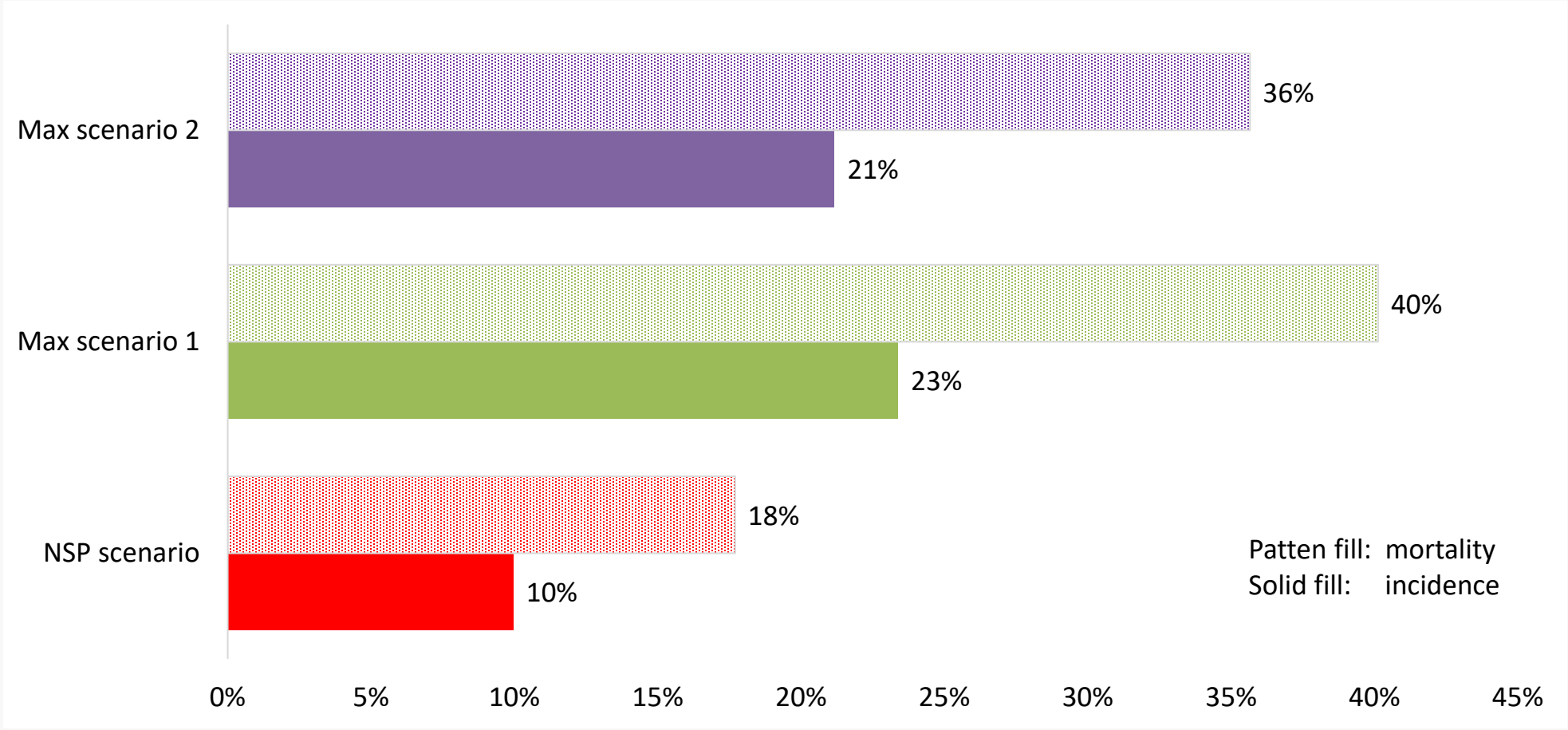
Intervention scenario	Estimated 2030 incidence/ mortality rate per 100,000	% reduction by 2030 vs 2015
Max scenario 1		
Incidence	443	43%
Mortality	67	55%
Max scenario 2		
Incidence	460	41%
Mortality	75	50%
NSP scenario		
Incidence	510	35%
Mortality	89	40%

NB: 2015 incidence rate/100,000 pop: 782; 2015 mortality rate: 149

% incidence and mortality reductions vs baseline (2023-2042)

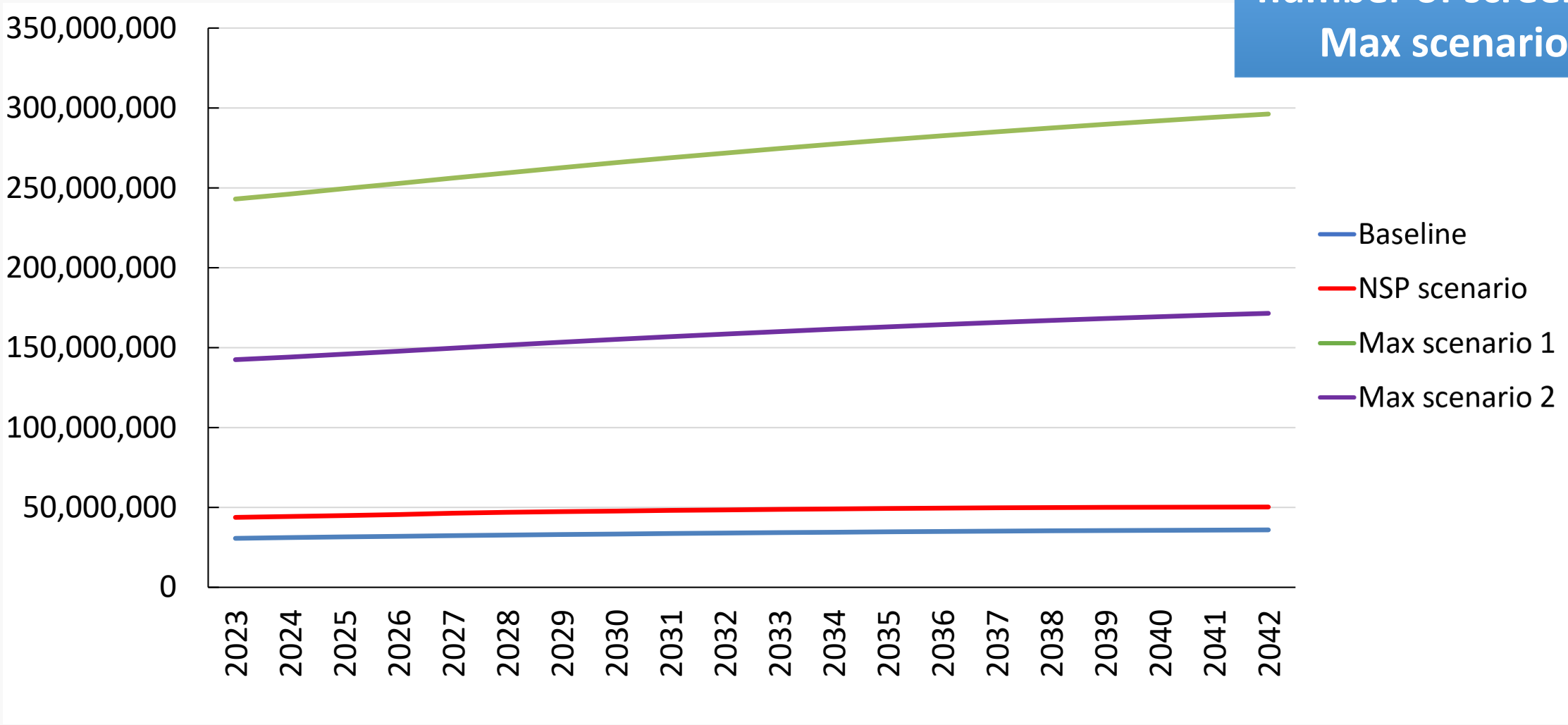


% incidence and mortality reductions vs baseline (2023-2042)

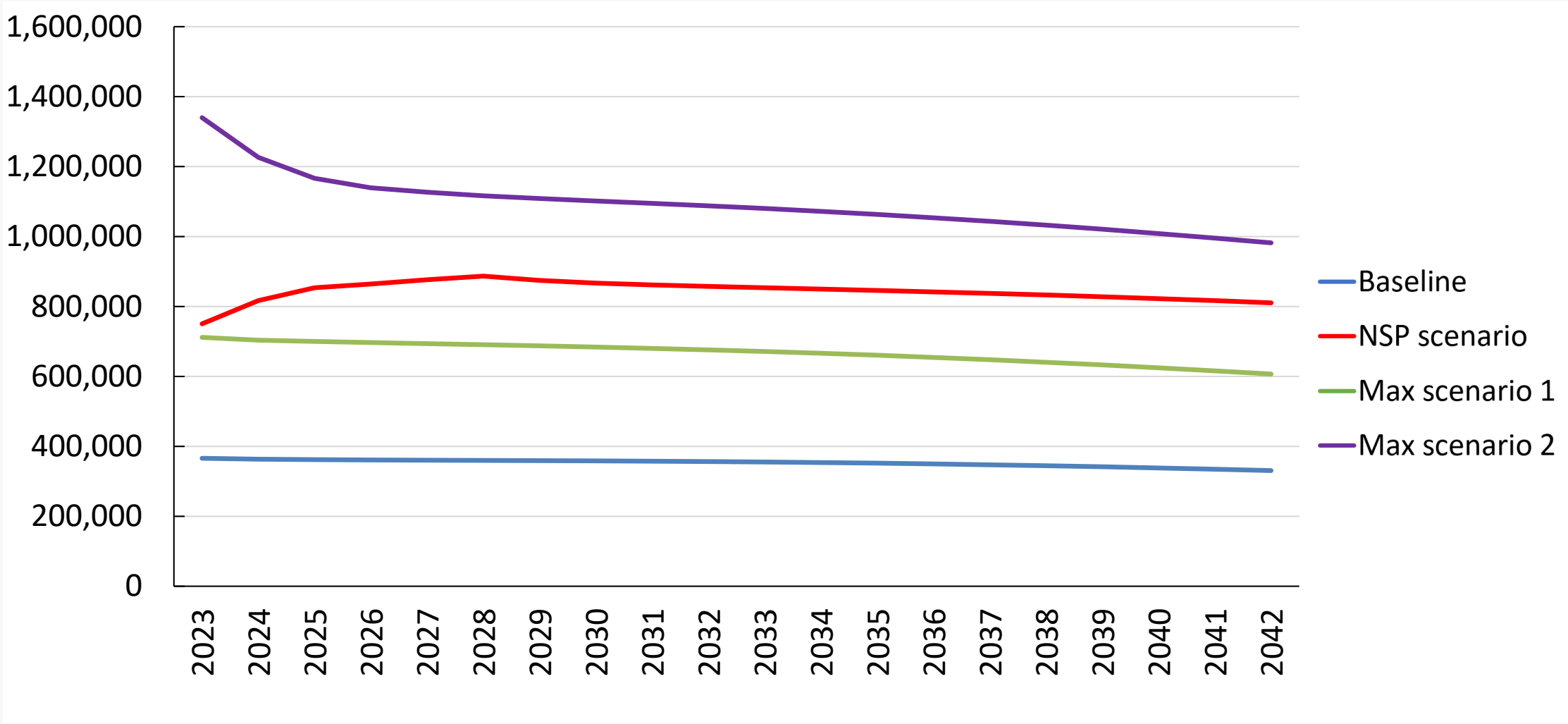


Number of screenings
(symptom screens and dCXR)

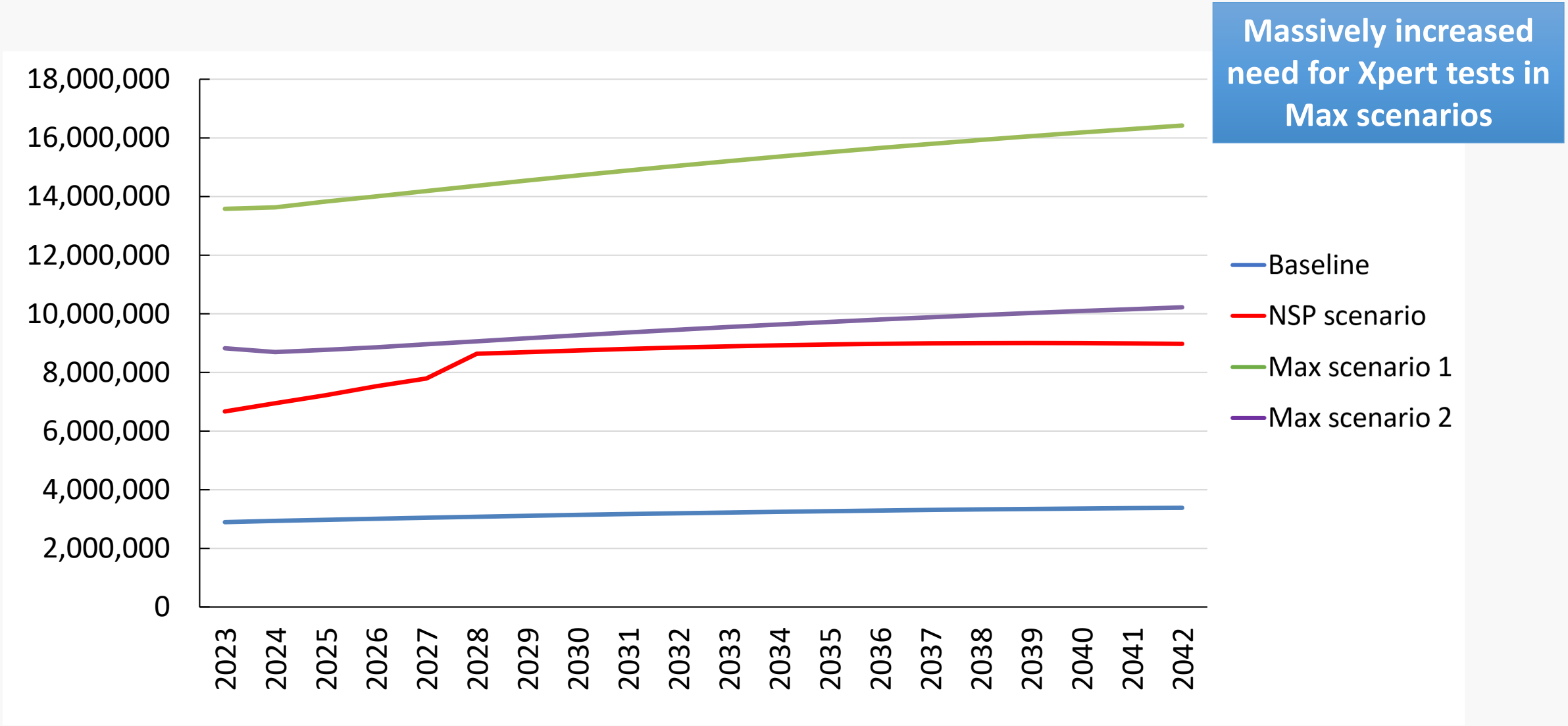
Unrealistically high number of screens in Max scenarios



Clients initiated on TPT

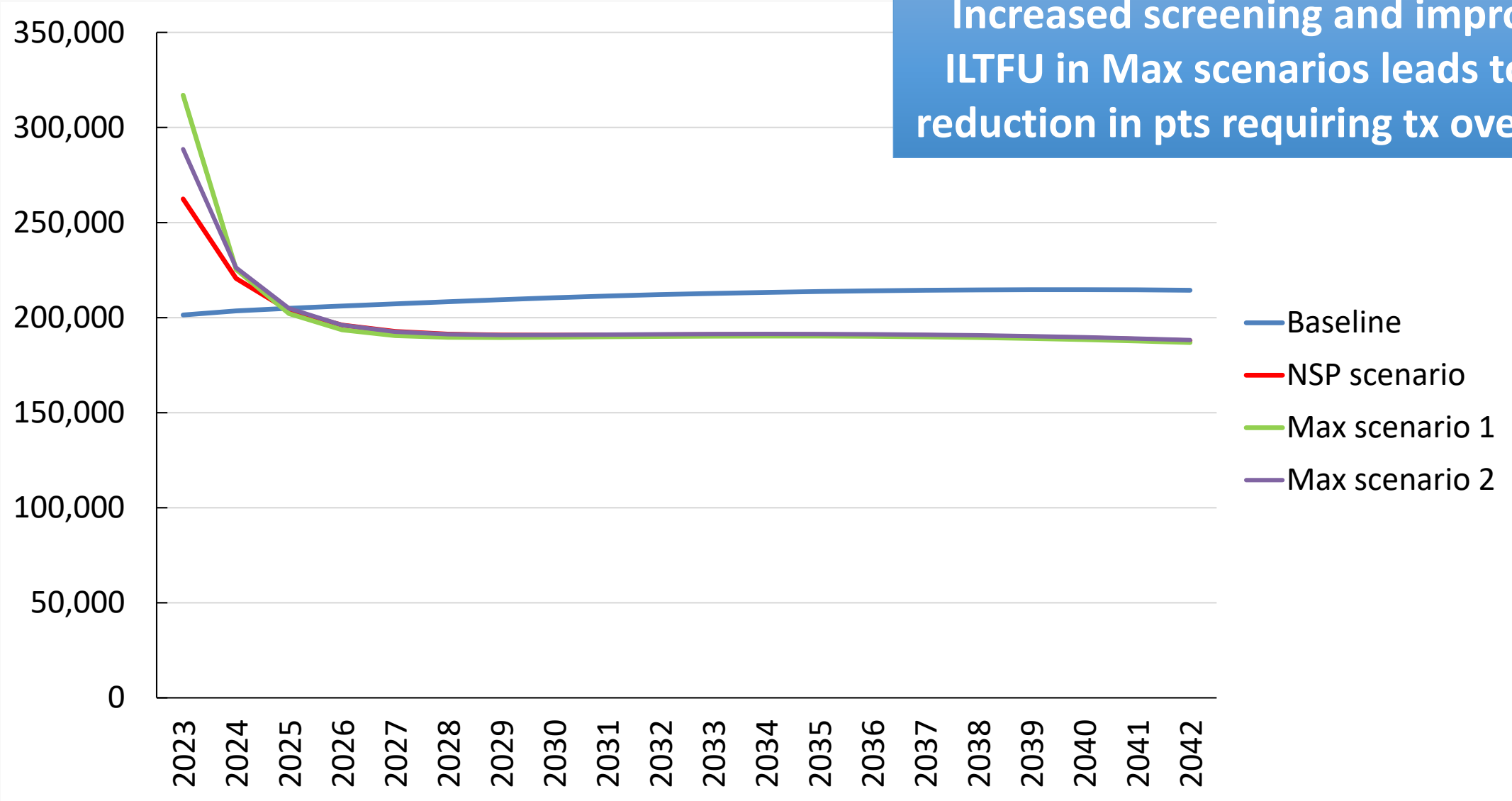


Clients tested with Xpert Ultra

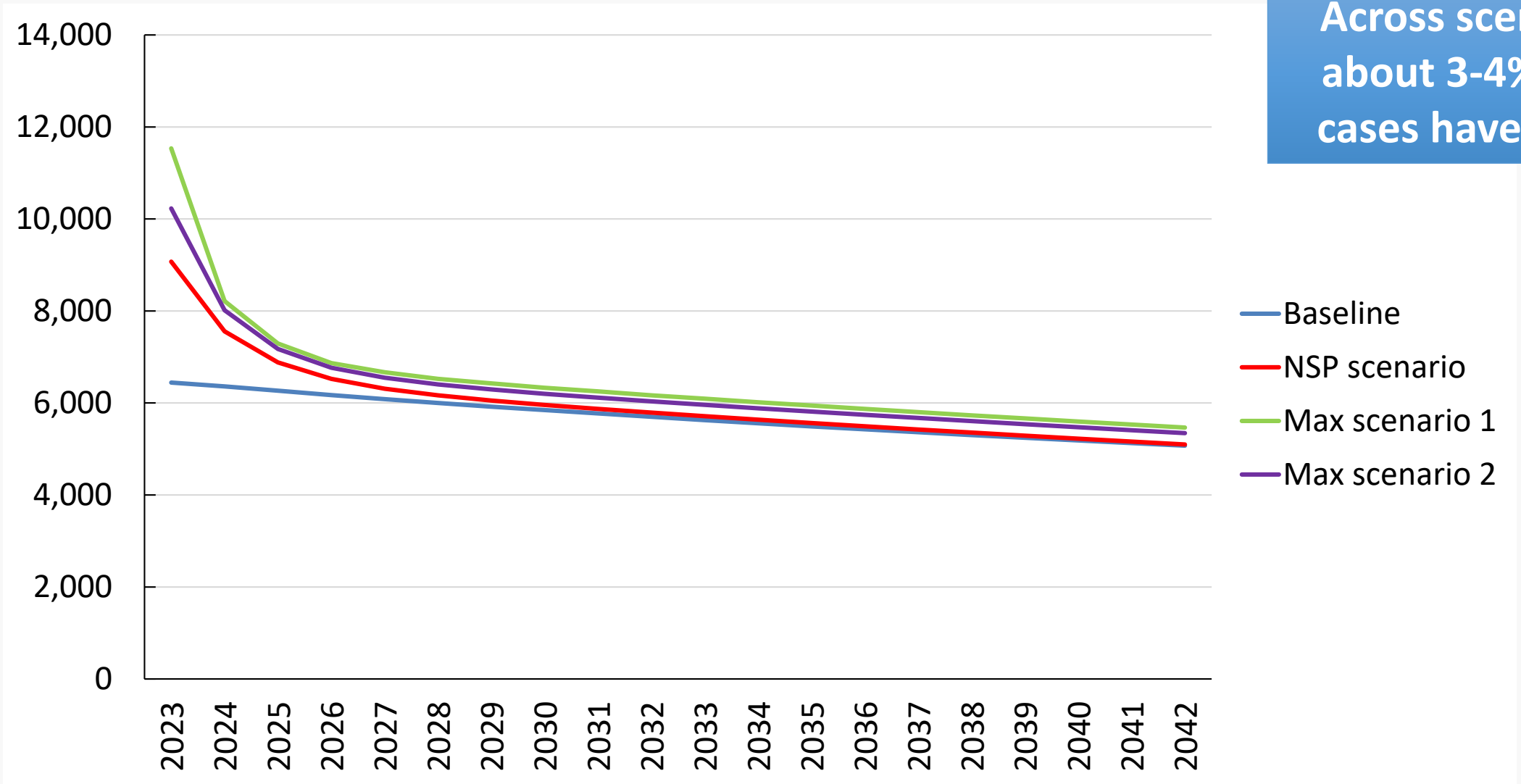


Clients treated (DS outpatient tx)

Increased screening and improved ILTFU in Max scenarios leads to net reduction in pts requiring tx over time

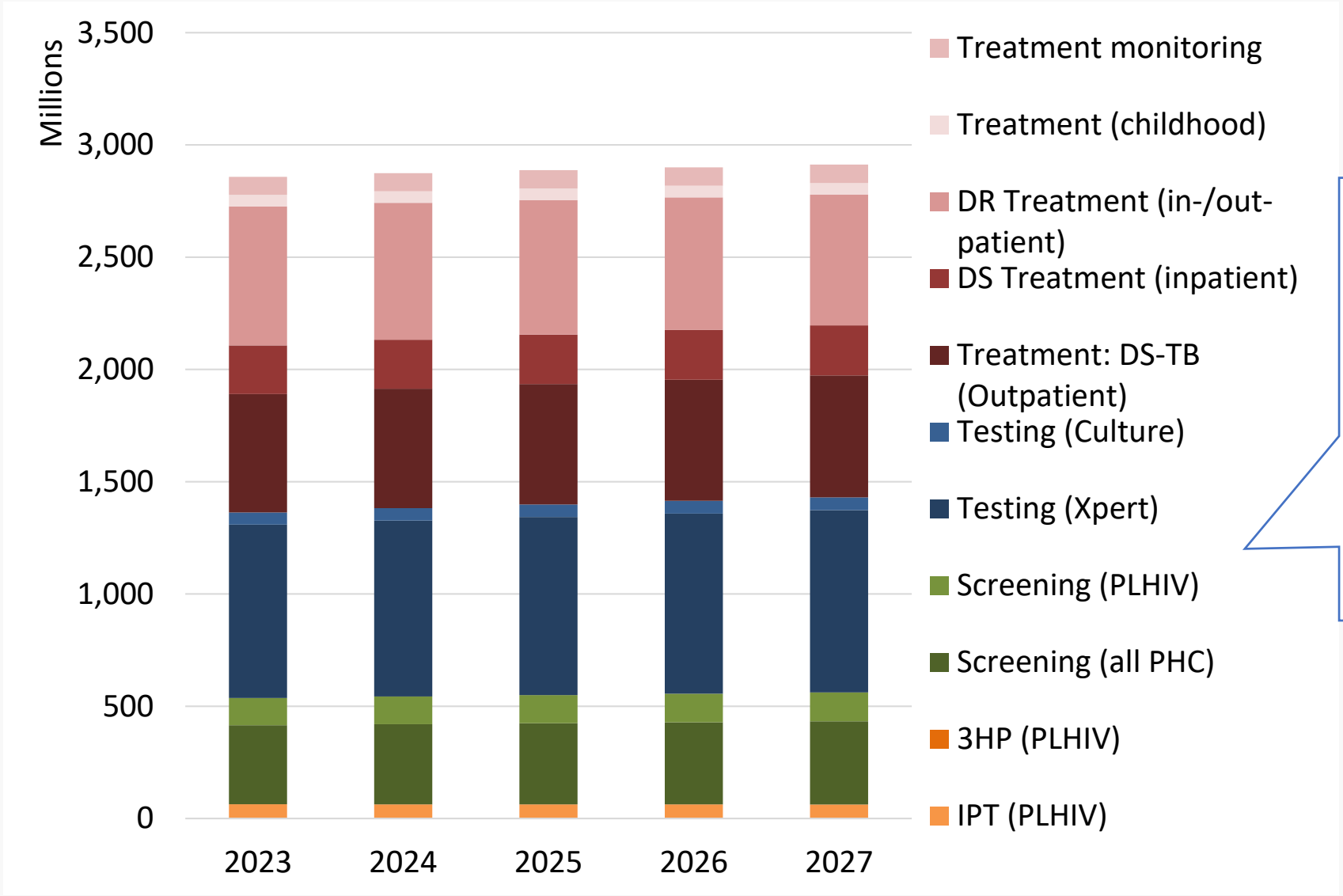


Clients treated (DR tx)



Across scenarios, about 3-4% of all cases have DR-TB

Total cost 2023-2027 (Baseline) [2021/22 ZAR]

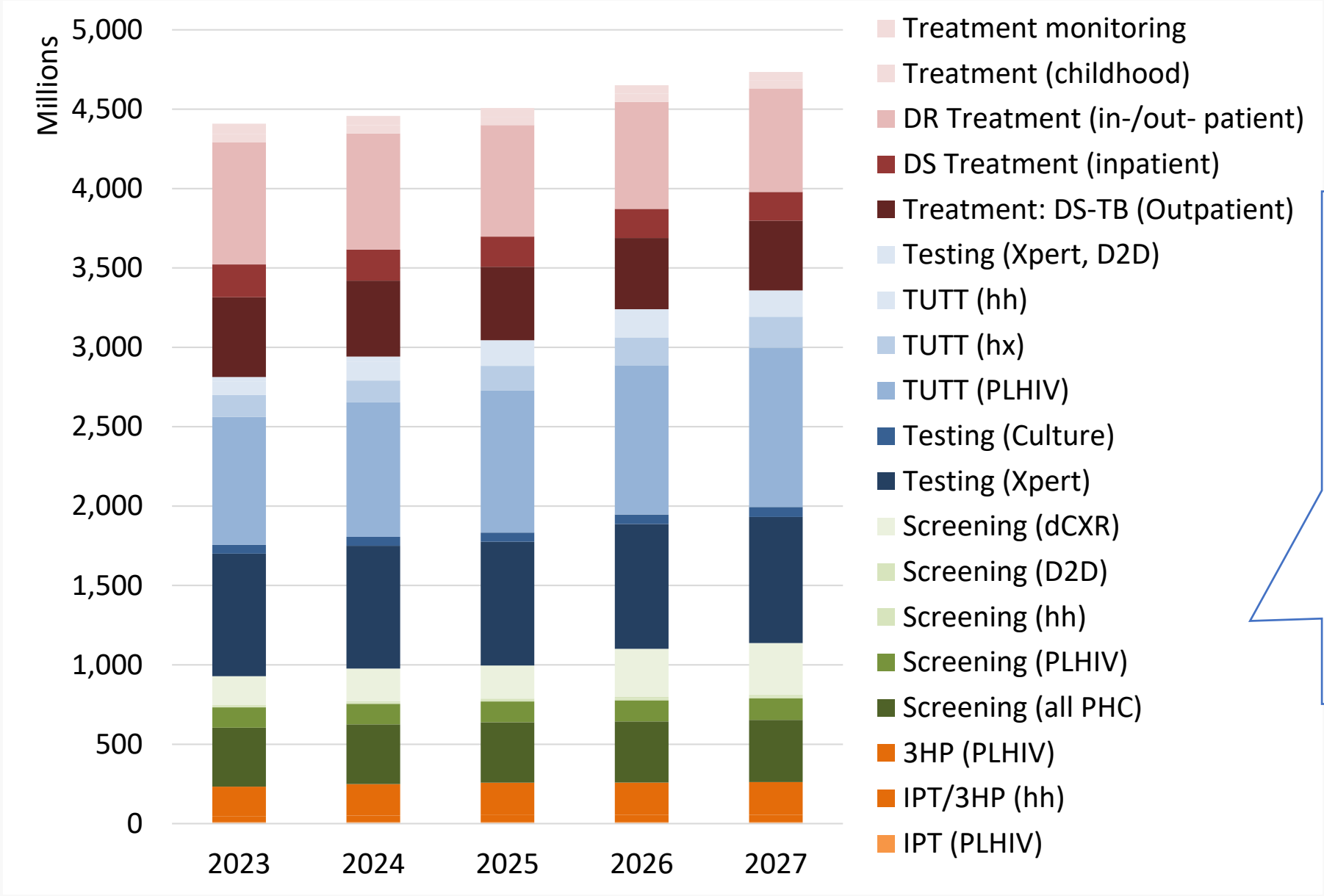


~R2.9 B/year
R14.4 B over 2023-2027

Driver of costs

- Xpert Ultra (27%)
- In-/outpatient DS-TB (26%)
- In-/outpatient DR-TB (21%)

Total cost 2023-2027 (NSP scenario) [2021/22 ZAR]

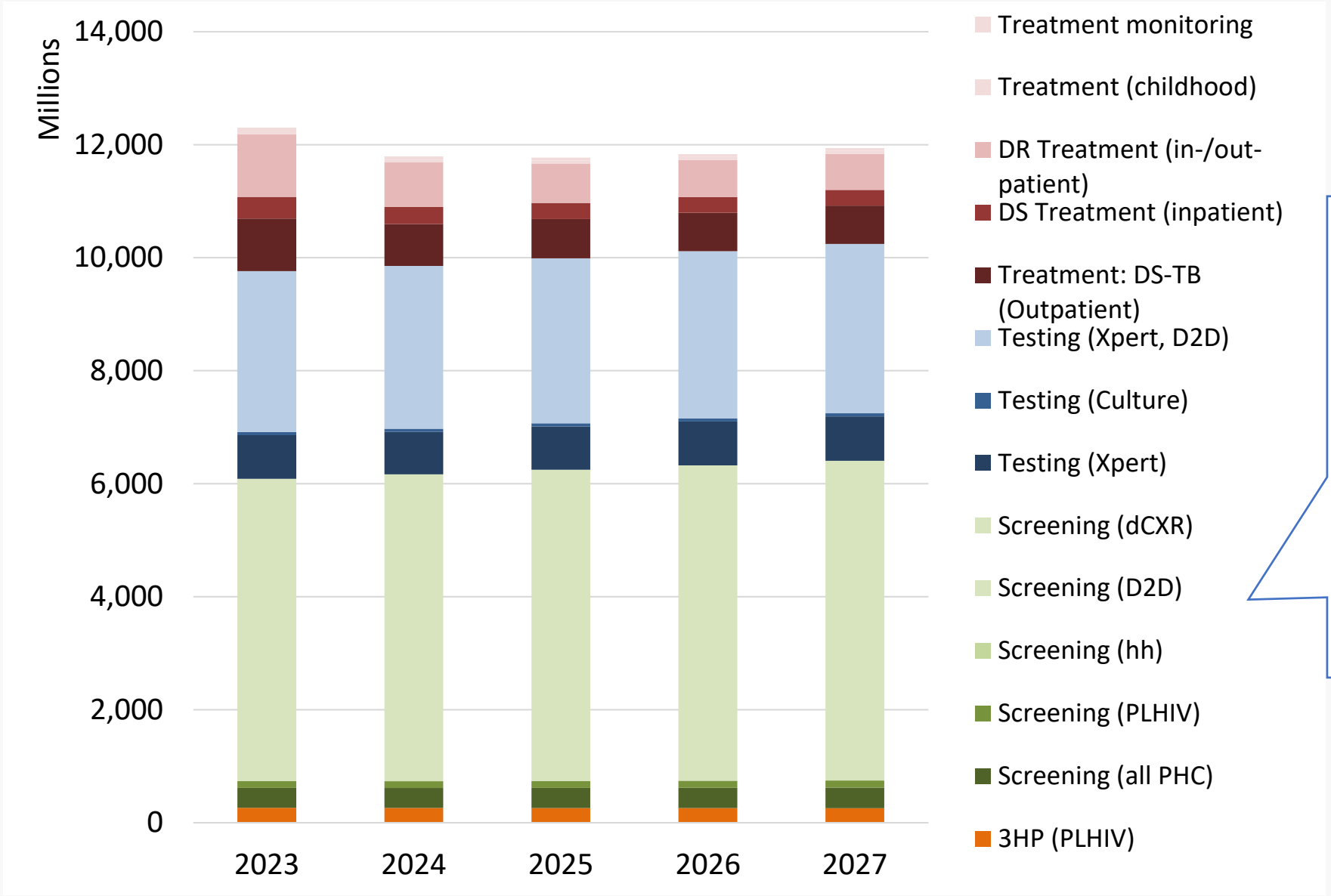


R4.4-R4.7 B/year
R22.8 B over 2023-2027

Driver of costs

- TUTT for PLHIV (20%)
- Xpert Ultra (18%)
- In-/outpatient DS-TB (16%)
- In-/outpatient DR-TB (14%)

Total cost 2023-2027 (Max scenario 1) [2021/22 ZAR]

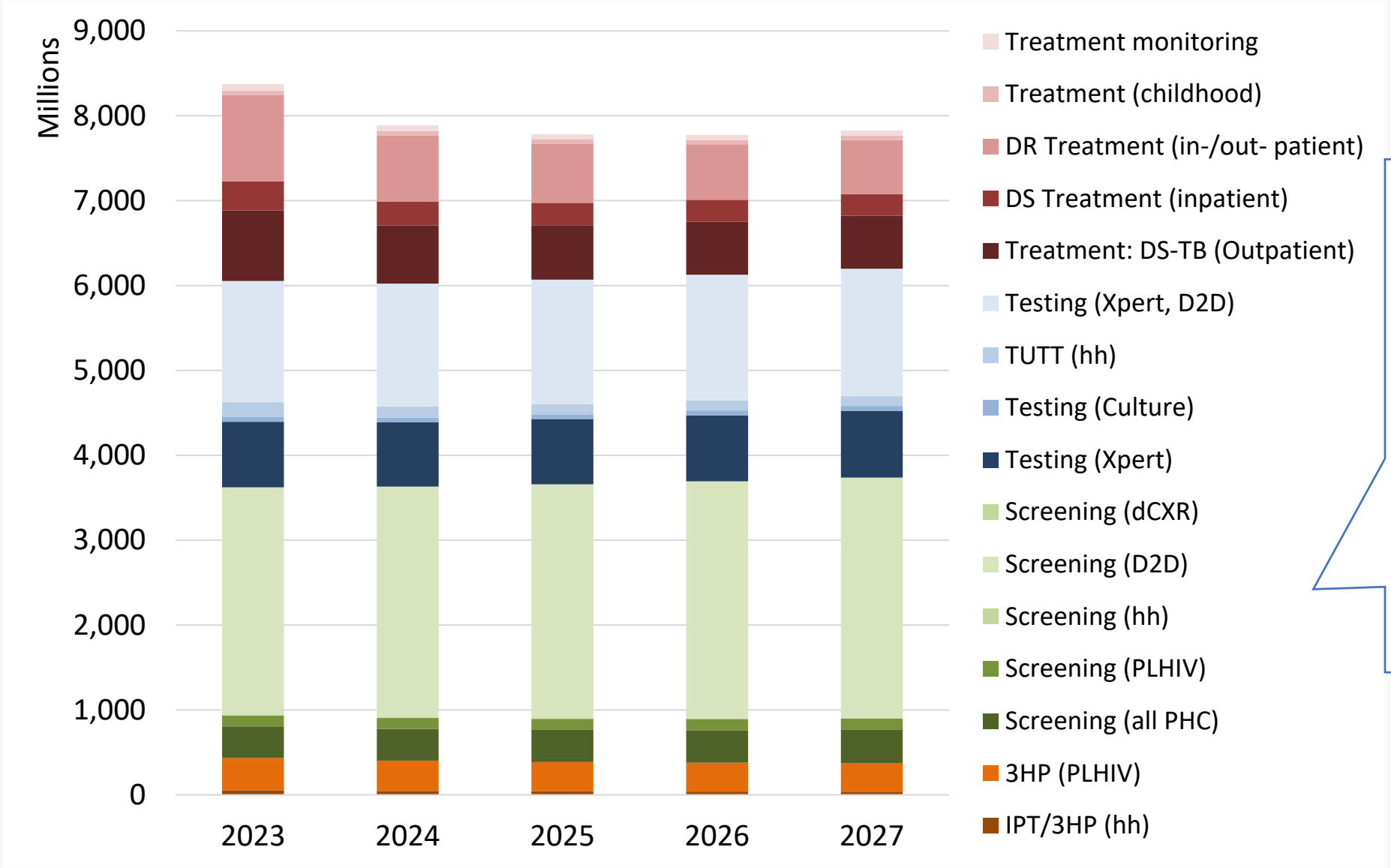


R 11.9 B/year
R 59 B over 2023-2027

Driver of costs

- D2D screening (46%)
- Xpert Ultra (31%)
- In-/outpatient DS-TB (9%)
- In-/outpatient DR-TB (7%)

Total cost 2023-2027 (Max scenario 2) [2021/22 ZAR]

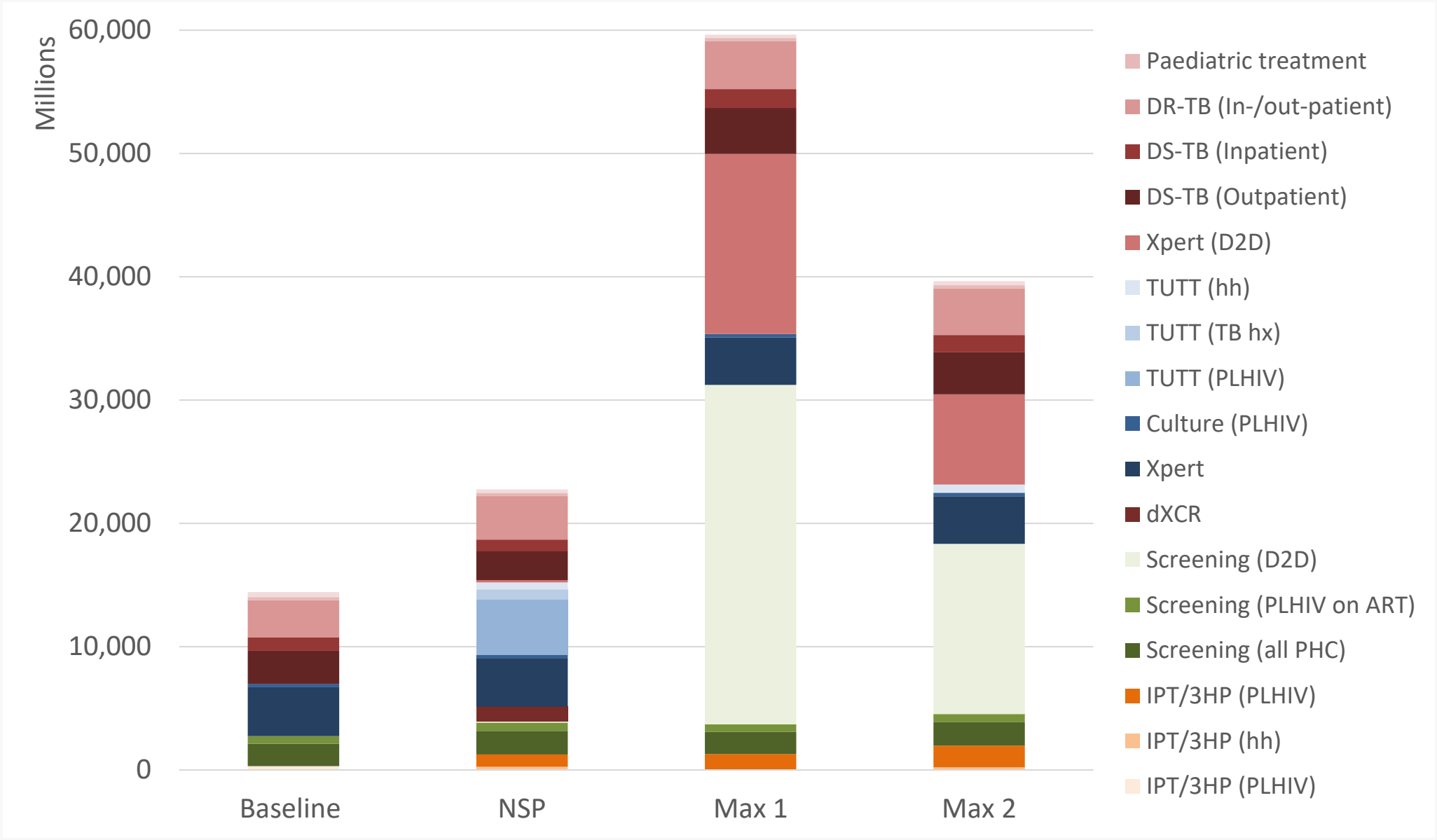


R7.9 B/year
R39.6 B 2023-2027

Driver of costs

- D2D screening (35%)
- Xpert Ultra (28%)
- In-/outpatient DS-TB (13%)
- In-/outpatient DR-TB (10%)

Total cost by scenario 2023-2027 [2021/22 ZAR]



Incremental cost-effectiveness

Individual interventions per NSP coverage targets	Average annual service coverage	Incremental cost (mil' ZAR 2021/2022) to TB programme over baseline (% increase)	Life years saved over baseline, millions (% increase)	ICER (ZAR 2021/22)
Xpert Ultra testing per diagnostic algorithm	3.3 million tests	2,712 (+5%)	3.0 (+9%)	902
TB screening in general PHC	34 million tests	2,124 (+4%)	2.0 (+6%)	1,044
Reduce ILTFU	Reduce by 50%	1,903 (+3%)	1.0 (+3%)	1,944
TB screening for HH contacts of persons with TB	0.4 million screens	4,643 (+8%)	2.0 (+6%)	2,359
TUTT for HH contacts of persons with TB	0.4 million tests	3,888 (+7%)	1.6 (+5%)	2,446
TPT (IPT/3HP) for HH contacts of persons with TB	0.26 million initiations	7,831 (+13%)	2.0 (+6%)	3,681
TB screening in PLHIV on ART	11 million screens	2,785 (+5%)	0.6 (+2%)	4,941
TUTT for individuals with history of TB	0.3 million tests	3,589 (+6%)	0.7 (+2%)	5,267
Annual D2D screening	5 million screens	5,695 (+10%)	0.8 (+2%)	6,847
TUTT for PLHIV	3 million tests	23,444 (+40%)	1.1 (+3%)	20,855
Culture testing per diagnostic algorithm (Xpert-, PLHIV)	0.7 million tests	1,796 (+3%)	0.05 (+0.1%)	39,912
dCXR	0.42 million screens	10,283 (+17%)	0.01 (+0.4%)	67,115
TPT (IPT/3HP) for PLHIV	0.3 million initiations	1,237 (+2%)	0.01 (0.03%)	139,732

Incremental cost-effectiveness

Description of interventions	Average annual service coverage	Incremental cost (mil' ZAR 2021/2022) to TB programme over baseline (% increase)	Life years saved over baseline, millions (% increase)	ICER (ZAR 2021/2022)
NSP scenario: All the interventions as per NSP targets	All the interventions as per NSP targets	44,692 (+78%)	5.1 (15%)	8,855
Max scenario 2 • TPT for PLHIV & HH contacts • Annual D2D screening x2 • TUTT (HH) • ILTFU = 0%	• 0.8 million TPT (PLHIV) initiations • 0.2 million TPT (HH) initiations • 95 million screens • 9.4 million Xpert tests • Reduce ILTFU by 100%	104,364 (+177%)	9.9 (30%)	10,019
Max scenario 1 • Annual D2D screening x4 • double TPT initiations for PLHIV • ILTFU = 0%	• 0.6 million TPT (PLHIV) initiations • 190 million screens • 15 million Xpert tests • Reduce ILTFU by 100%	191,374 (+326%)	11.7 (34%)	16,443

Limitations

- Paediatric TB is not modelled dynamically.
- Cost of interventions to link diagnosed patients to treatment not included.
- Cost of treatment for side effects not included.
- We did not report sex-stratified TB trends or impacts of interventions by sex strata.

Conclusions from 2023 TB Investment Case

- **Most cost-effective interventions**
  - Xpert testing, screening at PHCs, improving linkage, TUTT for household contacts

- **NSP scenario:**
  - Targets deemed realistic by NTP
  - Incidence reduction 35%, mortality reduction 40% by 2030 compared to 2015
  - Cost increase from ZAR 4.4 B to 5 B per year during NSP period

- **Max scenarios:**
  - Screening and Xpert test numbers unrealistically high
  - Incidence reduction ~40%, mortality reduction ~50% by 2030 compared to 2015 → short of 80%/90% targets
  - Total cost increases to ZAR 7.5 B to 10 B per year
  - But implementation is the bigger issue

Next steps

- **Thembisa TB:**
  - Re-calibration completed, results currently under review → 2024 TB IC
  - Paediatric TB
  - Impact of early treatment initiation on disease severity
  - Better cost of DR-TB
  - Provincial versions?

- **Optimisation:**
  - Multiple constraints (budget + HCW)
  - Multiple optimisation targets (cost-effectiveness + mortality/ incidence)