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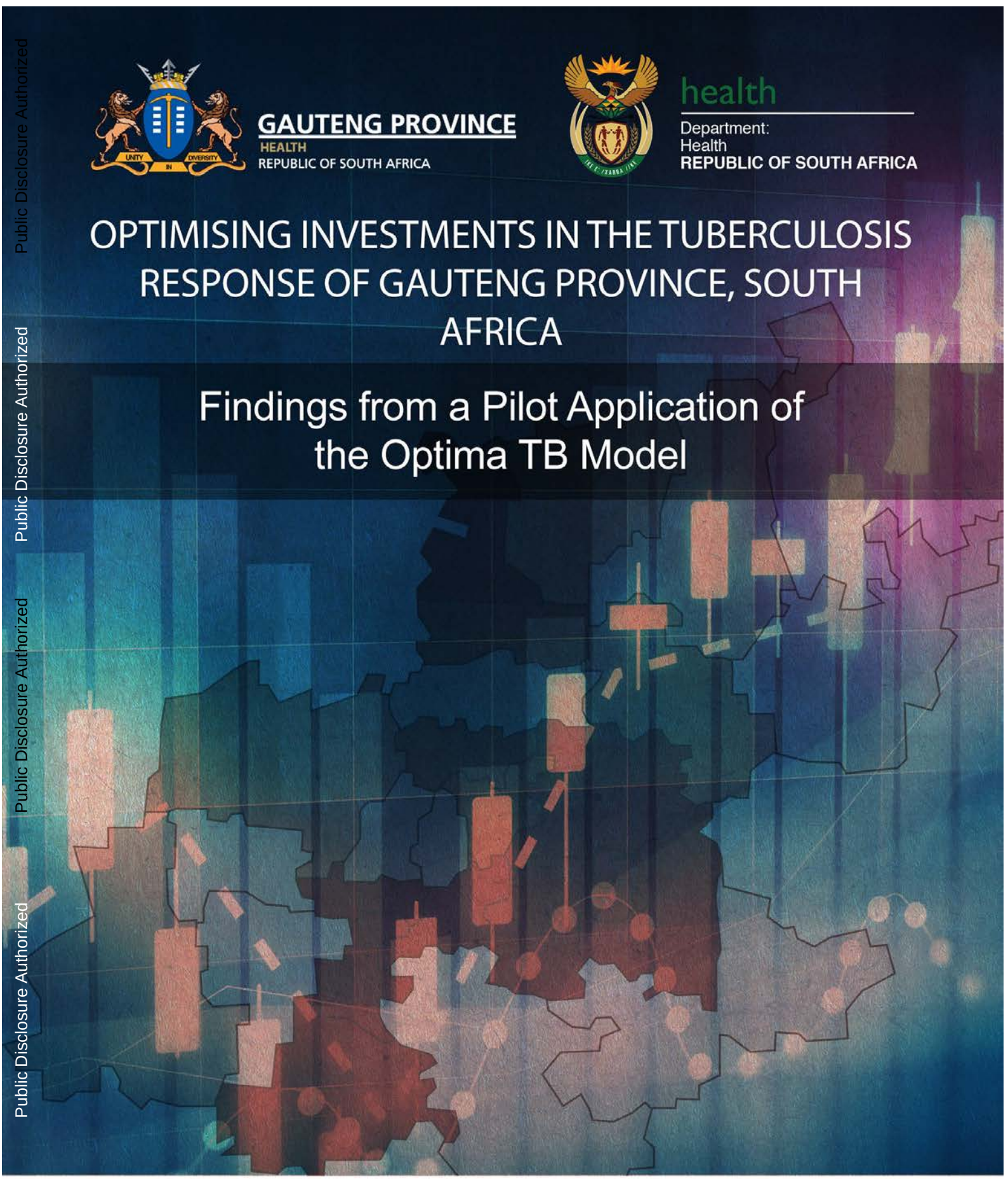
OPTIMISING INVESTMENTS IN THE TUBERCULOSIS RESPONSE OF GAUTENG PROVINCE, SOUTH AFRICA

Findings from a Pilot Application of the Optima TB Model



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Optimising Investments in theTuberculosis Response of Gauteng Province, South Africa

FINDINGS FROM A PILOT APPLICATION OF THE OPTIMA TB MODEL

OCTOBER 2019

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ABBREVIATIONS

ACF	Active case finding
APP	Annual Performance Plan
ART	Antiretroviral therapy
BAS	Basic Accounting System
BDQ	Bedaquiline
DOH	Department of Health
DR	Drug resistant
DS	Drug susceptible
FY	Financial year
HCW	Health care worker
HIV	Human immunodeficiency virus
IGRA	Interferon gamma release assay
IPT	Isoniazid preventive therapy
LAM	Test measuring lipoarabinomannan antigen
LPA	Line probe assay technology
LTBI	Latent tuberculosis infection
MDR	Multi-drug resistant
MTEF	Medium term expenditure framework
NDOH	National Department of Health
NHLS	National Health Laboratory Service
NSP	National Strategic Plan
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PHC	Primary health care
PLHIV	people living with HIV
Rif-R	Rifampicin resistant
SDG	Sustainable Development Goal
TB	Tuberculosis
TST	Tuberculin skin test
UHC	Universal health coverage
UVGI	Ultraviolet germicidal irradiation
WHO	World Health Organization
XDR	extensively drug resistant
Xpert	GeneXpert MTB/RIF, detecting DNA sequences specific for M. tuberculosis and rifampicin resistance
ZAR	South African Rand

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EXECUTIVE SUMMARY

This report summarises the experience and learning from the pilot application of the Optima TB model in a HIV/TB co-epidemic setting. Optima TB supports allocative efficiency analyses of TB responses and the pilot study was conducted in South Africa's Gauteng Province. The report also presents the findings obtained with this pilot application of Optima TB regarding epidemic trends, TB spending patterns, and the modelled effects of several resource allocation scenarios and optimization.

The pilot study was conducted jointly with the South African National Department of Health (NDOH) and Gauteng Department of Health. Together with other pilot applications, the experience and learning have enabled the Optima TB development team to refine the tool before its release as a global public good (for Optima TB, see http://ocds.co/tb/).

In recognition of the importance of the HIV epidemic in the Gauteng TB setting, several measures were taken to incorporate the effects of HIV. This included the use of the most recent Thembisa model estimates on HIV burden and trends and the calibration of Optima TB to HIV prevalence. ART coverage trends were also incorporated as well as the effect of ART on TB dynamics. HIV/TB co-infection directly impacted nine Optima TB model parameters whereby each parameter was influenced differently depending on co-infection rates and ART coverage. The parameters concerned mortality rates, susceptibility to TB infection, TB infectiousness, parameters associated with latent TB infection, among others.

Thanks to the learning from Gauteng's pilot application, the Optima TB model has been improved as follows:

a. The explicit inclusion of ART as a TB-sensitive programmatic intervention in Optima TB, rather than as a background assumption. While HIV and ART were already considered across multiple parameters and through HIV-disaggregated TB data, this model refinement is a valuable improvement for Optima TB use in the co-epidemic setting. It allows greater flexibility in defining scenarios and optimisations to provide the most relevant policy recommendations.

While HIV and ART were already considered across multiple parameters and through HIV-disaggregated TB data, this model refinement is a valuable improvement for Optima TB use in the co-epidemic setting.

b. The ability of Optima TB to perform uncertainty analyses as well as sensitivity analyses. This strengthens the robustness of results and conclusions and is a significant improvement over the univariate sensitivity analyses carried out during the Gauteng pilot.The updated Optima TB model has been expanded to explicitly track uncertainty.

Every input parameter can be entered with an uncertainty range of plausible limits around the best available data. Uncertainty relating to programme costs and efficacies can also be included, allowing a more rigorous comparison between alternative allocations. Uncertainty bounds for results are then generated by sampling from this parameter distribution. This will allow for the inclusion of more detailed uncertainty plots in future analyses.

Regarding the findings obtained with this pilot application of Optima TB, the following key findings can be highlighted under each of the policy questions:

► **POLICY QUESTION 1:** WHAT IS THE EPIDEMIC TRAJECTORY OF TB IN GAUTENG PROVINCE?

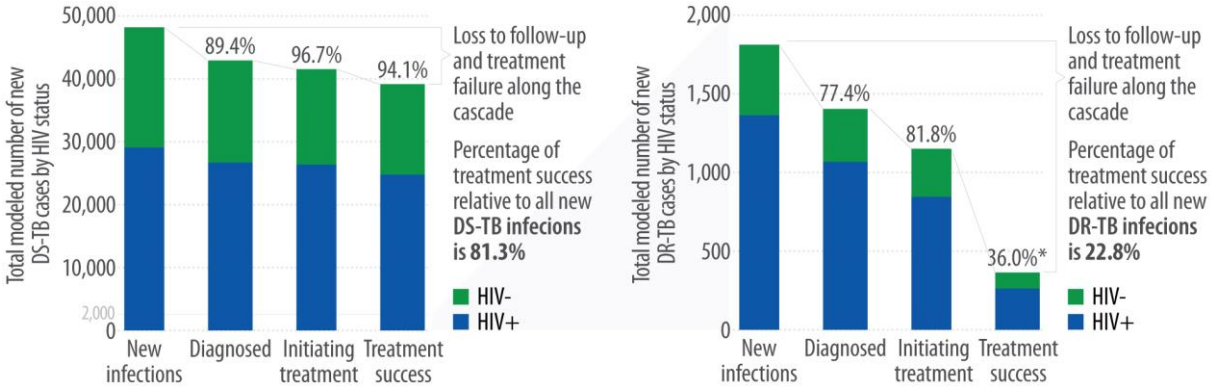
The TB epidemic in Gauteng is on a downward trajectory but the rate of drug-resistant cases has grown to 3.8% in 2015. Optima TB estimates 2.4 million latent TB cases in Gauteng for 2015. The number of latent TB infections is projected to increase significantly in the 15–64 PLHIV population as this population increases, however, latent TB prevalence is stable or decreasing across all populations.

Optima TB estimates the total of undiagnosed TB cases in Gauteng in 2016 at 37,000 ("missing cases") of which approximately 23,000 are PLHIV and 14,000 are HIV negative. Treatment initiation rates in Gauteng have significantly improved since 2012.

TB care cascades: Using a cross-sectional approach to cascades, we estimated that 89.4% of new DS-TB infections got diagnosed, using routine data available in 2016/17 (**Figure ES 1**). Among the diagnosed cases, 96.7% initiated DS-TB treatment, and 94.1% had treatment success. Treatment success relative to all new DS-TB infections was estimated at 81.3%.

For DR-TB, we estimated that 77.4% of new TB infections got diagnosed, 81.8% of diagnosed initiated DR-TB treatment, and 36% had treatment success. Treatment success relative to all new DR-TB infections was estimated at 22.8%.

Figure ES 1 Care cascade outcomes for DS-TB and DR-TB cases with current allocations, Gauteng



Source: Populated Optima TB model for Gauteng.

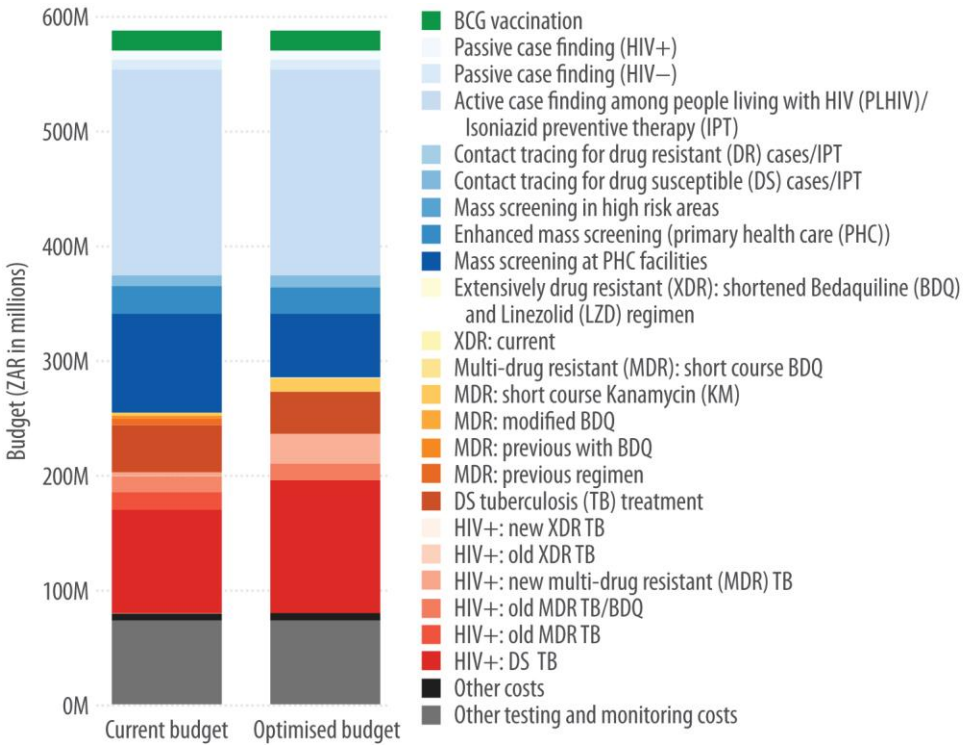
► **POLICY QUESTION 2:** UNDER CURRENT AND OPTIMISED FUNDING, WHAT IS THE PROGRESS THAT CAN BE MADE TOWARDS MEETING GAUTENG TB TARGETS?

The analysis estimated current TB funding levels and allocations in Gauteng. An estimated ZAR 589.6 million was spent on TB prevention and care in Gauteng in 2016, of which approx. ZAR 350 million was tracked as TB spend in the Basic Accounting System (BAS), and about ZAR 240 million was other TB-related spending financed from health sector resources. Laboratory consumables and other diagnostic costs combined, comprised 40.7% (ZAR 239.7 million) of total TB spending in 2016.

The analysis then determined the mathematically optimal funding allocations for Gauteng's TB programme (**Figure ES 2**). An optimal allocation to simultaneously avert TB infections, reduce prevalence and prevent deaths (combined optimisation objectives), would: Increase annual funding to strengthen mass screening at PHC and invest in targeted mass screening in high risk areas, as well as prioritise investment in linkage of diagnosed cases to treatment programmes (ZAR 30.1 million) in order to minimise pre-treatment losses.

Figure ES 2 Current allocation of TB resources and optimised allocations to simultaneously minimise cumulative TB disease incidence, prevalence and deaths from 2017–35 in Gauteng Province

Source: Populated Optima TB model for Gauteng.

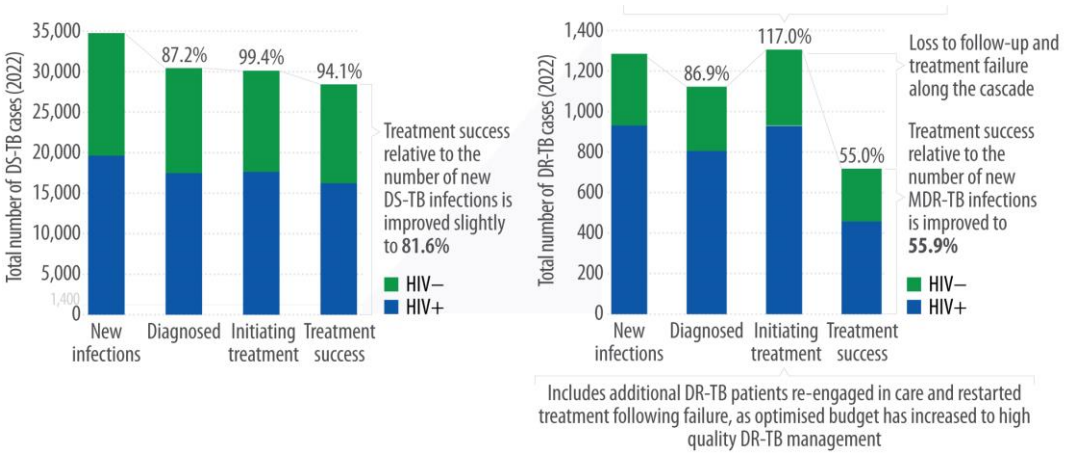


If the optimisation analysis was limited to TB treatment interventions, more could be learnt about the best allocations across patient groups and regimens. It recommended increases in annual funding for DS-TB treatment in co-infected patients (+20.5M ZAR), shortened Bedaquiline for HIV- patients with MDR-TB (+8.4M ZAR), and new MDR-TB regimens in co-infected patients (+14.3M ZAR).

The impact of the 2016 optimised budget on TB care cascades was then determined (**Figure ES 3**). Treatment success relative to the number of new DS-TB infections was improved

slightly to 81.6% (from 81.3%). Treatment success relative to the number of new MDR-TB infections is improved to 55.9% (from 22.8%, including additional DR-TB patients who have been re-engaged in care, and re-started treatment following failure).

Figure ES 3 Care cascade outcomes for DS-TB and DR-TB cases with optimised allocations, Gauteng



Source: Populated Optima TB model for Gauteng.
Notes: DR-TB = drug resistant tuberculosis; DS = drug susceptible tuberculosis MDR-TB = multi-drug resistant tuberculosis.

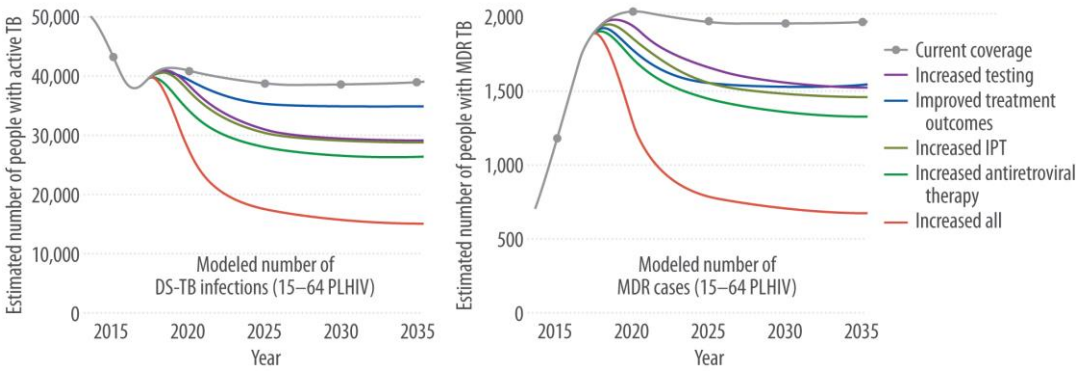
The analysis also explored the investment pattern for different levels of budget availability (**Figure 3.35**). Under conditions of increased budget availability (as should be the case if historical budget increases continue to apply) the following programmes were continuously prioritised: a) Active case finding in patients in HIV care, b) high quality mass screening and outreach in high-risk areas, and c) new MDR-TB regimens in PLHIV, and new XDR-TB regimens (the latter at 200% budget). In terms of impact of different funding levels, it was found that reducing the current budget by 50% would lead to significant increases in the numbers of TB infections and deaths. Budget increases would buy additional impact, however, large increases beyond 150% of current budget would have diminishing returns.

► **POLICY QUESTION 3:** CAN TARGETING TB PROGRAMMES AND INTERVENTIONS ACROSS SUB-POPULATIONS IMPROVE OUTCOMES?

The importance of ART scale-up for PLHIV:

- The largest observed decrease in PLHIV active-TB prevalence is from scaling up ART coverage among diagnosed PLHIV (Figure ES 4, green line)
- The scaling up of ART also yields the most substantial decrease in the projected number of MDR-TB cases
- Simultaneously increasing the coverage of key programmes for PLHIV (ART, TB diagnosis, Isoniazid Preventive Therapy), could reduce the number of DS- and MDR-TB infections by 65% by 2035 (red line).

Figure ES 4 Modelled number of active DS/MDR TB cases among PLHIV (2016–35)



Source: Populated Optima TB model for Gauteng.
Notes: IPT = Isoniazid preventive therapy; PLHIV = people living with HIV; DS = drug susceptible tuberculosis MDR = multi-drug resistant tuberculosis; TB = tuberculosis.

► **POLICY QUESTION 4:** CAN GAUTENG MEET THE STRATEGIC PLAN 2022 TARGETS WITH CURRENT/PROJECTED FUNDING?

Regarding the NSP 2017–22 target of reducing 2016 TB disease incidence by at least 30% by 2022 the model outputs suggest that (Figure ES 5, left chart):

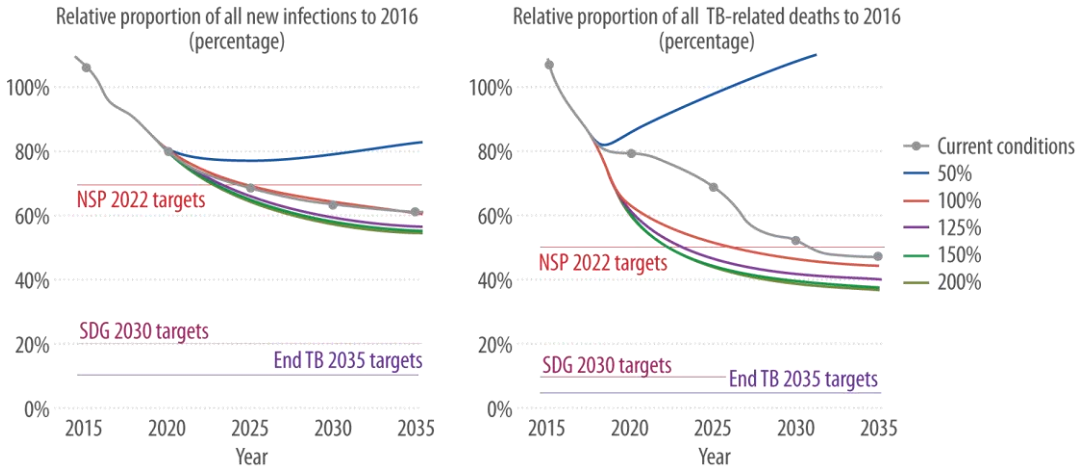
- This target is not achieved with the 2016 budget of ZAR 590 million per year
- The target could be achieved with optimised allocation and funding of 150% of the 2016 amount (assuming a 6% annual increase in dedicated TB funding in Gauteng, the 2022 funding amount would come close to 150% of the 2016 budget amount)

Regarding the NSP 2017–22 target of reducing overall TB mortality by 50% by 2022 (**Figure ES 5**, right chart):

- This target is not achieved with 2016 funding levels of ZAR 590 million per year
- With the 2016 budget amount optimally allocated, the target is projected to be reached in 2025, but not in 2022
- The target could be achieved with optimised allocation and 125% of the 2016 TB budget

Importantly, to reflect the reality of programme implementation, changes in programme funding between current and target funding levels were capped at either a maximum of 30% per year, for existing programmes, or a maximum of ZAR 15 million, for new programmes for the first year, and 30% in subsequent years, until the target level for the programme funding was reached.

Figure ES 5 Optimised allocation in relation to 2022, SDG 2030 and End-TB 2035 targets, Gauteng



Source: Populated Optima TB model for Gauteng.
Notes: NSP = National Strategic Plan; SDG = Sustainable Development Goal; Current budget: 2016 spending allocation of ZAR 590 million; 100%: Optimised 2016 spending allocation of ZAR 590 million; 50–200%: Optimised 2016 spending allocation of 50-200% of the 2016 budget of ZAR 590 million.

In order to meet the long-term 2030 and 2035 targets, new approaches and significant TB budget increases would be required, as well as rapid scale-up of universal ART for PLHIV supported by the HIV funding streams.

► **POLICY QUESTION 5:** HOW MUCH FUNDING IS REQUIRED TO ACHIEVE THE NSP 2022 TB TARGETS?

The modelling of intervention impact suggested that approximately ZAR 885 million should be spent on Gauteng's TB response from a combination of TB dedicated funding streams and health sector resources, and allocated optimally. This is projected to enable the Gauteng TB programme to meet the TB disease incidence target of a 30% reduction of the 2016 level by 2022.

The target of reducing TB mortality by 50% by 2022 is projected to be reached with a lower level of resources (approximately ZAR 738 million) allocated optimally.

It should be noted that reaching TB disease incidence targets is challenging due to the constant reactivation of latent TB which is especially high in PLHIV as well as an effect of co-factors such as the growing number of older people in Gauteng, and high levels of diabetes.

► **POLICY QUESTION 6:** WHAT IS THE EXPECTED FUTURE IMPACT OF SPECIFIC RESPONSE SCENARIOS?

Improving linkage to TB care

- If Gauteng's Annual Performance Plan (APP) 2020 testing targets are met and sustained, Optima TB predicts a significant reduction in active TB prevalence. The number of diagnosed cases would initially rise, then decrease as more cases are initiated on treatment. This would reduce the number of undiagnosed cases contributing to TB transmission.

- If the APP 2020 treatment initiation rate of 98% is met by 2020 and sustained, modeled TB prevalence will decrease. Further scale-up would yield additional gains for MDR/XDR-TB but the gains would be smaller than for DS-TB.
- If the APP 2020 MDR treatment outcome targets are met and sustained, a 35% decrease in the total number of MDR cases among HIV negative adults is projected for 2035. Despite the high treatment success rates currently achieved for DS-TB, there are still opportunities to reduce the total number of DS-TB cases through further improvements in treatment outcomes.
- Meeting and sustaining these 2020 APP targets would yield significant reductions in TB prevalence and could lead to a 50% reduction in the number of both MDR and XDR cases by 2035.
- The following actions would be important: a) Increasing the accessibility to PHC-provided TB screening and testing, in order to increase the proportion of diagnosed TB infections, b) Having fit-for-purpose routine data procedures, and c) Investing in early tracing of cases that are not linked to care.

Scale-up of MDR Short-course regimens

- Optima TB predicted that this would result in significant increases in successful treatment. It would likely minimise the costs associated with re-treating MDR-TB, the management of adverse drug effects, and help contain drug resistance challenges. It would reduce inpatient days, and therefore the risk of nosocomial TB transmission.
- Short-course regimens would offer better patient care, with less side effects, shorter treatment durations, and reduced challenges to adherence.
- To cover 75% of all diagnosed cases with current PLHIV MDR-TB regimens, a ZAR 10M increase in DR-TB spending would be needed. An additional 10% spending would be required to sustain treatment coverage while moving from older MDR regimens to short courses.

Intensifying case-finding, mass screening and active case finding in combination

- The analysis determined the effect of PHC-based symptom screen at different levels of implementation quality (asking only the cough question or asking all four questions consistently).
- TB screening among individuals in HIV/ART care was identified as the main way to find new TB cases.
- With the same amount of funding, an additional 2 000 active infections could be identified with higher quality mass screening at PHC (four questions consistently asked, improving the sensitivity of the approach).
- Some investment for outreach in high-risk areas to diagnose hard to reach populations would be desirable, but a significant increase in spending would be needed to identify a similar number of active TB cases.
- To sustain the current number of active-TB cases found, slightly less spending would be required if the currently sub-optimal coverage of DS-TB contact tracing was increased.

Improving treatment of MDR-TB through new second-line drugs

- To cover 75% of all diagnosed cases with current PLHIV MDR-TB regimens, a ZAR 10M increase in DR-TB spending would be needed.
- An additional 10% spending would be required to sustain treatment coverage but move from older MDR regimens to short courses.

Increasing preventive therapy to high risk populations including PLHIV

The effect of increasing IPT coverage in newly diagnosed PLHIV from 38% to 65%, as a distinct intervention or combined with other key interventions was explored.

- IPT had a positive impact on reducing DS-TB and MDR-TB in PLHIV. Increasing ART coverage among all PLHIV from 47% to 65% had however a larger effect.
- IPT scale-up in prison populations had a significant short- and medium-term effect on TB prevalence and expected TB cases. The effect was especially large in HIV-prisoners and to a lesser extent in HIV positive prisoners.

RECOMMENDATIONS

According to the pilot application of Optima TB, important health impact could be gained (35% reduction in active TB cases and 28% reduction in TB deaths by 2022) by sustaining 2016 TB financing of ZAR ~590 million and making specific changes/ reallocations towards optimal allocations, as follows:

- **Reduce pre-treatment loss-to follow-up and increase linkage to care, particularly for MDR-TB:** Facilitate treatment initiation by further integrating point of care, and strengthening de-centralization with healthcare staff and treatment capacity. Also, ensure fit-for-purpose patient monitoring systems including integration of systems between health facilities and laboratories. High-quality treatment initiation counselling (which is likely to make a positive contribution to treatment initiation and adherence) remains crucially important.

- **Use PHC mass-screening funding to strengthen its correct implementation:** Enhance population screening at PHC facilities, by consistently asking all four questions in the symptomatic screening protocol—this can nearly double screening sensitivity, from about 21% to 38%, and address the decreasing yield (approximate investment of ZAR 24 million into quality-enhanced PHC mass-screening replacing low-quality mass-screening services).

- **Transition to shorter drug-regimens for drug-resistant TB:** Investment in newer DR-TB regimens can significantly improve treatment success rates (from 23% treatment success among the estimated new DR-TB infections to as high as 56% treatment success), and accelerate smear-conversion. Estimated spending shifts are ZAR 8 million less for older MDR regimen types, and approximately ZAR 14 million more for new MDR regimens including short-course.

- **Maintain contact-tracing for drug-resistant TB cases:** Continued investment of approximately ZAR 1.4 million into DR-TB contact tracing is expected to identify about 144 MDR-TB infections annually.

- **Reallocate some funding from mass-screening to outreach in high risk areas:** Large investments in outreach programmes are not advisable if current diagnosis coverage levels are to be sustained and budgets remain at similar levels. Modest amounts of funding into outreach (approx. 0.3% of 2016 budget or ZAR 1.4 million), however, can be beneficial and increase TB diagnoses among hard to reach populations. Outreach needs to draw on spatial TB epidemic analysis.

- **Additional scale-up of IPT:** In prisons, IPT scale-up to 30% coverage will yield significant short-term gains in reducing active cases in prison populations (especially in HIV-positive prisoners where a 20-30% reduction in future DS-TB cases was projected). IPT scale-up in the PLHIV population from 38% to 65% will yield moderate to small short-term gains in reducing active cases among adult PLHIV (estimated gains through further ART scale-up to 65% of PLHIV were considerably larger).

- **Improve linkage to TB care in correctional services:** Significant improvements have been achieved in screening practices, treatment initiation and outcomes for prisoners. Additional improvements in diagnosis rates (to 85% for DS-TB) and treatment outcomes (to 90% treatment success for DS-TB), however, could yield up to a 50% reduction in DS-TB prevalence.

- **Maintain Active Case Finding coverage levels in PLHIV:** Uphold current spending of approximately ZAR 178 million on active case finding during HIV/ART routine consultations at PHC, estimated to have identified almost 30 000 TB cases among PLHIV, or 75% of all TB/HIV notified cases, in 2017.

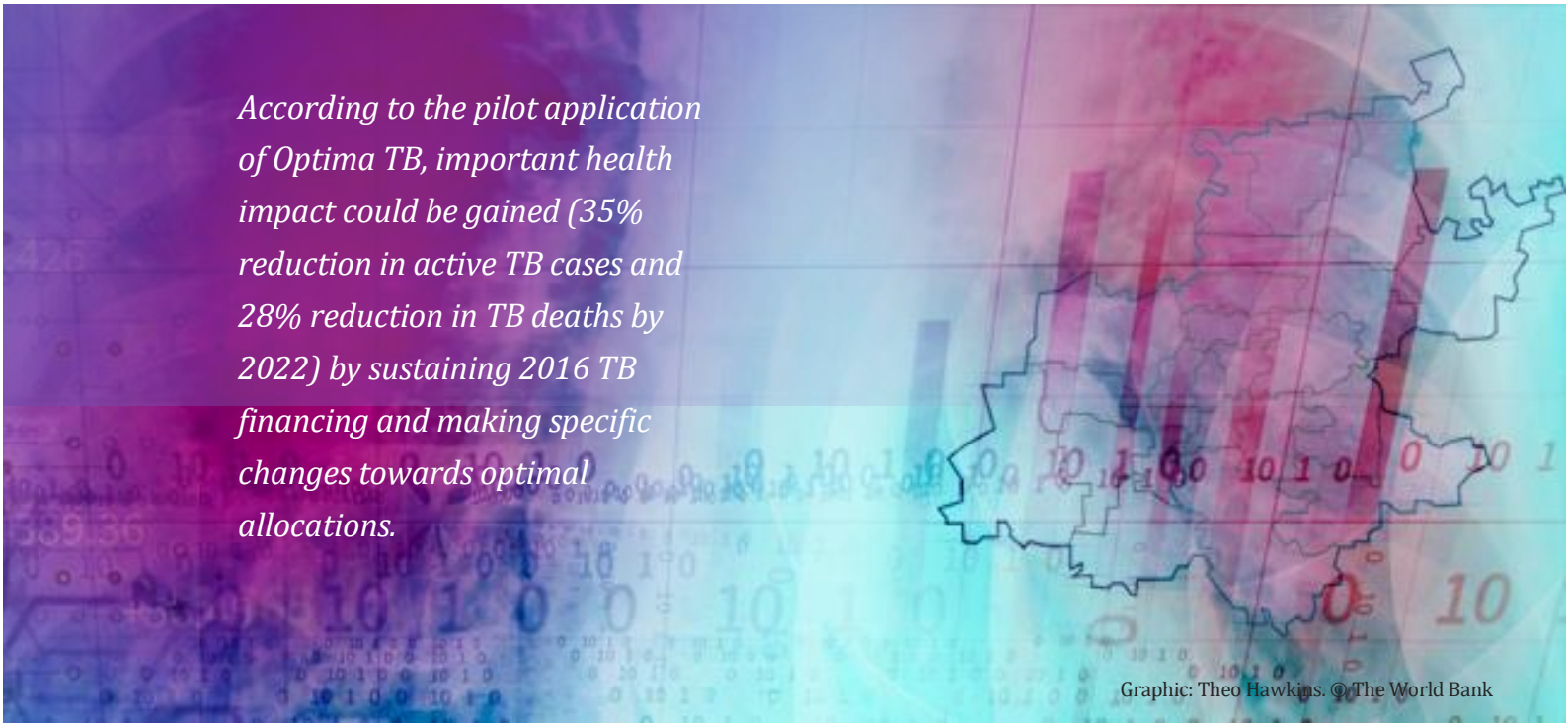
- **Institutionalise DR-TB reporting from all correctional facilities:** All Gauteng prison facilities should report into the national TB surveillance system for DS and DR-TB to track TB in these high-risk settings (and enable analyses like the present one).

- **Enhance TB infection prevention and control for the approx. 55,000 public health care workers in Gauteng:** There is a lack of epidemiological and programmatic data on TB in HCWs in Gauteng (this analysis was not able to include HCWs as a sub-population due to lack of critical data for modelling). A concerted effort is needed to appropriately monitor and analyse the disease burden in this population, ensure that all personal TB protection measures are taken, and that the TB medical surveillance programme is fully implemented.

- **Maximise the integration and use of TB routine data to strengthen programme implementation, and ensure specific M&E activities such as:** Tracking of TB-specific expenditures within the health sector; Reporting of how TB cases are identified (by intervention modality); Systematic analysis of TB treatment outcome data in mining sector (by commodity, TB drug sensitivity and HIV status); Geospatial analysis of key

indicators to target TB interventions; and Exploring patient perspectives on TB prevention, treatment and care services.

- **Further scale-up of ART in the general population:** Increasing ART coverage to 65% of all PLHIV would have a significant positive impact on the TB burden in PLHIV by decreasing active TB prevalence and the number of MDR-TB cases by around 30%



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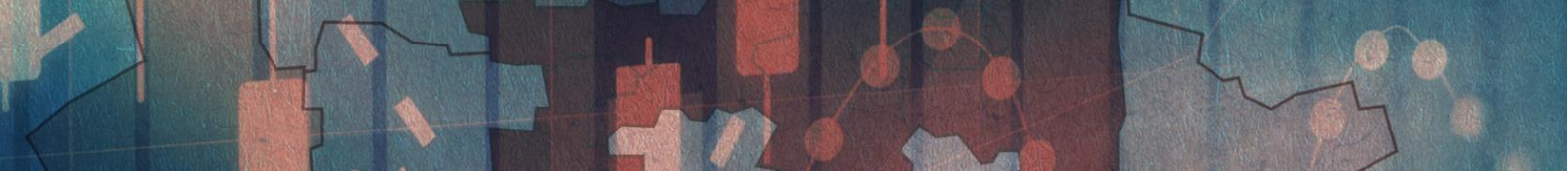


1. INTRODUCTION

This allocative efficiency analysis was designed to pilot and refine a new decision support tool for TB responses, called Optima TB. The report presents the rationale for conducting allocative efficiency studies in TB, the application experiences with Optima TB in Gauteng Province, and the findings of the pilot study. These findings cover both the learning from the model application for the further development of Optima TB, and the analysis results regarding the allocative efficiency of Gauteng's TB response. The Gauteng pilot study was conducted jointly with the South African National Department of Health and Gauteng Department of Health. It was specifically planned to help refine the Optima TB model for the HIV/TB co-epidemic setting.

1.1 NECESSITY FOR ALLOCATIVE EFFICIENCY IN SOUTH AFRICA'S TB RESPONSE

South Africa continues to experience severe TB and HIV epidemics. Despite significant progress in many aspects of the TB response, TB has remained a major public health threat. The disease has been the leading cause of death in 2014, 2015 and 2016, although the proportion of deaths due to TB declined in the three-year period from 8.3% in 2014 to 6.5% in 2016.[1] Nationally, the TB disease incidence rate has been on a slow downward trajectory.[2] For 2016, the rate was estimated at 781 per 100 000 population, resulting in an estimated 438 000 new TB infections, 59% of which were among people living with HIV (PLHIV).[3] South Africa has the highest burden of HIV co-infected TB cases globally, estimated at 258 000.[4] Given the sustained transmission of TB, the TB prevalence rate has not been reducing much since 2010 according to government's assessment underpinning the National Strategic Plan on HIV, STIs and TB 2017-2022 (NSP).[5] Multidrug-resistant TB (MDR-TB) is a growing problem with the number of diagnosed MDR-TB cases doubling from 7 350 notified cases 2007 to 14 161 cases in 2012).[6] Survey data point to the increase in the rate of rifampicin resistance (RIF-R) from 3.4% in 2001 to 4.6% in 2012–2014.[7] The high HIV/TB co-infection rate implies careful case management to ensure adherence to the sometimes complex treatment regimens.

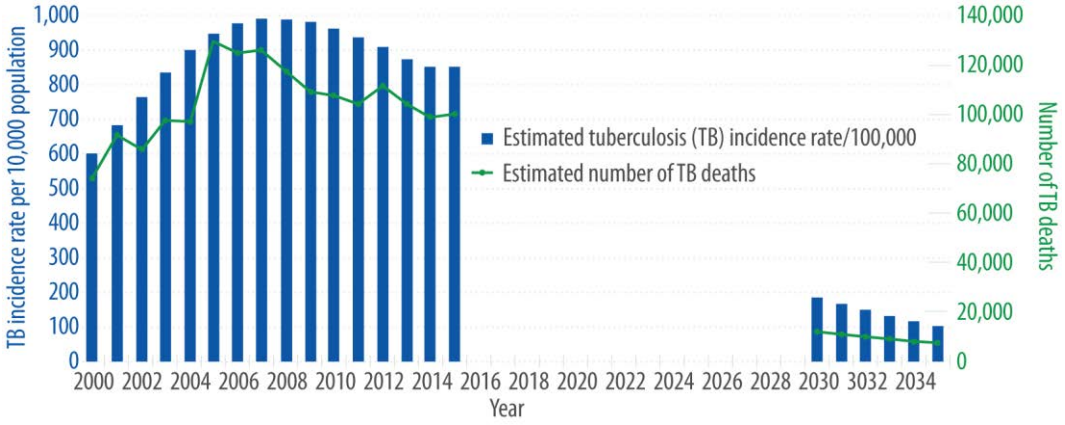
At the heart of NSP 2017–22 is the strategy to "focus for impact" using best data and evidence. This is being operationalised via a geographical focus on the 19 districts with the highest TB burden and the 27 districts that account for 82% of all PLHIV and the majority of new HIV infections.

At the heart of NSP 2017–22 is the strategy to "focus for impact" using best data and evidence. This is being operationalised via a geographical focus on the 19 districts with the highest TB burden and the 27 districts that account for 82% of all PLHIV and the majority of new HIV infections. It also means that efforts to address TB and HIV in high-risk key and vulnerable populations are redoubled by government. The NSP highlights the following high-risk groups for TB: Prison inmates and staff[8], gold mine workers with TB rates of 3 000–7 000 per 100 000[9,10], diabetes cases with an estimated TB rate of 2 760 per 100 000[11] and

health care workers (HCW) who experience high exposure to TB, including drug-resistant (DR) strains.[12,13]

While the estimated national TB disease incidence rates and TB mortality have, as mentioned above, been on a downward trajectory, the rate of decline has been found too slow to meet the 2030 Sustainable Development Goals (SDG) or the 2035 End TB Strategy targets.[14] Naidoo et al. (2017), by extrapolating from WHO estimates, projected that by 2030 and 2035, TB disease incidence rates for South Africa would need to decrease to 167 and 83 cases per 100 000 population, respectively, and mortality would need to fall to 9800 and 4900 cases, respectively (**Figure 1.1**). The analysis by Naidoo and colleagues concluded that reaching these targets would require an improved response from the National TB Programme.

Figure 1.1 Estimated tuberculosis incidence and mortality in South Africa and projected sustainable development goals and End TB Strategy targets



Source: Naidoo et al. (2017), "The South African Tuberculosis Care Cascade: Estimated Losses and Methodological Challenges".

Notes: Data on the estimated TB disease incidence rates and mortality for 2000 to 2015 are from the revised time series analysis of global tuberculosis burden published by the WHO in 2016. Projected figures for 2030–2035 are based on targets relative to the 2015 estimates and assume a straight-line decline in TB disease incidence rates and mortality in this period

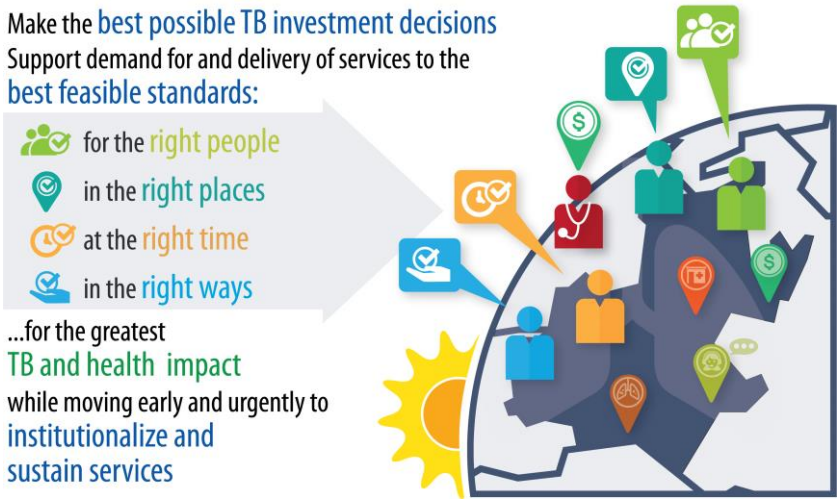
The need for an efficient and targeted TB response is clearly stated in the NSP 2017-2022. The strategy emphasises, among others, the need to:

- allocate resources strategically to achieve impact
- find the missing 150 000 cases who need to receive TB treatment and their contacts
- introduce new TB regimens for TB to reducing the burden of disease and improve the quality of life for those on TB treatment
- close gaps in the treatment cascade, with dedicated resources applied to improving quality and strengthening of adherence support
- linking and integrate services to better address co-morbidities
- succeed in the various prevention interventions to reduce new active TB infections
- provide differentiated care, to ensure a people-centred approach which can also contribute to the reduction of stigma and discrimination

Importantly, the NSP 2017-2022 promotes a vision of "moving from TB control to targeted elimination". This requires targeted, data-informed interventions which progressively improve TB prevention and cure.

In order to meet the ambitious vision and strategic TB targets, and to maximise what can be achieved with available TB resources, it is therefore important to **assess the best funding allocations across the different TB interventions**. **Optimal allocation distributes budgets to the most efficient, targeted interventions and services, based on evidence**. Allocative efficiency analysis asks *How can available resources be optimally allocated to achieve the stated objectives?* **Figure 1.2** summarises the concept making reference to the importance of delivering the right services to the correct target groups, at the right time and in the right places, in order for TB investments to succeed.

Figure 1.2 Allocative efficiency in the TB response



Source: Adapted for authors' design.

1.2 SPENDING PATTERNS ON TB IN SOUTH AFRICA

TB services in South Africa are funded through public revenue, external development partners, and the private sector, which includes company contributions and some individuals' out-of-pocket expenses. The latter are low because the government provides TB diagnosis and treatment for free. Spending within the HIV programme is of course equally important in order to control TB, since TB is the main opportunistic infection in individuals with advanced HIV. The public HIV allocations in the health budget have seen significant growth from ZAR 966 million in 2004/5 to ZAR13.6 billion in 2014/15, representing a 1400% growth over a decade.[15] The HIV budget allocations grew by 15% between 2013/14 and 2015/16 on an annual average nominal basis.[16] Spending on both TB and HIV in South Africa happens within a context of very limited fiscal space overall.

Spending within the HIV programme is of course equally important in order to control TB, since TB is the main opportunistic infection in individuals with advanced HIV.

The comprehensive spending assessment on HIV and TB undertaken for the South African HIV/TB Investment Case found that the total spending on HIV and TB combined in South

Africa increased from ZAR 17.4 billion in 2011/12, to ZAR 19.2 billion in 2012/13 and to ZAR 22.1 billion in 2013/14, representing an average annual increase of 16% over the three years.[17] Of these amounts, the largest and growing contribution came from the South African government. These public contributions formed 80% of the total HIV and TB spending in 2013/14 and occurred at a time when the South African economy was declining, and public expenditures were being reduced. Almost all public revenue for HIV and TB (93.4%) flows through the Department of Health in South Africa.

PEPFAR provided the second largest share at ZAR 3.7 billion (17%) in 2013/14 while the Global Fund contribution was ZARR 662 million (3%) in the same financial year. Of the total spending, HIV-related activities accounted for 82% and TB for 18%.[18] Total amounts reported from the HIV/TB spending assessment are shown in **Table 1.1**. These total amounts were split across the nine provinces with the bulk of the funding going to KwaZulu-Natal (23%), Gauteng (16%) and Eastern Cape (12%), and much smaller amounts going to Limpopo, Free State, North West (6% each), and Northern Cape (2%).[19]

Table 1.1 Total spending by TB, HIV/TB and HIV in South Africa (ZAR, 2011/12–2013/14)

Spending (ZAR)	2011/12	2012/13	2013/14	Grand total	% share (over 3 years)
TB	3 376 879 676	3 347 469 461	3 741 386 861	10 465 735 998	18%
HIV/TB	226 762 744	170 405 661	388 817 295	785 985 700	1%
HIV	13 774 978 081	15 686 235 058	17 999 562 790	47 460 775 929	81%
Grand Total	17 378 620 502	19 204 110 179	22 129 766 946	58 712 497 627	100%

Source: Guthrie et al. (2015). Consolidated spending on HIV and TB in South Africa (2011/12–2013/14). Results for Development, November 2015.

The same detailed spending assessment also classified the TB spend of FY2013/14 using the public sector's Basic Accounting System (BAS), which government uses for planning and resource purposes as well as for broad tracking of expenditures. **Table 1.2** shows Government and PEPFAR spend by BAS category. Hospital-based TB treatment and TB diagnostics each made up about a quarter of the total spend, followed by ambulatory TB treatment and HIV/TB integration activities.

Table 1.2 TB total spending according to the SA BAS categories (ZAR, 2013/14)

Spend by BAS category	Government	PEPFAR	Total	% share
TB control/management/surveys	70 224 101	–	70 224 101	1.7%
TB treatment (clinics or outpatient)	832 439 237	–	832 439 237	20.4%
TB treatment (hospitals)	1 076 390 840	–	1 076 390 840	26.4%
TB treatment not disaggregated	–	294 094 020	294 094 020	7.2%
TB XDR/MDR treatment	447 238 662	–	447 238 662	11.0%
TB/HIV (Integration)	341 110 731	–	341 110 731	8.4%
TB Diagnostics	1 021 000 000	–	1 021 000 000	25.0%
Total	3 788 403 572	294 094 020	4 082 497 592	100.0%

Source: Guthrie et al. (2015). Consolidated spending on HIV and TB in South Africa (2011/12–2013/14). Results for Development, November 2015.

Table 1.3 summarises DOH public TB spending by funding stream and BAS category. For TB (as opposed to HIV with its conditional grants), the largest portion of funding becomes available through the voted portion of the budget, the equitable share. This Government allocation is revenue raised nationally to enable provinces and municipalities to provide TB services and perform functions allocated to them within the response. Of all of the DOH public funds for TB, a large portion (87.5%) was channelled through the equitable share, followed by the DOH's conditional grant (11.8%).

Table 1.3 Total DOH public spending on TB by funding source and BAS category (ZAR, 2013/14)

DOH HIV & TB Interventions	DOH HIV CG	DOH Voted (Equitable Share)	Other DOH public funds	Grand Total	% Share (2013/14)
TB control/management/ surveys	14 485 421	47 712 869	8 025 811	70 224 101	1.8%
TB treatment (clinics or outpatient)	–	832 439 237	–	832 439 237	21.3%
TB treatment (hospitals)	(15 711)	1 058 829 158	17 577 392	1 076 390 840	27.5%
TB XDR/MDR treatment	–	447 238 461	201	447 238 662	11.4%
TB/HIV (Integration)	340 892 100	218 632	–	341 110 731	8.7%
Training	107 092 488	15 761 541	–	122 854 030	3.1%
Workplace prevention	–	1 703 248	–	1 703 248	0.0%
TB Diagnostics	–	1 021 000 000	–	1 021 000 000	26.1%
Total	462 454 298 (11.8%)	3 424 903 146 (87.5%)	25 603 404 (0.7%)	3 912 960 849	100.0%

Source: Guthrie et al. (2015). Consolidated spending on HIV and TB in South Africa (2011/12–2013/14). Results for Development, November 2015—using DOH national and provincial BAS records 2013/14.

In line with the vision of the national development plan and outcome 2 (a long and healthy life for all South Africans), the DOH focus over the medium term is to sustainably expand HIV and TB treatment and prevention, to revitalise public health care facilities, and ensure the provision of specialised tertiary hospital services.[20] According to the Treasury, spending on these three areas take up 85% of the department's total budget over the 2014-2019 MTEF period. **Table 1.4** shows the seven-year expenditure trends for TB, HIV and health programmes overall, as well as annual and average growth. The following observations can be made:

- TB expenditure grows at a much lower rate (6.7% on average) than the expenditure for HIV (16.5%) or for health programmes (11.3%)
- The annual growth rates for TB fluctuate whereas HIV and health have more stable growth rates
- Dedicated TB funding streams are a small fraction of the budget for health programmes (0.1%), and a large share of health spend is for HIV (41.6%)

Table 1.4 Expenditure trends in TB, HIV and health (MTEF, 2014/15–2020/21)

ZAR (million)	Audited outcome			Adjusted appropriation	Medium-term expenditure estimate			Average growth (%)
	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21	2017/18–2020/21
TB	**21.8**	**20.1**	**24.3**	**26.3**	**27.2**	**27.7**	**30.6**	–
Growth	–	-7.8%	20.9%	8.2%	3.4%	1.8%	10.5%	6.7%
HIV	**12 572.8**	**13 962.5**	**15 712.5**	**18 024.4**	**20 441.5**	**22 582.3**	**25 008.2**	–
Growth	–	11.1%	12.5%	14.7%	13.4%	10.5%	10.7%	16.5%
Health	**33 539.0**	**35 984.9**	**38 496.2**	**42 595.6***	**47 142.9**	**51 453.4**	**56 269.3**	–
Growth	–	7.3%	7.0%	10.6%	10.7%	9.1%	9.4%	11.3%
TB as % of health	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*
HIV as % of health	*37.5%*	*38.8%*	*40.8%*	*42.3%*	*43.4%*	*43.9%*	*44.4%*	*41.6%*

Source: Treasury 2018 estimates (tables Vote 16) in: National Treasury (2018). Estimates of National Expenditure 2018; * = Revised estimate.

1.3 SOUTH AFRICA'S NATIONAL HIV AND TB INVESTMENT CASE

The government developed in 2015 a national HIV and TB investment case to identify and set out funding priorities and describe the long term returns.[21] Based on a systematic review of cost-effectiveness data, the most cost effective mix of interventions to combat HIV and TB were identified. The Published in March 2016, the investment case helps to guide national-level decisions about which interventions are the "best buys" for achieving HIV and TB targets. It made the following conclusions:

On reducing TB disease incidence - Even with combined aggressive strategies for TB and HIV, the 2030 and 2035 WHO targets will be missed, with TB disease incidence plateauing around 2020. Additional reductions in incidence will require new tools for TB prevention and diagnosis which also result in reducing TB disease incidence among HIV-negative individuals.

On reducing TB mortality - The TB 90-90-90 scenario likely reaches the 2025 target for 75% reduction in TB deaths, but further interventions or new tools would be necessary to bring down TB mortality to the 2035 target of a 95% reduction. Implementing at the same time the HIV 90-90-90 scenario, the reduction in TB mortality will be considerably greater.

The investment case also demonstrated the importance of collaborative HIV/TB programmes. It concluded, for instance, that ART expansion could serve as a platform to strengthen monitoring and linkage of patients at high risk of developing active TB.

For TB, the investment case recommended that additional investment is needed for finding and successfully treating TB cases, and that the package should include comprehensive intensified case finding, diagnosis and high quality treatment (as well as a continued focus on investment in the HIV treatment programme). To support the implementation of the TB recommendations, and to ensure the sustained expansion of HIV treatment, the Treasury considered the need to allocate increased funding amounts (see **Table 1.4** for most recent

Treasury estimates). The prioritised investment into the *Comprehensive HIV, AIDS and TB conditional grant* was expected to improve case detection and to increase the TB treatment success rate from 83% to 90% by 2018/19.[22]

1.4 STUDY FOCUS ON GAUTENG PROVINCE

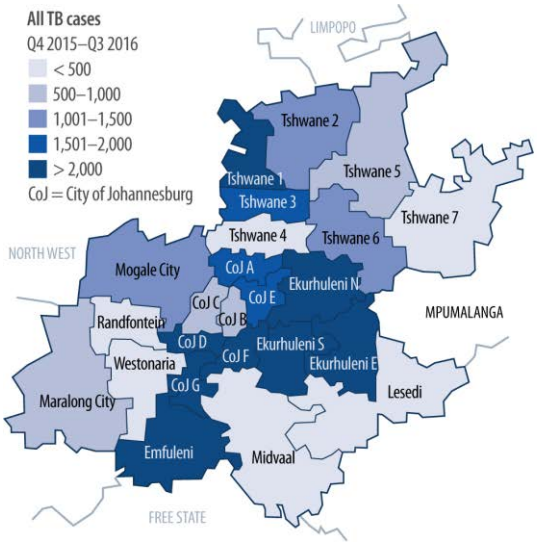
The NSP 2017-2022 identifies 19 districts of South Africa as TB high-burden districts. Of the five districts of Gauteng Province, four are classified in the NSP as **high-burden** (City of Johannesburg, Ekurhuleni, City of Tshwane, West Rand), emphasising the weight the TB epidemic poses on Gauteng.

Gauteng is the most urban province of South Africa with three metros and an estimated population of 14.3 million in 2016.[23] There are areas of very high population concentrations, and socio-economic inequalities are especially large in this province. As per 2016 estimates, HIV prevalence was 13.1% and ART coverage among all PLHIV about 54% (2017 Thembisa model Gauteng, ART coverage under universal eligibility). The local TB burden is determined by dynamic and varying co-factors ranging from living conditions to social and health determinants as well as health system factors.[24]

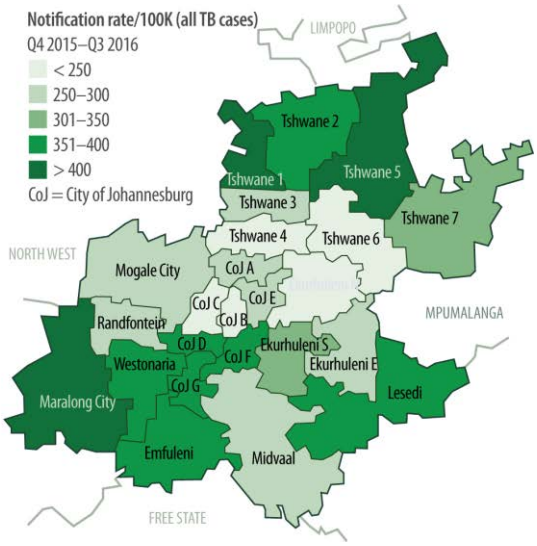
As part of the allocative efficiency analysis, geospatial mapping of key TB indicators was carried out to explore the heterogeneity of the TB epidemic in Gauteng and capture the spatial dimension of the epidemic across its sub-districts, using 12 months of routine surveillance data (**Figure 1.3**, Ekurhuleni only disaggregated to district level). Regarding TB cases notified (left map), there was large heterogeneity across the province indicating the differential burden of cases the local services have to manage. Notification rates (right map) also varied significantly but the pattern was different as the population denominator is factored in in this metric. It ranged from below 150/100 000 population (Tshwane 4, Joburg B and C) to over 400/100 000 population (Tshwane 1 and 5, Merafong City).

Figure 1.3 Geospatial maps of notified TB cases by sub-districts, Gauteng (2016)

LEFT: Number of all TB cases notified



RIGHT: TB notification rate/100 000 population

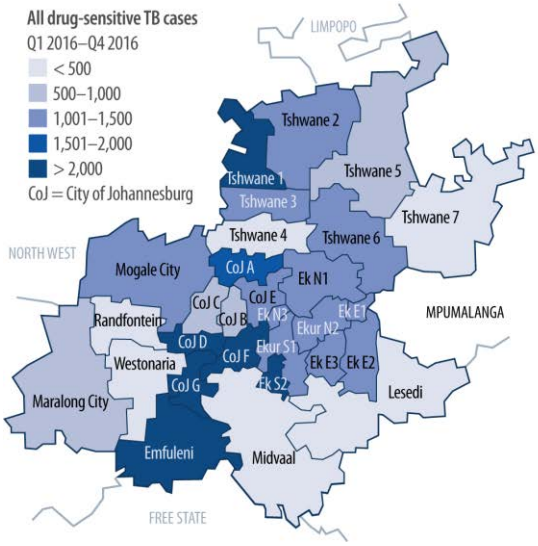


Source: Routine TB surveillance data from October 2015 to September 2016.
Note: Ekurhuleni only disaggregated to district level, Q = quarter; TB = tuberculosis

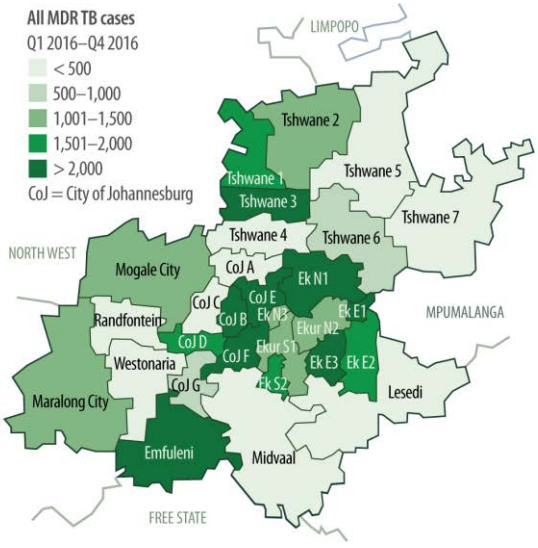
Figure 1.4 shows strain-specific notification data for the 27 sub-districts for 2016. The number of cases of DS-TB (left map) and MDR-TB (right map) notified at the respective health facilities was also highly disparate with DS-TB ranging from below 500 cases to over 2000 cases per sub-district and year and MDR-TB ranging from below 15 to over 90 cases.

Figure 1.4 Geospatial maps of notified DS and MDR TB cases by sub-districts, Gauteng (2016)

LEFT: All DS-TB cases notified



RIGHT: All MDR TB cases notified



Source: Routine TB surveillance data from October 2015 to September 2016.
Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; Q = quarter; Additional spatial maps are presented in **Appendix D.**

By early 2017, the TB situation in Gauteng Province was characterised in brief by:

- Progress in many aspects of the TB response, but facing ambitious strategic targets
- A steady increase in DR-TB case numbers
- Insufficient treatment initiation and success for MDR-TB
- New treatment regimens and strategic options available

The Gauteng DOH Strategic Plan for Health 2015/16-2019/20 states

> *We want to **reduce the number of TB cases** even further.*
> *We want to increase the **quality, efficiency and accessibility** of our care.*
> ***To achieve this, we need to think differently and do things differently.***

Given the burden of TB morbidity and mortality in this populous province, the approximately 2 million PLHIV present in Gauteng, the continued importance of the mining sector, labour migration and industries, as well as the good data availability and the relatively tight fiscal space, the South Africa National Department of Health (NDOH) requested the World Bank as technical partner (**Box 1.1**) to conduct an allocative efficiency analysis for the TB response in this province.

Box 1.1 World Bank support to improve allocative efficiency in health

The World Bank supports countries in their efforts to achieve Universal Health Coverage (UHC) through a range of strategies relating to health sector reform, health financing as well as analytical support to enhance efficiency and effectiveness of health service delivery. Within the broader **support towards enhancing efficiency and effectiveness of health programmes**, the concept of allocative efficiency refers to the maximization of health outcomes, with the least costly mix of health interventions.

As part of its wider support, the World Bank in collaboration with other partners has supported **disease-specific allocative efficiency studies** in more than 40 countries. Initially, the focus of allocative efficiency studies was on HIV responses. The focus has now expanded towards TB, nutrition, malaria, NCDs and health service prioritisation. TB allocative efficiency studies generally try to answer the question, "How can TB funding be optimally allocated to the combination of TB response interventions that will yield the highest impact?"

There is wide consensus that better outcomes could be achieved in many settings with a given amount of TB funding; or that given outcomes could be achieved with less TB funding if resources are distributed optimally or if resources are used in the most efficient ways. Mathematical modelling is one way to determine optimised TB resource allocation.

An allocative efficiency study of Johannesburg's HIV response was carried out within the District Implementation Plan process and the Fast-Track Cities Initiative in 2016, using the Optima HIV model.[25,26] On the basis of this previous collaboration it was suggested that a similar analysis be undertaken of the Gauteng TB response, using an early version of the Optima TB model. The South African National Department of Health (NDOH) and Gauteng Department of Health agreed, jointly with the health authorities in Belarus and Peru, to participate in the piloting phase of Optima TB and document application lessons. This would then enable the development team of Optima TB to refine the tool before its release as a global public good (for Optima TB, see http://ocds.co/tb/).

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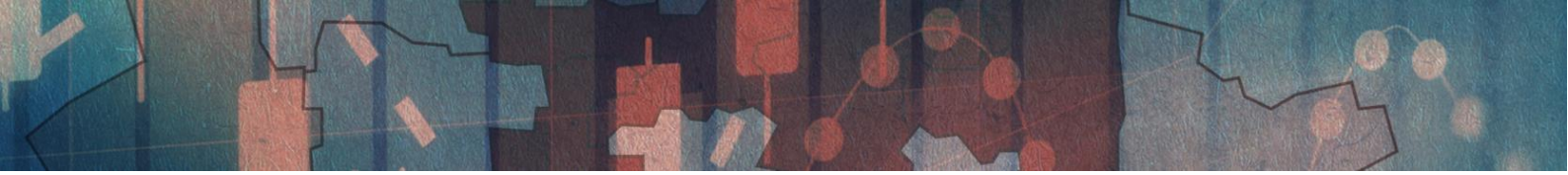

2. STUDY QUESTIONS AND METHODOLOGY

This section outlines the questions posed in this pilot application of Optima TB, and the main steps taken to carry out the analyses presented in this report. Additional details are available in **Appendix A** (Technical summary of Optima TB) and **Appendix B** (Data inputs into the model).

2.1 ALLOCATIVE EFFICIENCY QUESTIONS ADDRESSED

To support Gauteng in its decision-making on TB resource allocations, this pilot study set out the answer several policy questions which were developed with the key stakeholders in the initial planning and methodology workshop. These are:

- A. WHAT IS THE EPIDEMIC TREND OF TB IN GAUTENG?

  What are the number of active TB cases, latent infections, TB disease incidence, TB prevalence and TB-related deaths, by age group, HIV status, general/key-population status, and by resistance type?

- B. HOW CLOSE CAN GAUTENG GET TO ITS 2020 PROVINCE-LEVEL TB TARGETS?

  Over the period of the *Gauteng Provincial DOH Strategic Plan for Health 2015/16 - 2019/20*, how close can Gauteng get to the 2020 strategic TB targets:

  - With current funding, allocated according to current expenditure?
  - With current funding, allocated optimally?

- C. TARGETING TB PROGRAMMES AND INTERVENTIONS ACROSS SUB-POPULATIONS: CAN TARGETING RESOURCES TO SELECTED KEY POPULATIONS IMPROVE OUTCOMES?

- D. CAN GAUTENG MEET THE 2022 NSP TARGETS WITH CURRENT/PROJECTED FUNDING?

  Over the period of the *National Strategic Plan on HIV, STIs and TB 2017-2022*, how close can Gauteng get to 2022 strategic TB targets?

  - With available funding, allocated according to current expenditure?
  - With available funding, allocated optimally?
  - How will Gauteng's TB trends change under different funding scenarios?

- E. HOW MUCH FUNDING IS REQUIRED TO ACHIEVE THE 2022 NSP TB TARGETS?

  Given current programme implementation practices and costs:

  - How much total funding is required to meet the NSP targets?
  - How could this funding be optimally allocated between interventions?

- F. WHAT IS THE EXPECTED FUTURE IMPACT OF SPECIFIC RESPONSE SCENARIOS IDENTIFIED?

  - Improve links to TB care
  - Scale-up short-course regimens for MDR

- Intensify case-finding, mass screening and active case finding in combination
- Improve treatment of MDR-TB through new second-line drugs
- Increase preventive therapy to high risk populations including PLHIV

Progress toward the END-TB 2035 targets and the intermediate 2025 WHO TB milestone are also reflected in this analysis.

2.2 METHODOLOGY

Collaboration and stakeholder involvement

This pilot application of Optima TB was a collaboration between the South Africa NDOH, the Gauteng Provincial Department of Health, the National Health Laboratory Service (NHLS), the World Bank and the Optima Consortium of Decision Sciences (OCDS).

Focal Points were assigned within each of the organisations to implement the analysis and coordinate contributions. A group of experts and key informants was brought together in two workshops to provide input into the policy questions and analytical framework, share data and expertise, and review the outputs of the analysis.

The proposed analysis was described in a Scope of Work document and agreed upon. Epidemiological, programme, and cost data were collected in a joint effort using an adapted Excel-based Optima TB data entry spreadsheet. WamTechnology, on behalf of the NDOH, provided detailed breakdowns of TB routine data based on the model compartments and sub-populations defined for the analysis. In order to establish baseline spending on TB, the BAS was used on TB specific funding streams, with the Gauteng DOH Finance Unit providing a level 4 expenditure analysis and overall guidance. The disaggregated expenditure data was then triangulated with unit cost estimates to estimate TB spending by intervention.

Input data, model calibration and cost-coverage-outcome relations were reviewed and validated by the in-country study group. The team then consulted with government experts and other in-country partners on the preliminary results and summarised them in this report. Findings were brought into the Gauteng APP 2018/19 in order to ensure the insights gained from the analysis could be used in priority setting in Gauteng's TB response.

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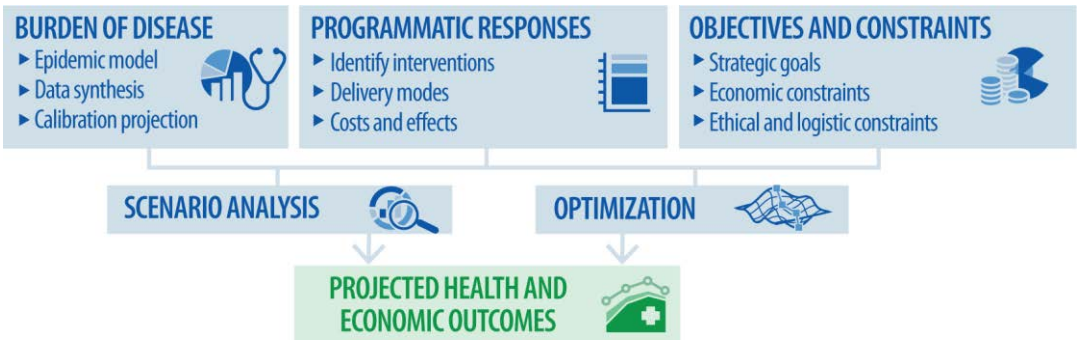
Technical review

The TB Think Tank organised the peer review of the draft report by local experts and provided detailed comments in writing. Additional material on the model calibration was made available to the local reviewers upon request. The report writing team then responded point-by-point to the TB Think Tank. Using a comments-response matrix, the authors proposed specific edits to be made in the report in order to address each review comment. No re-analysis or re-modelling was conducted at this stage, as per agreement with the review team. However, the authors outlined in the report how the new version of Optima TB incorporated the learning from the Gauteng analysis, and expanded the report as needed to do justice to the many excellent points raised during the technical review process.

Optima TB model

Optima TB, a mathematical model of TB transmission and disease progression integrated with an economic and programme analysis framework, was used (**Figure 2.1**).

Figure 2.1 Schematic on the Optima approach to TB modelling



Source: Adapted for authors' design

Optima TB incorporates evidence on biological transmission probabilities, detailed infection progression and population mixing patterns, in a compartmental model, which disaggregates populations into different model compartments including *susceptible, vaccinated, early latent, late latent, undiagnosed active TB, diagnosed active TB, on treatment and recovered* populations. In addition, compartments are further disaggregated by drug resistance types into drug susceptible (DS), multi-drug resistant (MDR) and extensively drug resistant (XDR). A more detailed illustration of the compartmental model structure is included in **Appendix A**.

In consultation with national and province-level experts and in the absence of a TB prevalence survey, Optima TB was calibrated primarily based on data on TB case notifications and registered TB deaths.

To assess how incremental changes in spending affect TB epidemics and determine an optimised funding allocation, the model parameterises relationships among the cost of TB interventions, the coverage level attained by these interventions, and the resulting outcomes (cost-coverage outcome relations). These relationships are specific to the place, population, and intervention being considered.

Using the relationships among cost, coverage, and outcome in combination with Optima TB's epidemic module, it is possible to calculate how incremental changes in the level of funding allocated to each intervention will impact on overall epidemic outcomes. Furthermore, by using a mathematical optimisation algorithm, Optima TB is able to determine an optimised allocation of funding across different TB interventions. Additional details about Optima TB and the Gauteng application are included in **Appendices A and B**.

By using a mathematical optimisation algorithm, Optima TB is able to determine an optimised allocation of funding across different TB interventions.

Analytical framework

Model parameters are summarised in **Table 2.1** and detailed in **Appendix B.**

Table 2.1 Model parameterisation

Category	Parameterization in the Optima model	Description/Assumptions
Populations defined in the model	General Population (0–4 years)	Male and Female Children aged 0–4
	General Population (5–14)	Male and Female Young Population aged 5–14
	HIV+ adults (15–64)	Male and Female PLHIV aged 15–64
	HIV– adults (15–64)	Male and Female HIV negative aged 15–64
	HIV+ adults (65+)	Male and Female PLHIV aged 65+
	HIV– adults (65+)	Male and Female HIV negative aged 65+
	HIV+ prisoners	Males and Female HIV positive prisoners
	HIV– prisoners	Male and Female HIV negative prisoners
	HIV+ mining employee	Male and Female PLHIV employed in gold mines
	HIV– mining employee	Male and Female HIV negative employed in gold mines
Programme expenditure areas defined in the model and included in optimisation analysis	Old MDR and XDR Regimens	These include the standardised MDR-TB drug regimen (24 months), as well as the standardised MDR-TB regimen with the addition of BDQ. These old MDR/XDR regimens were not included for prisoners and miners.
	Short-Course MDR Regimens	These include the 9-12-month Kanamycin drug regimen (24 months), as well as the mentioned treatment course with the addition of BDQ
	New MDR Regimens for PLHIV and Key Populations	These include the new,[27] shortened BDQ 20-month regimen, 9-12-month Kanamycin short-course, as well as the mentioned short-course with the addition of BDQ
	Isoniazid Preventive Therapy	IPT is added on for non-active TB cases identified through contact-tracing, and new HIV+ cases on ART identified through ACF in PLHIV: Assumed the average cost and treatment outcomes of 6- and 12-month regimens
	BCG Vaccination	Vaccination with Bacillus Calmette-Guérin targeting the 0–4 population
	Passive Case Finding across all Populations	Diagnosis package for people who present to the health facility with symptoms; includes a GenXpert test, two sputum smear microscopies and two cultures or culture coupled with LPA
	Mass Screening at PHC	Current practice of mass screening PHC clients with symptom screen
	Enhanced Mass Screening at PHC	Improved mass screening of PHC clients asking all four symptom questions consistently for improved sensitivity
	Active Case Finding among PLHIV Populations	Active case-finding by targeted screening of high-risk groups with chest X-rays
	Screening Outreach in High-risk Areas	Active case-finding in hotspots/high transmission areas
	Contact Tracing of DS-TB cases	Investigation of DS TB-contacts and follow-up treatment with IPT preventative therapy for suspected LTBI
	Contact Tracing of DR-TB cases	Investigation of DR TB-contacts and follow-up treatment with IPT preventative therapy for suspected LTBI

Table 2.1 continued…

Table 2.1 Model parameterisation (continued)

Category	Parameterization in the Optima model	Description/Assumptions
Expenditure areas not optimised	The components of TB spending that were not included in the optimisation analysis	Some programme areas have not been optimised but instead were fixed at agreed amounts. This was done for different reasons: Due to an unclear relationship between an intervention and its effect on TB disease incidence, morbidity or mortality, or because there was no detail on what the expenditure was for.
	Passive case finding (HIV+)	Fixed at ZAR 7,956,362
	Passive case finding (HIV–)	Fixed at ZAR 9,020,991
	Other testing & monitoring	Fixed at ZAR 75,371,510
	Other costs	Fixed at ZAR 5,082,944
Years and time horizons	2000	Year of model initiation, start year for data entry
	2016	Base year
	2017/18–2019/20	Timeframe Gauteng Province APP TB targets
	2017–22	Timeframe National Strategic Plan on HIV, STIs, TB
	2030	Target year for achievement of SDG targets
	2035	Target year for End TB Strategy
Baseline scenario funding	As per authors' expenditure analysis	Total spending on TB in 2016 as per this study's expenditure analysis drawing on level 4 BAS analysis by DOH and costings

Based on spending per person reached with an intervention, cost-coverage-outcome relations were developed. Calibrations and cost-coverage outcome relations were produced in collaboration with in-country experts and are further explained in **Appendix A**, while unit costs are included in **Appendix B.** Scale-up scenarios presented in this report use gradual increases from 2017 until 2035.

Factoring in of the HIV epidemic

In recognition of the importance of the HIV epidemic in the Gauteng TB setting, the following measures were taken to incorporate HIV effects:

- **HIV trends**: The most recent Thembisa model estimate for the number of PLHIV in year 2000 coupled with annual estimates for HIV incidence from 2000 to 2016 for Gauteng were used (Thembisa 2.5 Provincial Outputs were available at the time of this analysis). Optima TB model calibration was performed by first matching to the population size for each population, including to the population size for PLHIV (this is equivalent to calibrating to the prevalence of HIV). The 2016 PLHIV value was held constant to 2035.
- **ART coverage:** Although the provision of ART is financed from non-TB resource streams, it was essential to incorporate the effect of ART on TB dynamics. The ART coverage level for 2000-2016 as per Thembisa 2.5 Gauteng model was therefore factored in. The coverage level under universal ART eligibility was 47.3% for 2016, the base year for the Optima TB model (note that in the latest Gauteng Thembisa model, version 4.1, ART coverage for 2016 and 2017 are at similar levels at 46.0% and 47.7%, respectively). In Optima TB, ART coverage was then kept constant for the projected PLHIV population in order to not make unsupported assumptions about the

future investment in ART within the HIV program. The impact of increased ART coverage on TB dynamics was explored in scenario 8.

- **Optima TB model parameters impacted by HIV:** Co-infection directly impacted nine model parameters whereby each parameter was influenced differently depending on co-infection rates and ART coverage (see Appendices on Optima TB and on TB epidemiological parameters full further details):
    1. Mortality rates (excluding TB-related deaths)
    2. Mortality rates (including TB-related deaths)
    3. Susceptibility to TB infection
    4. TB infectiousness
    5. Departure rate from early TB latency
    6. Probability of latent TB infection versus active TB infection
    7. Proportion of new active TB cases with different smear/strain combinations
    8. Rate of TB diagnosis (by population which may be targeted differently)
    9. Proportion of TB treatment outcomes for each smear/strain combination

Strategic TB targets used in the analysis

The strategic goals under the Gauteng Provincial DOH Annual Performance Plan 2017/18–2019/20 informed the modelling analysis (**Table 2.2** gives targets by year). Targets from the NSP 2017–22 were also consulted, as well as the 2030 SDG and the 2035 End TB Targets, as follows:

- INCIDENCE: Decrease the number of new TB infections by 50% by 2019/20 (NSP: Cut 2016 TB disease incidence by at least 30% by 2022 (SDG global level: Decrease TB disease incidence by 80% by 2030; End TB Strategy by 90% by 2035).
- SYMPTOM SCREEN: Increase number of people screened for TB from 440 000 in 2013/14 to 4 million by 2019/20 (and screen 90% of total population with HIV by 2019/20)
- TREATMENT INITIATION: Increase % of patients diagnosed with MDR-TB initiated on treatment from 75% to 80% by 2019/20
- TREATMENT OUTCOMES: a) Reduce treatment default rate from 5.4% to <5% by 2019/20; b) Increase DS-TB treatment success rate from 89.1% to 95% by 2019/20; and MDR-TB treatment success rate from 55% to 65% by 2019/20 (NSP: Attain at least a 90% treatment success rate for DS-TB and at least 65% treatment success rate for MDR-TB); c) Increase the percentage of people cured of TB from 83% to 85% by 2019/20; d) Decrease TB death rate from 6% to 3.5% by 2019/20 (NSP: Reduce overall TB mortality by 50%. Global level: Reduce DS-TB mortality by 90% by 2030 and by 95% by 2035).

Table 2.2 Annual targets in Gauteng's Annual Performance Plan 2017/18–2019/20

	Audited actual performance		Estimated performance		Medium term		End of plan target
TB Indicator	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20
TB treatment initiation in symptomatic children aged 5+	84%	85%	87%	89%	90%	91%	92%
Treatment success rate	84.5%	85.7%	87.1%	90%	87%	89%	90%
Loss to follow up rate	5.1%	4.8%	5%	5.1%	5.5%	5.5%	5.0%
Death rate	<5%	4.5%	4.4%	<5%	5.5%	5.5%	5.0%
MDR treatment success rate	40%	51.5%	51%	55%	55%	60%	65%
TB/HIV co-infected on ART rate	–	–	75%	85%	88%	90%	90%

Source: Gauteng Annual Performance Plan 2017/18–2019/20

Costing of the diagnostic algorithms

At the time of analysis, Gauteng had rolled out GeneXpert positive and negative algorithms for initial diagnosis. We estimated unit costs of TB tests and the diagnostic pathways using 2016 data in Gauteng province (see **Figure B.1**). The NHLS was the main partner in unit costing, as a similar costing exercise had already been completed in association with the National HIV/TB Investment Case (Market assessment 2012/13). The unit costing of nine major TB tests was conducted by NHLS, based on reagent and consumable costs obtained in the latter half of 2016. Original templates from the previous market assessment by Kate Schnippel were modified and used. Unit costs were built up from costs of consumables, instrument utility, labour and overheads (20%, composed of sample transport 8% and operating expenses 12%). Costs were obtained from the Oracle ERP system and all reagent costs included VAT at 14%. Mid-point cost-to-company salaries were used for all labour costs. The NHLS costing excluded TST (as done at clinics), IGRA (only provided at private labs) and Adenosine deaminase tests (only for EP-TB). Diagnostic algorithms were costed based on guidance in force in 2016/17 (Xpert positive and Xpert negative algorithms, PC101) and literature (Cox H et al., 2015; Pooren A et al., 2013). The various pathways based on lab results were considered for overall TB diagnostic costs, such as Xpert+/Rif-S, Xpert+/Rif-Res, and Xpert-/HIV+, among others. Triage to short-course MDR treatment was included in diagnostic costs. Xpert fails and repeats (2%) were accounted for, as well as other tests/X-rays. The costings extended to case monitoring during treatment and the ascertainment of treatment outcome.

Costing of treatment interventions

We worked closely with partners from the Gauteng DoH to cost TB treatment interventions based on published protocols for implemented interventions and guidance from experts for prospective interventions. We combined the average cost per inpatient day (Sinanovic et al. 2015) and outpatient visit (Pooran et al. 2013) with the number of inpatient or outpatient days specified in protocols or by experts for a given treatment intervention (*see supplementary information:Gauteng Treatment Cost Calculations for Report*). Medication costs were sourced from the 'South Africa Provincial TB Budget Tool' (Version 1.5) and the Master Procurement Catalogue (2017) and

We worked closely with partners from the Gauteng DoH to cost TB treatment interventions based on published protocols for implemented interventions and guidance from experts for prospective interventions.

multiplied by the treatment dose and duration required for different interventions. Other costs related to treatment monitoring and baseline tests were also captured in the costing analysis, for which costs were sourced from the NHLS State Price List (2013) and the TB budget tool. The estimated total cost for each treatment intervention was then validated by comparing with patient management costs estimated by Schnippel et al. 2012, outpatient costs by Cox et al. 2015, and costs reported in the TB consolidated spending report (Guthrie et al., 2015).

Estimation of TB spending in Gauteng

Following the estimation and validation of diagnostic and treatment costs, a bottom-up approach was used to estimate total spending on TB-related activities in Gauteng. Epidemiological and intervention coverage data were combined with diagnostic costs and annualised treatment costs to estimate spending on interventions implemented in Gauteng. With guidance from the Gauteng DoH financing unit, intervention spending was mapped and aggregated to categories tracked in the Basic Accounting System (BAS). The BAS did not track resources used for DS-TB, and only captured budget or expenditure lines related DR-TB, hospital care or medical equipment. However, where available, aggregated intervention spending estimates were in line with spending tracked in the BAS. The spending categories captured in the BAS enabled a validation of 60% of total estimated spending (see **Figure 3.9**).

Limitations of the analysis

Similar to any mathematical modelling analysis, this study encountered challenges of missing data, and therefore had to make assumptions, which necessarily imply certain limitations:

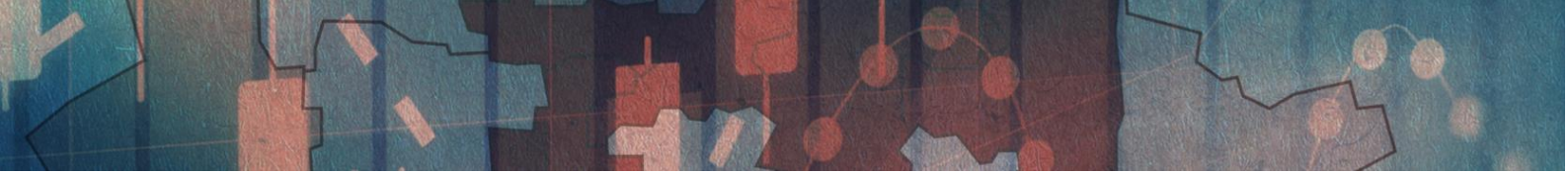
- **Active TB prevalence:** This parameter includes diagnosed and undiagnosed active TB cases and is of key importance in TB modelling (see for example the modelling study by Andrews et al. 2012 "The cost-effectiveness of routine tuberculosis screening with Xpert MTB/RIF prior to initiation of antiretroviral therapy in South Africa: a model-based analysis" which concluded that the most influential parameter on the results was undiagnosed TB prevalence). By mid-2017, there was no TB prevalence survey data available for Gauteng Province or the national level. This meant that routine data on TB notifications formed the basis for estimating disease burden instead of active TB prevalence.
- **People living with HIV:** Relationships between HIV-induced immune depletion, HIV treatment effects and activation of LTBI are complex, and a model necessarily needs to make simplifications. Since the importance of HIV is large in a co-epidemic setting like Gauteng's, limitations on the ability to capture HIV and ART effects in the model may have significant effects. In the model, the main effect of HIV is to increase the probability of progression from latent-TB (esp. early latent) to active-TB. ART among co-infected populations reverts their probability of progression back towards its original value.
- **ART coverage:** In Optima TB, ART coverage was kept constant for the projected PLHIV population which may not have been an ideal choice given NDOH's commitment to roll-out ART to all diagnosed PLHIV within the universal treatment policy. The study team did not want to make assumptions about resource allocations outside the TB funding streams. Retrospectively, the conservative approach appears

acceptable as the Thembisa model reduced ART scale-up expected by 2020 between Thembisa Gauteng versions 2.5 and 4.1 from 71.3% to 59.2%, respectively.

- **TB in key populations:** In response to South Africa's TB Investment Case which found that key populations should be included in TB modelling analyses,[28] an attempt was made to include PLHIV, prisoners, gold mine employees and health care workers. While the study team succeeded with including the first two, it was not possible to include the 57 813 gold mine employees and 54 875 Gauteng public sector HCWs in the full analysis due to major data gaps (see **Table B.2** for all sub-populations defined in this analysis).
- **Relapse and reinfection:** In consultation with the Gauteng TB Programme, the best available evidence on relapse/re-infection were used to inform the model, however, data availability and quality were insufficient to separate the two pathways. Therefore, this aspect was represented in the model by the transition from a 'recovered' compartment (see **Figure A.1**), which included successfully complete treatments, to the active-TB junction upon re-infection rather than re-entering the latency pathway. A constant annual 2% (global average at the time) was applied for the transition rate to capture both re-infection and relapse.
- **TB expenditure data:** Although some TB expenditure assessments has been done, they were generally not current for the model's 2016 base year, or they provided national level data without disaggregation for Gauteng Province, or reported TB spend in very broad expenditure areas only (while this analysis looked at discrete TB interventions). The main source of expenditure data was the Gauteng DOH's Basic Accounting System which is not built to give sufficiently detailed breakdowns of costs by intervention. Also, many expenditures in the TB response don't enter as TB-specific spend in the BAS (e.g., medication for drug-susceptible TB). These limitations were addressed by data triangulation within a level 4 BAS analysis, and estimating spend per category via the use of unit costs (which came from own bottom-up costing and from partners' working documents and the published literature).
- **Cost-outcome relationships:** Cost functions are a critical driver of outcomes in resource optimisation modelling. In the absence of data to inform non-linear cost-coverage curves, linear cost-coverage curves were assumed, and constant unit costs as the study team lacked evidence to make informed assumptions on future changes. The modeling approach used to calculate relative cost-effectiveness among programmes also included assumptions concerning the impact of increases or decreases in funding for interventions. These assumptions were partially based on costs per person reached and observed ecological relationships among outcomes of intervention coverage and the amount of money spent on interventions in the past or in other contexts..
- **Implementation efficiency:** The analysis included considerations of implementation efficiency in a limited way only, as it was beyond the scope of the study. For instance, a reduced drug prices (leading to lower unit costs, better efficiency and cost-effectiveness) were not modelled, although treatment regimens were carefully costed by component cost. Lower unit costs would potentially affect the resource allocation recommendations.
- Intervention effectiveness: Modelling the optimisation of allocative efficiency depends critically on the availability of evidence-based parameter estimates of the effectiveness of individual interventions. Although these estimates were derived from a global systematic literature review, they may vary in specific countries and

populations depending on various factors, particularly the quality of implementation and levels of adherence to interventions. All interventions and spending categories, for which such parameters could not be obtained were not included in the mathematical optimisation. Because they still have important functions in the TB response and use TB budget, they were treated as fixed costs and, in some specific scenarios, adjusted with specific justifications (see **Table 2.1**).

- **Robustness of results:** At the time this pilot study was conducted, the model was not yet set up to conduct sensitivity analyses and uncertainly was therefore not accommodated in this study (which, focussed on adapting the Optima TB model for the HIV/TB setting, running intervention-level expenditure and cost analyses, and providing the stakeholder-requested scenario and optimisation analyses). However, the study team did explore two types of model outputs (active TB cases, diagnosed DS-TB cases) when diagnosis rate and/or ART coverage were varied as these two parameters are both drivers of model results and have some uncertainty attached (see **Figure 3.26** and accompanying interpretation). The conclusions section offers further considerations on sensitivity analysis in this type of modelling study.
- **Non-TB benefits:** Effects outside the TB endpoints are complex to consider (such as the non-TB benefits of different TB treatment modalities). Given the complexity of interactions among interventions and their non-TB benefits, the model did not seek to take into account wider health, social, human rights, ethical, legal, employment-related or psychosocial implications; but acknowledges that they are important aspects to be considered in planning and evaluating TB responses.



3. RESULTS

3.1 WHAT IS THE EPIDEMIC TREND OF TB IN GAUTENG?

This section addresses the first question on the epidemic trends for DS, MDR and XDR TB in in different Gauteng populations since year 2000.

Estimates for the 2016 base year of the Gauteng analysis

Given year 2016 was used as the base year for the analysis, the below tables present Optima TB estimates on active TB (**Table 3.1**), and TB disease incidence, latent infections and TB-related deaths (**Table 3.2**), by sub-population for 2016.

Table 3.1 Model estimates on active TB in Gauteng, by sub-population (2016 base year)

Population	Active TB cases	Active DS-TB cases	Active MDR-TB cases	Active XDR-TB cases	Active TB prevalence
0–4 years	5532	5504	23	4	0.4%
5–14 years	3958	3877	73	8	0.2%
15–64 years HIV–	19883	19045	819	19	0.2%
65+ years HIV–	1760	1686	68	6	0.3%
15-64 years HIV+	55208	49213	2914	80	2.6%
65+ years HIV+	394	382	12	0	2.2%
Prisoners HIV–	370	369	1	0	1.3%
Prisoners HIV+	299	296	2	0	3.2%
Subtotal (HIV–)	31503	30481	986	36	–
Subtotal (HIV+)	52901	49892	2929	81	–
Total	84405	80373	3915	116	–

Source: Optima TB model output, based on data extracted from South Africa's TB surveillance system, demographic data from available national population census surveys and estimations of HIV prevalence using published HIV survey data.

Table 3.2 Model estimates on TB disease incidence, latent infections and TB deaths in Gauteng, by sub-population (2016 base year)

Population	Incidence per 100k	New DS-TB infections	New DR-TB infections	Latent TB cases	TB-related deaths per year
0–4 years	284	3882	16	57 859	298
5–14 years	110	1960	35	172 243	195
15–64 years HIV–	137	11 113	354	1 507 354	1511
65+ years HIV–	161	953	19	147 025	261
15–64 years HIV+	1147	22 384	1063	405 838	5861
65+ years HIV+	1004	176	3	3911	83
Prisoners HIV–	841	239	0	20 399	19
Prisoners HIV+	1712	161	0	4837	30

Source: Optima TB model output, based on data extracted from South Africa's TB surveillance system, demographic data from available national population census surveys and estimations of HIV prevalence using published HIV survey data.

Past trends in Gauteng's TB epidemic

All historical TB notification data for Gauteng were explored and used in the model calibration and the assessment of the past epidemic trends (*see supplementary data Gauteng Historical EPI Data for Report*). Notification data for recent years suggest that the Province's TB epidemic is slowly declining but with an increasing percentage of drug-resistant cases notified:

- 57,283 notified TB cases in 2011 (of which 1.1% DR)
- 52,457 notified TB cases in 2013 (2.1% DR)
- 46,534 notified TB cases in 2015 (3.8% DR)

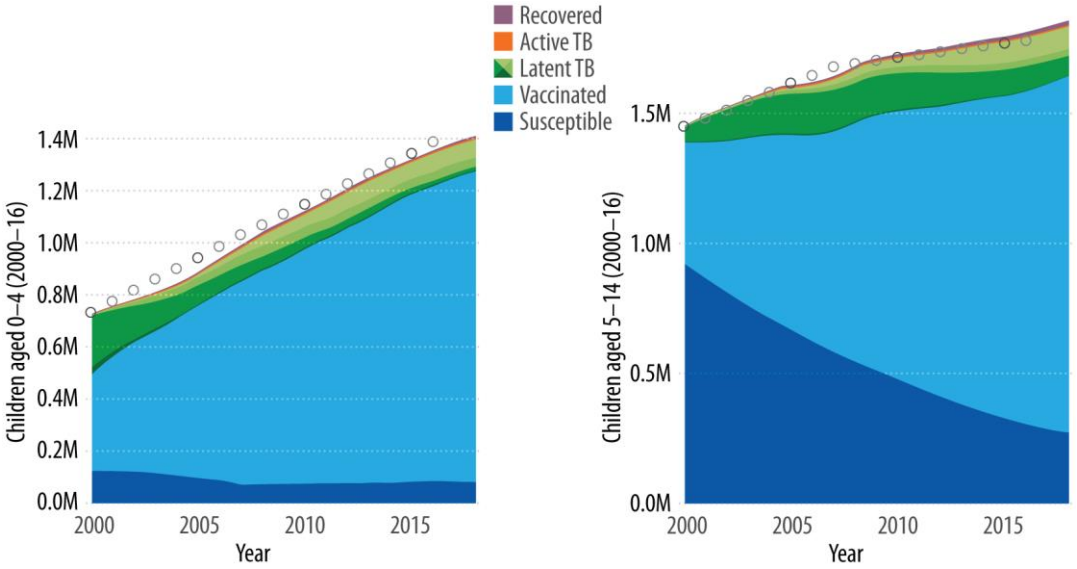
Overall and population-specific model calibrations for sputum smear positive and negative TB case notifications (by TB strain) are shown in **Appendix C**. The modelled estimates produced by the calibrated Optima TB model for TB disease incidence and active TB prevalence are also presented in **Appendix C.**

Past epidemic trends for the period 2000 up to 2016 showed very significant differences across the sub-populations defined for this analysis. Results are presented for children (**Figure 3.1**), adults aged 15–64 (**Figure 3.2**), adults aged 65 and above (**Figure 3.3**), Gauteng prisoners (**Figure 3.4**) and Gauteng gold mine employees (**Figure 3.5**).

The following observations can be made:

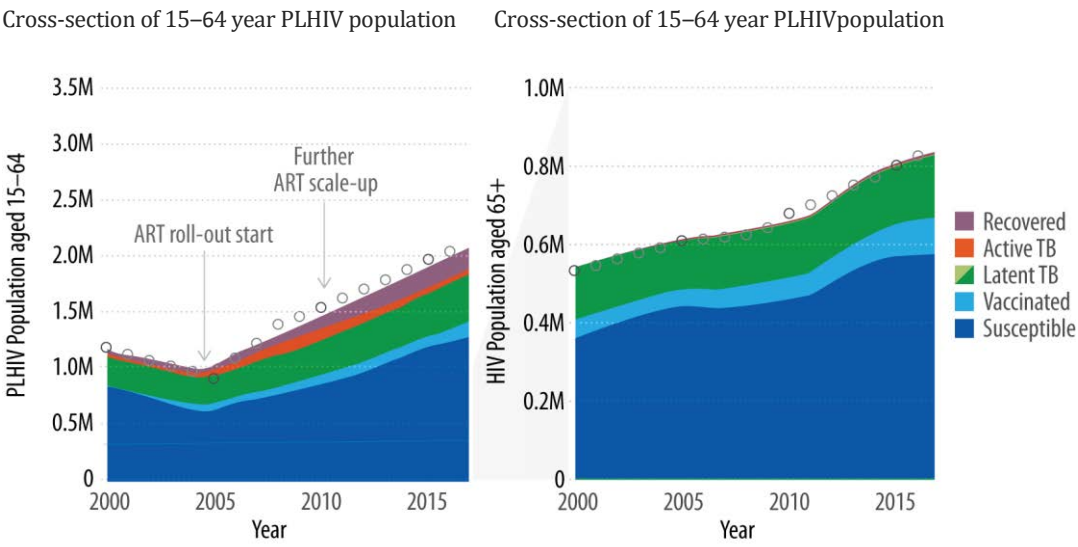
- **Children:** Both child populations have been expanding in size, especially the under 5 population has seen major growth. The majority of children are in the BCG-vaccinated model compartment, with increased BCG coverage over the years. Latent TB is at a relatively low level in children.
- **HIV+ adults:** ART introduction and scale-up lead to a significant increase in population size among and with it to growing numbers of PLHIV who are either susceptible to TB infection, have latent TB or are recovered from TB.
- **HIV– adults:** The main observation is a rapidly expanding population in both adult age groups, and with this population growth comes an expanding pool of TB susceptible persons.
- **Prisoners:** The model suggests a large proportion of prisoners having latent TB infections. This sub-population has been growing, in line with the increasing number of prisoners in Gauteng correctional institutions (from approx. 23 thousand in year 2000 to approx. 37 thousand in 2016). A sizable proportion of HIV+ prisoners have a history of TB.
- **HIV+ gold mine employees:** The main observation is a rapidly decreasing population size since year 2000, from approx. 96 thousand in year 2000 to about 56 thousand in 2016. The decrease is steeper for HIV+ miners, which might arise through retirement and death.

Figure 3.1 Modelled epidemic trends in Gauteng for children aged 0–4 and 5–14 (2000–16)



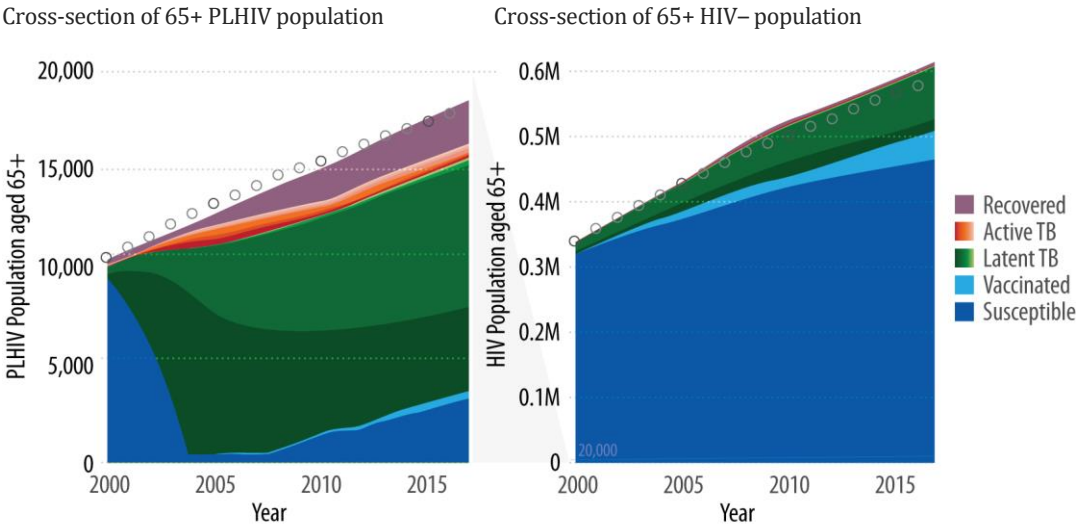
Source: Calibrated Optima TB model Gauteng.

Figure 3.2 Modelled epidemic trends in Gauteng for adults aged 15–64, by HIV status (2000–16)



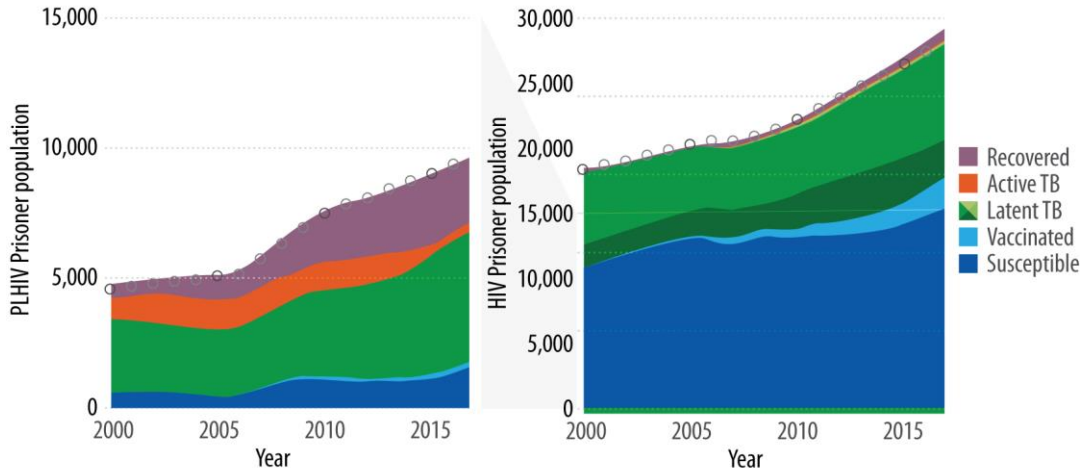
Source: Calibrated Optima TB model Gauteng.

Figure 3.3 Modelled epidemic trends in Gauteng for adults aged 65+, by HIV status (2000–16)



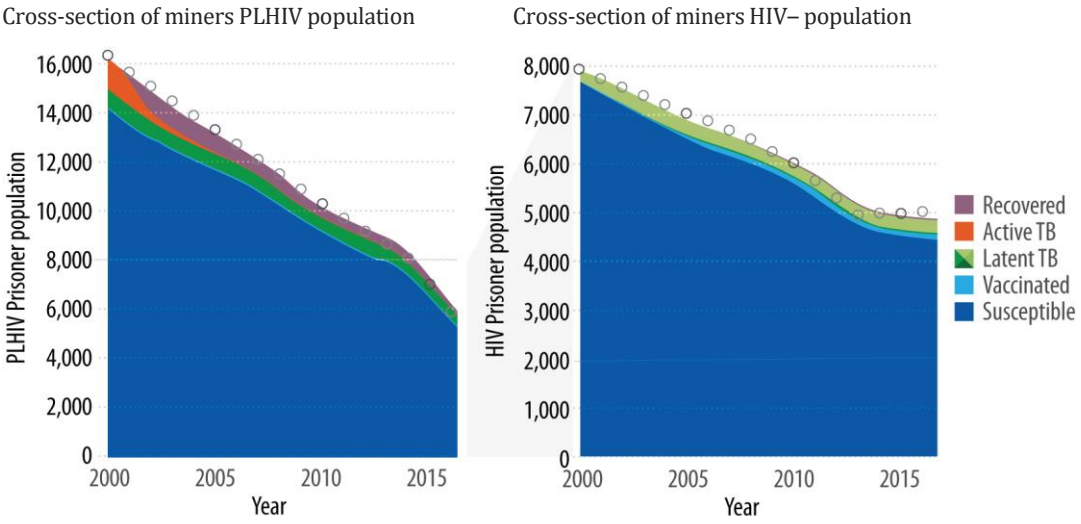
Source: Calibrated Optima TB model Gauteng.

Figure 3.4 Modelled epidemic trends in Gauteng for prisoners, by HIV status (2000–16)



Source: Calibrated Optima TB model Gauteng.

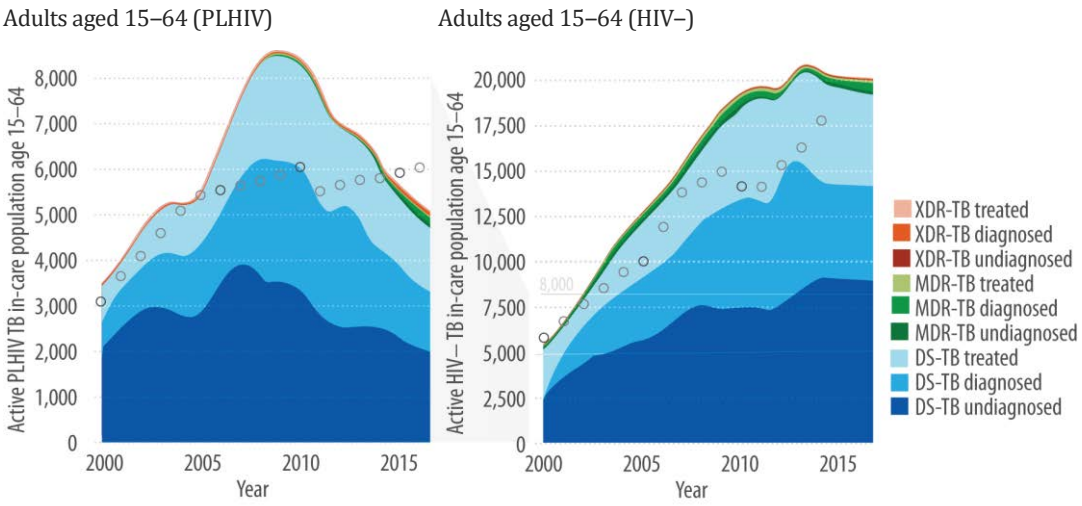
Figure 3.5 Modelled epidemic trends in Gauteng for gold mine employees, by HIV status (2000–16)



Source: Calibrated Optima TB model Gauteng.

Finally, **Figure 3.6** focuses on the modelled trends of active TB infections only, disaggregated by TB strain and care status. In the population with the largest number of active infections (PLHIV aged 15–64), the model's overestimate of active infections around year 2010 is likely driven by dynamics of increased PLHIV populations and TB prevalence, rapid ART scale-up and subsequent reduction in TB prevalence. Gaps in the surveillance data[29] may have amplified these effects in the model (with the model compensating for unexpectedly low treatment numbers by increasing predicted TB transmission and hence active infections). Model overestimates due to notification gaps in Gauteng have equally been reported by Nanoo et al. (2015).

Figure 3.6 Modelled trends of active TB infections in adults aged 15-64, by care status (2000–16)



Source: Calibrated Optima TB model Gauteng.

Notes: ○ = Data based on WHO Prevalence Estimates; DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; PLHIV = people living with HIV; XDR = extensively drug resistant tuberculosis.

Medium-term projected incidence trends in Gauteng's TB epidemic

Epidemic projections into the future are highly dependent on the assumptions regarding intervention coverage and resource availability. Longer-term projections under specific conditions are shown later in the report. Here, we merely show mid-term projections for TB disease incidence rates for FY 2019/20 and FY 2021/22, assuming TB intervention coverage and outcome conditions as per 2016. **Table 3.3** shows projected incidence by sub-population. Given these conditions, the projected incidence rates per 100 000 were on a further downward trajectory from 2016 and 2021/22. Prisoners and adult PLHIV would continue to have much higher TB risk than the general, HIV negative population groups.

Table 3.3 Modelled TB disease incidence in Gauteng, by sub-population (2016, 2020 and 2022)

Sub-population	TB disease incidence rate 2016	TB disease incidence rate 2019/2020	TB disease incidence rate 2021/22
0–4 years	284	211	184
5–14 years	110	91	81
15–64 years HIV–	137	118	108
65+ years HIV–	161	129	115
15–64 years HIV+	1147	831	724
65+ years HIV+	1004	734	635
Prisoners HIV–	841	635	576
Prisoners HIV+	1712	1443	1342

Source: Populated Gauteng Optima-TB model.

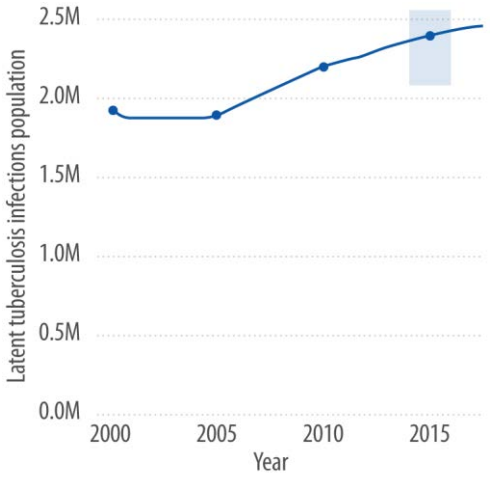
Temporal trends in latent TB infections

Latent TB infections represent the reservoir sustaining the TB epidemic. The actual prevalence of latent TB in Gauteng is unknown.

Given the global drive to eliminate TB and national targets, there is an increasing interest to address TB latency better. Optima TB, based on observed active TB infections in Gauteng, estimated 2.4 million latent TB cases in Gautena for 2015.

Given the global drive to eliminate TB and national targets, there is an increasing interest to address TB latency better.[30] Optima TB, based on observed active TB infections in Gauteng, estimated 2.4 million latent TB cases in Gauteng for 2015 (**Figure 3.7**). This is consistent with Houben & Dodd's[31] national estimate when adjusted for Gauteng (these authors estimated 15.7–19.7 million latent TB cases in South Africa with a best estimate of 17.2 million). While Optima TB predicts latent TB prevalence to be stable or decreasing across all populations, the number of latent TB cases is projected to increase especially in the 15–64 PLHIV population as this population's size increases.

Figure 3.7 Model-derived latent TB infections in Gauteng Province (2000–16)

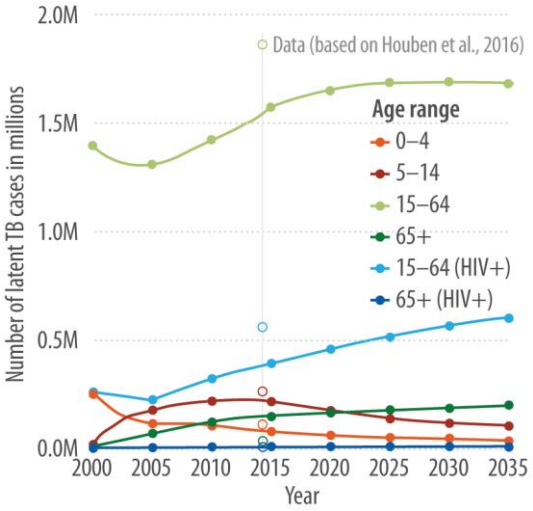


Source: Calibrated Optima TB model.
Note: Gauteng and estimates of latent prevalence from Houben & Dodd 2016 (shaded area).

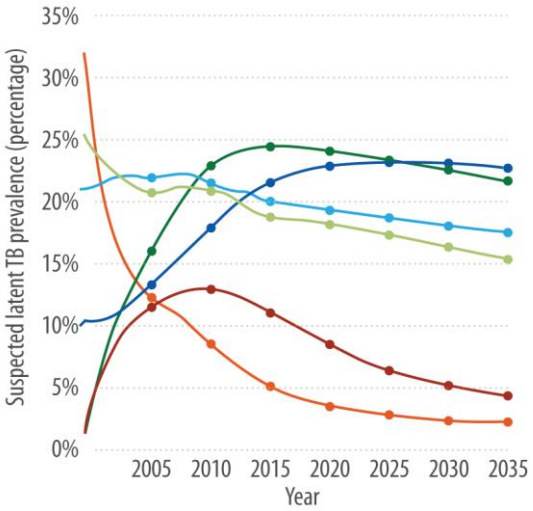
Figure 3.8 shows long-term latency trends under base case assumptions. The number of latent TB infections is projected to increase significantly in the 15–64 PLHIV population as this population increases[32], and rise slightly in the 15–64 and 65+ HIV– populations. Latent TB prevalence is stable or decreasing across all populations

Figure 3.8 Modelled latent TB infections in Gauteng Province over time (2000–35)

Modeled number of latent TB cases



Modeled latent TB prevalence



Source: Calibrated Optima TB model Gauteng.
Note: ○ = Data (based on Houben et al., 2016).

3.2 WHAT IS THE TB EXPENDITURE IN GAUTENG, AND WHAT IS THE IMPACT?

This section describes the programmatic focus of TB spending in Gauteng Province and the corresponding epidemiological outcomes if current spending patterns were sustained.

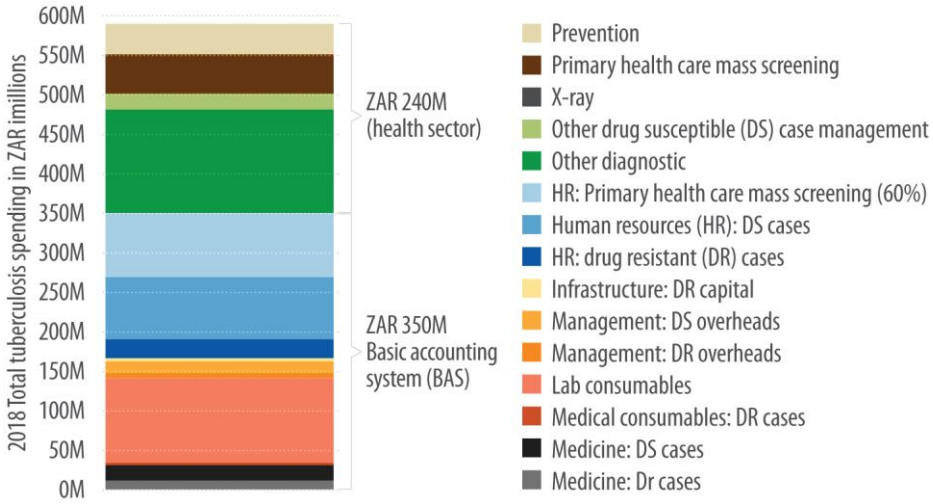
Note that spending on ART for PLHIV by the HIV program was not included in the expenditure for TB, and was not assumed to increase despite NDOH's intention to further scale-up ART in the future.

TB expenditure pattern in 2016 in Gauteng

This analysis estimated that in 2016 (base year), ZAR 589.6 million spent on TB prevention and care by the public sector in Gauteng Province. This was composed of ZAR 350 million detailed in the BAS (TB funding streams) and an estimated ZAR 240 million of other TB-related spending financed by the health sector. **Figure 3.9** provides a breakdown of TB spending in 2016 by intervention area.

Laboratory consumables and other diagnostic costs combined, comprised 40.7% (ZAR 239.7 million) of total TB spending in 2016. Overall, expenditure was dominated by screening and diagnostic costs and human resource costs, whereas drug costs were a relatively small expenditure component.

Figure 3.9 Estimated TB expenditure in Gauteng by intervention area, ZAR (2016)



Source: Populated Optima data entry spreadsheet for the Gauteng, based on BAS level 4 analysis and authors' own component costing as per Appendix B.

Without TB programmes, TB disease incidence and deaths would rise substantially

A scenario analysis was performed to assess the impact of current TB spending (**Figure 3.10**). This analysis assumed that the level of 2016 resources would be sustained up to 2030 and funding allocated in the same way as it was allocated in 2016 (as per **Figure 3.9**). The effect of this 'current conditions' scenario was compared to a scenario of zero public sector spending on TB. The effects of 'current conditions' and 'no TB funding' on active TB cases, MDR TV cases and TB deaths were established.

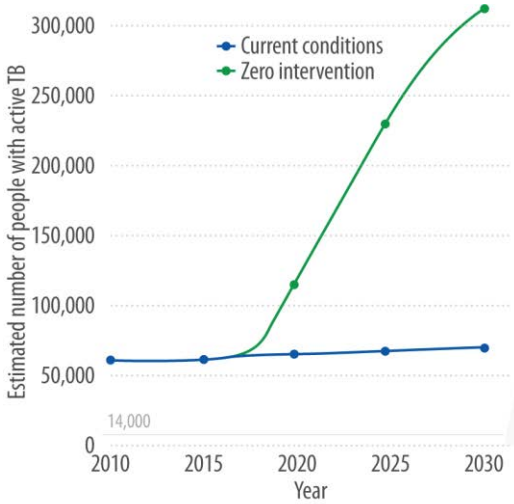
The scenario analysis suggests that current funding for TB interventions is making a very significant impact on the TB epidemic and TB cases and associated deaths would rise very rapidly if this investment ceased. Without spending ZAR ~590 million annually (from TB and health budgets), by 2030:

- TB-related incidence in HIV– could **increase three times**
- TB-related mortality could **increase six times**
- The number of active TB cases **could increase five times**

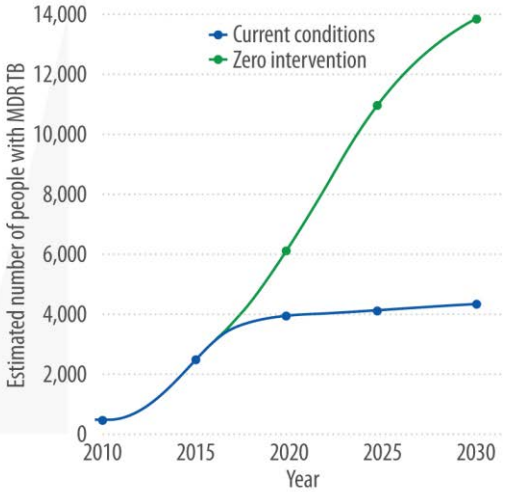
While current TB spending allocations are clearly beneficial compared to no public spending on TB, it would likely lead to stable case numbers and deaths, and possibly a rise in MDR (**Figure 3.10 a–c**). Importantly, spending allocations as per the 2016 base year would not be able to contain TB disease incidence, and incidence would actually increase (**Figure 3.11**). This implies that according to projections performed in Optima TB, national and global targets would not be achieved with current allocations of resources. The following sections therefore explore alternative resource allocation scenarios.

Figure 3.10 Epidemiological outcomes of current TB spending patterns versus no TB-spending between 2016 and 2030

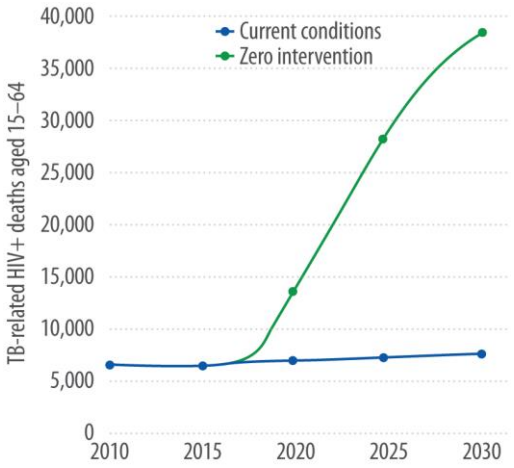
a. Modelled number of active cases, 15–64 HIV+



b. Modelled number of MDR cases, 15–64 HIV+

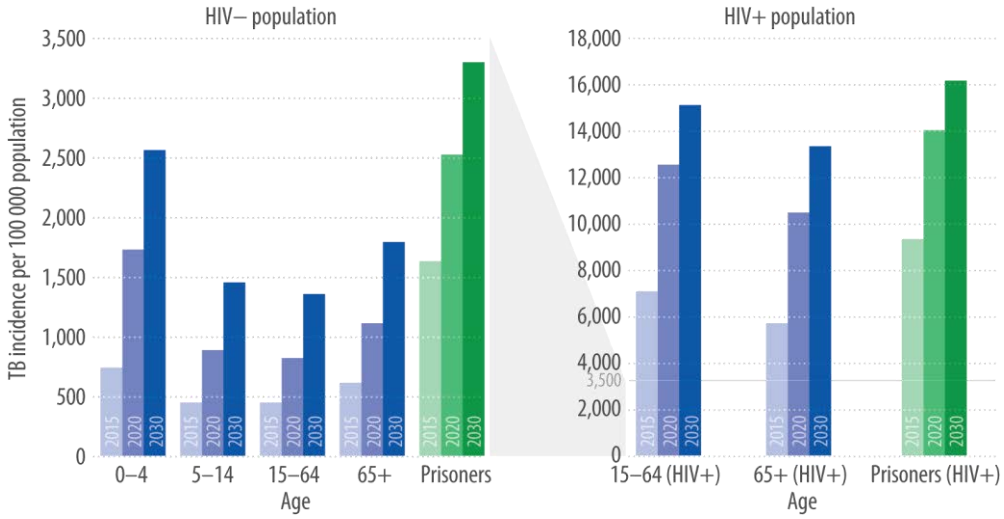


c. Modelled TB-related deaths per year, 15–64 HIV+



Source: Populated Optima model for Gauteng.
Note: Current conditions refers to continued coverage of TB interventions at 2016 levels.

Figure 3.11 Projected TB disease incidence with current TB spending allocations continuing to 2030, assuming no increase in ART coverage



Source: Populated Optima model for Gauteng.

3.3 WHAT WOULD BE THE IMPACT OF DIFFERENT PROGRAMME IMPLEMENTATION SCENARIOS?

This section summarises different scenario analyses, which were conducted to understand the effect that specific programmatic changes would have on Gauteng's TB indicators. The scenarios were identified during an initial planning workshop for the analysis with a mix of stakeholders invited by the provincial and national study focal points. They respond to the study questions of intervention targeting (whether targeting of resources to selected key populations improve outcomes) and future impact of specific response scenarios (including better case-finding strategies, improved linkage to TB care, and further scale-up of MDR short-course).

SCENARIO GROUP 1: Testing and treatment scenarios to reach 2020 and 2035 targets

This group of scenarios models the impact of reaching 2020 APP and 2035 End TB targets for:

- TB screening/testing
- TB treatment initiation (linkage to care)
- TB treatment outcomes

These effects are then combined to assess what impact on Gauteng's TB epidemic could be obtained if meeting 2020 APP targets and 2035 milestones. Scenarios with scale-up's assume that the scale-up is gradual from 2017 to the end year of analysis.

Improved TB screening/testing

This scenario asks, what is the impact of reaching 2020 and 2035 targets for treatment initiation? A key model parameter in this scenario on screening/testing is the 'diagnosis rate', which in the model represents the probability of movement from the undiagnosed to the diagnosed compartments over a year (see Appendix A for model structure). This

therefore includes TB disease incidence, as well as the number of undiagnosed people with active TB from previous years (after accounting for other rates such as mortality and natural recovery).

Table 3.4 summarises the parameters, which were modified in the model to assess the effect of the scenario (note that case finding in PLHIV is addressed separately in scenarios). Although in the 2020 target scenario, coverage targets are achieved by 2020, the impact of achieving and sustaining 2020 coverage levels is tracked up to 2035.

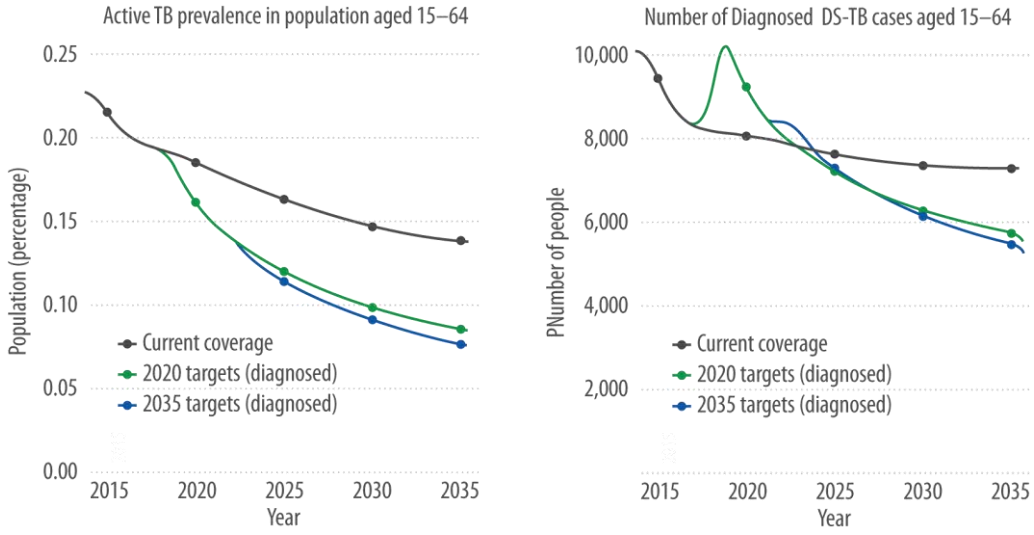
Table 3.4 Scenario: Improved TB screening/Testing

Improved TB screening/testing	Current conditions (2016)*	APP 2020 Targets	END-TB 2035 Targets
Case detection for DS-TB in HIV–	67%	90%	95%
Case detection for MDR-TB in HIV–	67%	90%	95%
Case detection for XDR-TB in HIV–	67%	90%	95%

Sources: Populated Gauteng Optima TB model; Gauteng APP; and 2035 End TB Targets.
Note: * = The model's "diagnosis rate" was calculated using notified as a proportion of total prevalence and not incidence.

Figure 3.12 presents the impacts on active TB prevalence in the HIV negative adult population, and the effect on diagnosed DS-TB cases up to 2035. When APP 2020 testing targets are met and sustained, a significant reduction in active-TB prevalence is observed in the model. The number of diagnosed cases initially rises, then decreases as more cases are initiated on treatment. This reduces the number of undiagnosed cases contributing to new active TB infections.

Figure 3.12 Modelled impact of meeting TB screening/testing targets (2016–35)



Source: Populated Optima model for Gauteng.
Notes: DS-TB = drug susceptible tuberculosis; TB = tuberculosis.

Improved treatment initiation (better linkage to care)

What is the impact of reaching 2020 and 2035 targets for treatment initiation? **Table 3.5** lists the parameters varied in the model to determine the effect of linkage to TB care using treatment initiation targets as proxy.

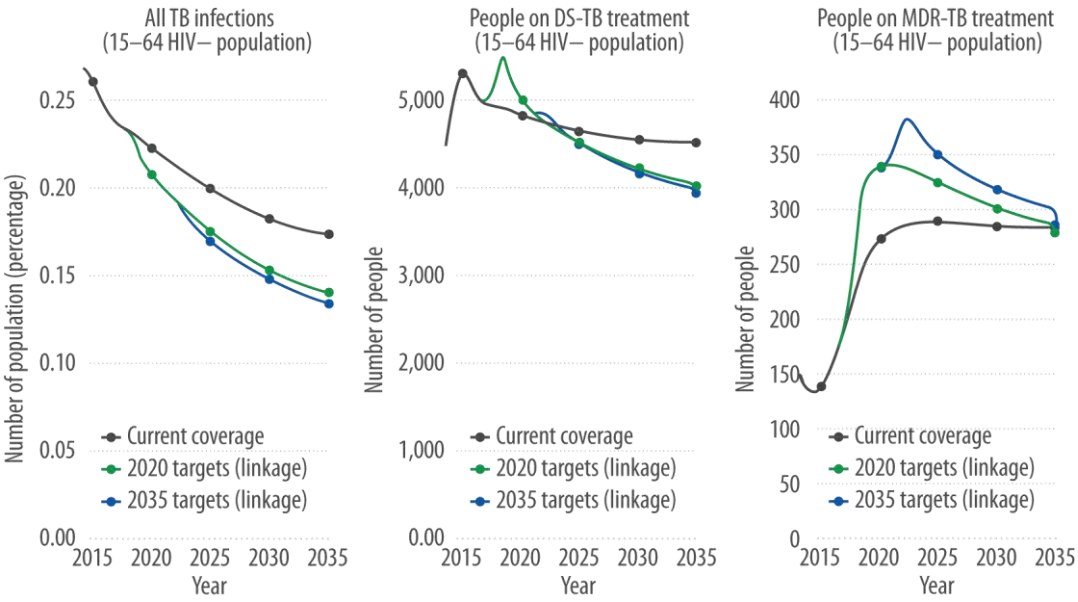
Table 3.5 Scenario: Improved treatment initiation (for linkage to care)

Improving treatment initiation and averting pre-treatment loss to follow up	Current conditions (2016)	APP 2020 targets	END-TB 2035 targets
Treatment initiation for DS-TB regimens	90%	98% (assumed)	99%
Treatment initiation for MDR-TB regimens	57.4%	80%	92%
Treatment initiation for XDR-TB regimens	100%	100%	100%

Sources: Prepared by authors in consultation with local experts.
Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; XDR-TB = extensively drug resistant tuberculosis.

Figure 2.13 presents the impacts of meeting treatment initiation targets on TB infections, DS and MDR treatment numbers in HIV negative adults. Treatment initiation rates in Gauteng have significantly improved since 2012, however, the model suggests that gains can still be made from further improvements in treatment initiation. Modelled TB prevalence decreases when the APP treatment initiation rate of 98% is met by 2020 and sustained. Further scale-up yields additional gains for MDR-TB but smaller gains for DS-TB due to the pre-existing 2016 baseline levels.

Figure 3.13 Modelled impact of meeting TB treatment initiation targets (2016–35)



Source: Populated Optima model for Gauteng.
Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; TB = tuberculosis.

Improved treatment outcomes

What is the impact of reaching 2020 and 2035 targets for treatment outcomes? Table 3.6 displays the various targets related to improved treatment outcomes in the TB care cascade. Note that treatment failure does not include TB-related death. Cases 'transferred out' as per the TB surveillance database are also not included.

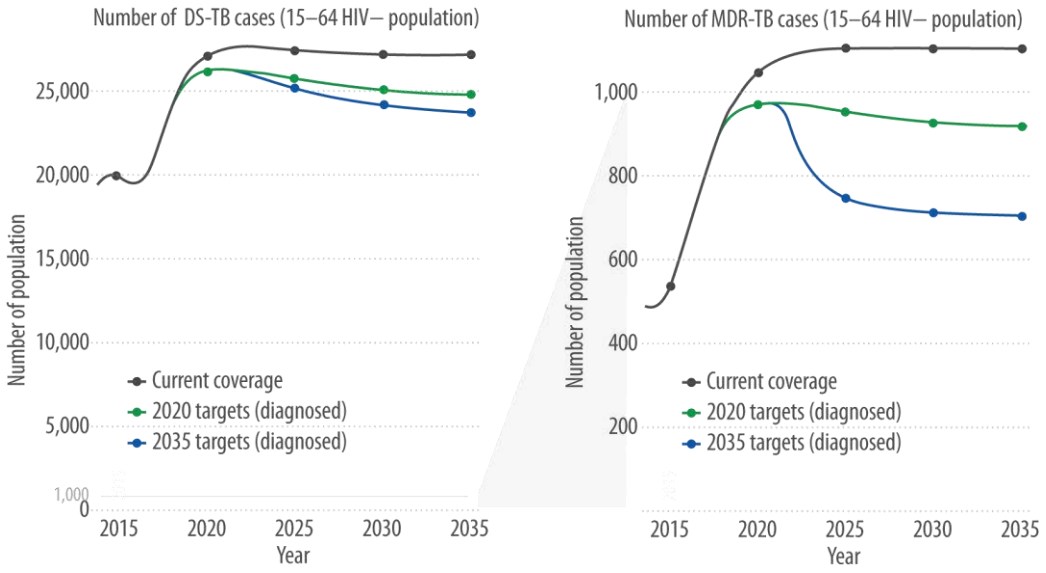
Table 3.6 Scenario: Improved treatment outcomes

Improved treatment outcomes	Current conditions (2016)	APP 2020 Targets	END-TB 2035 Targets
Treatment failure* including loss to follow up, regimen failure and relapse for DS-TB	7%	5%	5%
Treatment failure including loss to follow up, regimen failure and relapse for MDR-TB	47%	35%	10%
Treatment failure including loss to follow up, regimen failure and relapse for XDR-TB	80%	35%	20%
Treatment success rates for DS-TB regimens	89%	95%	98%
Treatment success rates for MDR-TB regimens	55%	65%	90%
Treatment success rates for XDR-TB regimens	63%	65%	80%

Source: Prepared by authors in consultation with local experts.
Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; XDR-TB = extensively drug resistant tuberculosis.

Figure 3.14 shows the modelled impact on DS- and MDR-TB cases in the HIV negative population up to 2035. If MDR treatment outcomes meet the APP 2020 targets and are sustained, a 35% decrease in the total number of MDR cases among HIV- adults is projected for 2035. Despite the high treatment success rates currently achieved for DS-TB, there are still opportunities to reduce the total number of DS-TB cases through further improvements in treatment outcomes.

Figure 3.14 Modelled impact of meeting TB treatment outcome targets (2016–35)



Source: Populated Optima model for Gauteng
Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis.

Improved TB care cascade

What is the impact of meeting the APP targets regarding the TB care cascade on Gauteng's TB epidemic? **Table 3.7** summarises the targets applied in this combined scenario of improved diagnosis, treatment initiation and treatment outcomes, for DS-, MDR- and XDR-TB.

Table 3.7 Scenario: Improved TB care cascade

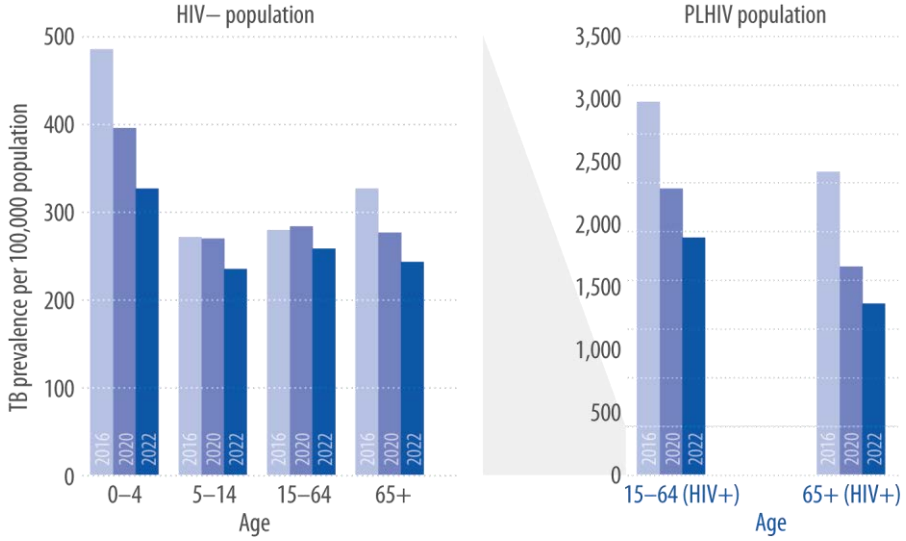
Scenario group 4: Improved care cascade	Current conditions (2016)	Improved diagnosis (APP 2020 targets)	+ Treatment initiation (APP 2020 targets)	+ Treatment success rate (APP 2020 targets)
Diagnosis of prevalent cases	67%	90%	90%	90%
DS-TB care				
Treatment initiation	90%	90%	92%	92%
Treatment success	87%	87%	87%	95%
MDR-TB care				
Treatment initiation	57%	57%	80%	80%
Treatment success	54%	54%	54%	65%
XDR-TB care				
Treatment initiation	100%	100%	100%	100%
Treatment success	38%	38%	28%	65%

Source: Prepared by authors in consultation with local experts.
Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; XDR-TB = extensively drug resistant tuberculosis.

The impacts of this important scenario on the improved TB care cascade are presented in several figures.

Figure 3.15 shows the effect on active TB prevalence in the medium-term (by 2020 APP and by 2022 NSP end-years) for HIV negative and positive populations. Meeting and sustaining the 2020 APP targets, yields significant reductions in TB prevalence per 100k for most general population groups by 2022. A particularly sharp decrease is observed among the 0–4, 15–64 PLHIV, 65+ HIV negative and 65+ PLHIV, with reductions of up to 40% in the prevalence of all TB infections.

Figure 3.15 Modelled impact of improved care cascade on TB prevalence (2020, 2022)

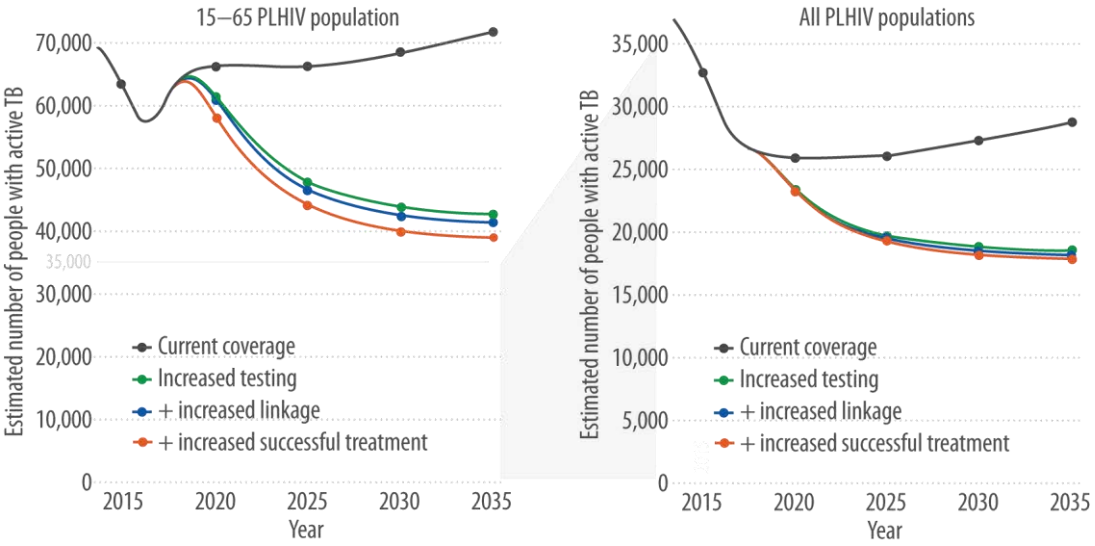


Source: Populated Optima model for Gauteng
Notes: PLHIV = people living with HIV; TB = tuberculosis.

Figure 3.16 displays the long-term impact up to 2035 just for PLHIV. Simultaneously meeting and sustaining the APP 2020 targets could, by 2035, achieve a 45% reduction in the

total number of active TB cases co-infected with HIV. It would reduce the number of new active TB infections by approximately 40% in PLHIV. This highlights the importance of increasing the accessibility to PHC-provided TB screening and testing, in order to increase the proportion of diagnosed TB infections. It also suggests that having fit-for-purpose routine data procedures is important to track people along the cascade, and that there is a need to invest in early tracing of cases that are not linked to care.

Figure 3.16 Modelled impact of improved care cascade on active TB cases and annual TB disease incidence among PLHIV (2016–35)



Source: Populated Optima model for Gauteng.
Notes: PLHIV = people living with HIV; TB = tuberculosis.

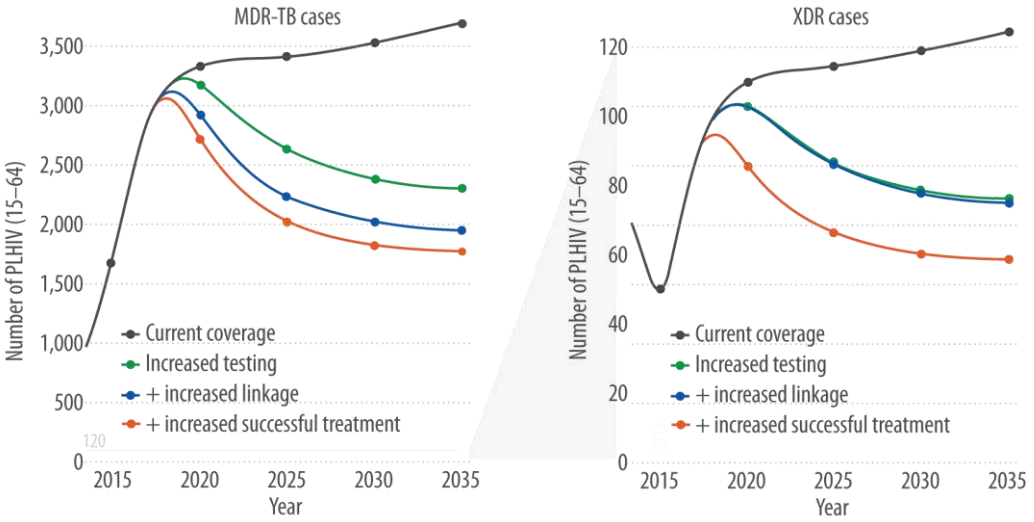
As in the PLHIV population, meeting and sustaining the APP 2020 targets yields significant gains for the adult HIV negative population too. The modeled total number of active TB cases in the adult HIV negative population is projected to be reduced by around 40% by 2035.

Figure 3.17 shows the impact of meeting and sustaining the 2020 APP targets on DR-TB. Overall, a strong impact is projected with a 50% reduction in the number of both MDR and XDR cases by 2035. Improving the proportion of TB infections that are diagnosed has the most substantial effect on reducing the total number of resistant cases, followed by improvements to pre-treatment loss to follow-up for MDR-TB cases. Improvements in treatment success from 54% to 65% (APP 2020), generates significant reductions in the number of DR-TB infections.

Simultaneously meeting and sustaining the APP 2020 targets could, by 2035, achieve a 45% reduction in the total number of active TB cases co-infected with HIV. It would reduce the number of new active TB infections by approximately 40% in PLHIV. This highlights the importance of increasing the accessibility to PHC-provided TB screening and testing.

Photo: ©Alamystockphoto.com

Figure 3.17 Modelled impact of improved care cascade on MDR and XDR cases among PLHIV (2016–35)



Source: Populated Optima model for Gauteng

Notes: MDR-TB = multi-drug resistant tuberculosis; PLHIV = people living with HIV; XDR-TB = extensively drug resistant tuberculosis.

SCENARIO GROUP 2: Alternative screening and treatment interventions

This group of scenarios models specific questions on programmatic changes and their effect on the Gauteng TB epidemic, which were found relevant by the provincial TB managers. They regard treatment outcomes of alternative DR short-course regimens, the impact and cost of quality-improved PHC-level symptom screening, and case finding through different screening interventions.

Alternative DR short-course regimens

How do alternative DR short-course regimens impact on treatment outcomes? This scenario explores the projected effects of transitioning to newer, shorter and more effective DR-TB drug regimens over 20 years from 2015. The projected effect of increasing DR-TB treatment coverage is also explored. Targets are shown in **Table 3.8** (see **Appendix B** for details on treatment regimens).

Table 3.8 Scenario: Targets for transition to short-course MDR regimens

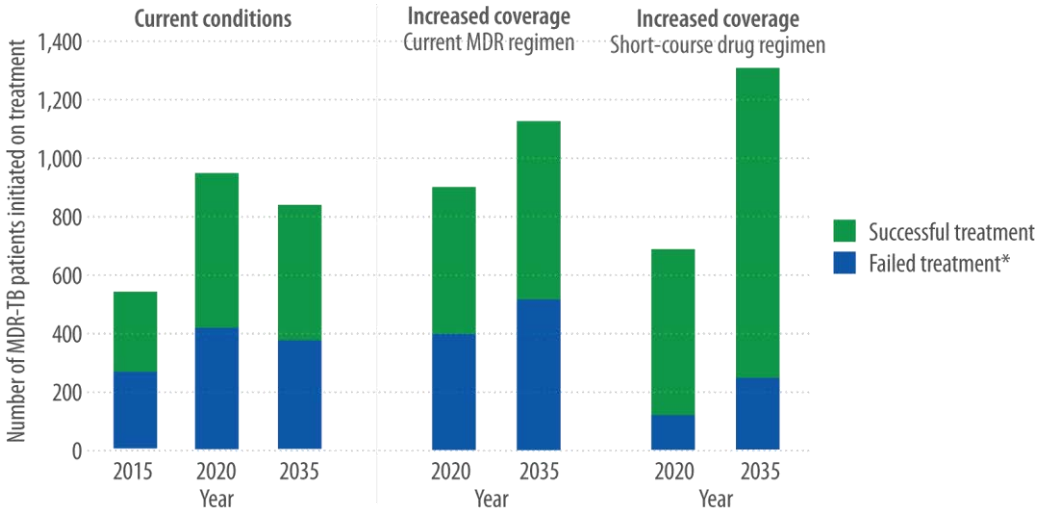
DR-TB treatment regimen comparison	Current conditions	Increased coverage, current drug regime	Increased coverage, short-course drug regimen
Number of people diagnosed with MDR (2015)	1950	1950	1950
Coverage for initiation on to drug regimens for DR-TB (2015) as percentage (APP 2020 Targets)	57%	80%	80%
Coverage for initiation on to drug regimens for DR-TB (2015) as number	1120	1463	1463
Of which, component of current drug regimen	100%	100%	10%
Of which, component of new short-course drug regimen	0%	0%	90%

Source: Prepared by authors in consultation with local experts.

Notes: DR-TB = drug resistant tuberculosis; MDR-TB = multi-drug resistant tuberculosis.

Figure 3.18 shows that transition to shorter MDR-TB regimens results in significant increases in successful treatment. This can minimise the high future costs associated with re-treating MDR-TB, treatment of adverse drug effects, and the risk of developing additional resistance. It is also likely to reduce the number of inpatient days, and therefore the risk of nosocomial TB transmission. Therefore, short-course regimens offer better patient care, with less side effects, shorter treatment durations, and reduced challenges to adherence.

Figure 3.18 Modelled impact of transition to short-course MDR regimens

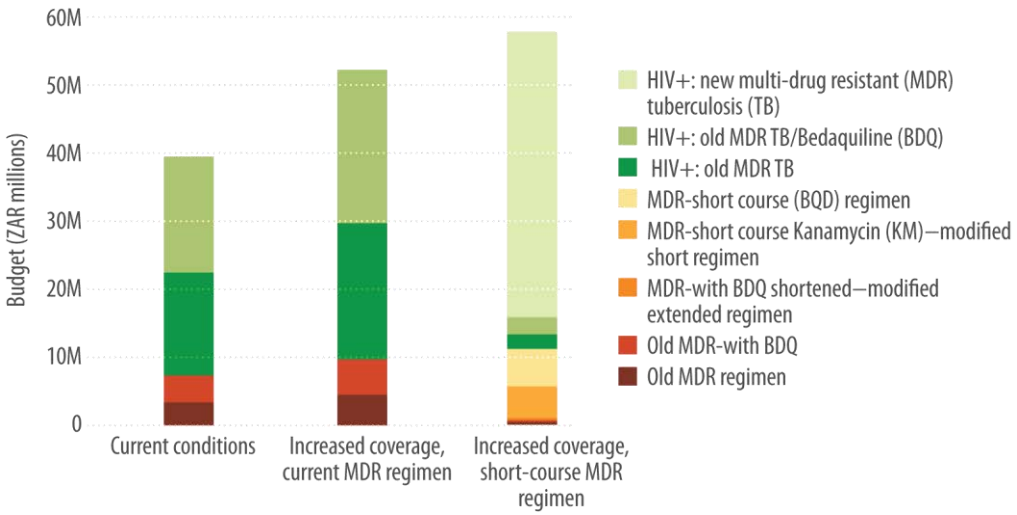


Source: Populated Optima model for Gauteng.

Notes: * = Failed treatments: In the model, this includes 'loss to follow-up' during treatment, 'treatment failure', and 'not evaluated'. Treatment success includes 'cured' and 'treatment completion', as per the WHO. Note that death during TB treatment is not included in treatment failure, but is considered separately; MDR-TB = multi-drug resistant tuberculosis.

Figure 3.19 presents the budget amounts required to sustain current treatment coverage with different MDR regimens. To cover 75% of all diagnosed cases with current MDR-TB regimens suitable for HIV positive cases, a ZAR 10M increase in DR-TB spending is needed. An additional 10% spending is required to sustain treatment coverage but move from older MDR regimens to short courses.

Figure 3.19 Estimated budget amounts required to transition to alternative MDR treatment regimens



Source: Populated Optima model for Gauteng.

Alternative screening approaches

What is the impact and cost of moving to enhanced mass screening? This scenario explores the projected effectiveness of "incomplete" and enhanced mass-screening at PHC, as well as geographically targeted mass screening (**Table 3.9**). Gauteng Province has a relatively high achievement of the indicator "Proportion of clients 5 years and older attending PHC facilities who were screened for TB", only KwaZulu Natal reported higher coverage for 2016/27.[33]

"Incomplete" mass screening refers to local programme implementers' comments that often only the cough question is asked in the PHC-based universal symptom screen, instead of all four TB symptom questions (see also **Appendix B**). The number of active TB cases identified was estimated by considering the total available spending allocated across the different interventions.

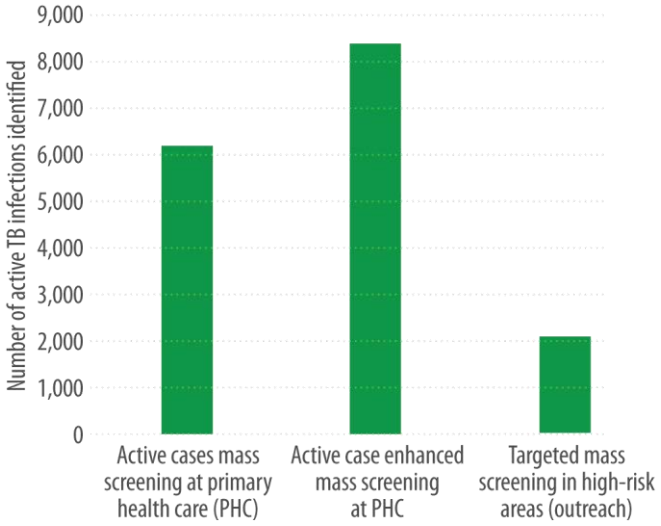
Table 3.9 Scenario: Alternative screening interventions

Alternative screening interventions to mass-screening at PHC	Current conditions – PHC Mass screening (2016)	Enhanced PHC mass screening	Targeted mass screening in high-risk areas
Total spending considered (ZAR)	111M	111M	111M
Estimated cost per person screened (ZAR)	6.5	13.1	1089.03
Delivery modality	PHC staff	PHC staff	Mobile unit with health staff

Source: Prepared by authors in consultation with local experts
Notes: PHC = primary health care.

Figure 3.20 presents the findings suggesting that with the same amount of funding, an additional 2000 active infections could by identified with higher quality mass screening at PHC (full set of four symptom questions consistently asked). Note that while more comprehensive symptom screening increases sensitivity in case finding, it also leads to a loss in specificity (estimated drop from 95% to 85%, Claassens et al. 2017). This can result in unnecessary Gene Xpert tests due to identification of a higher number of screen-positive individuals. Also, some investment for outreach in high-risk areas to diagnose hard to reach populations may be desirable, but a significant increase in spending would be required to identify a similar number of active cases.

Figure 3.20 Modelled impact of different screening approaches for active case finding



Source: Populated Optima model for Gauteng
Notes: PHC = primary health care; TB = tuberculosis.

Active case finding with focus on contact tracing

How could investment in different screening interventions improve case finding? This scenario explores the projected impact of increasing or decreasing the coverage of different screening and case finding programmes currently implemented. Parameters are detailed in **Table 3.10**. Given that contact tracing (CT) guidelines are poorly implemented, according to the TB coordinators, it was assumed that CT will be carried out for only 1 in 5 DS-TB cases and 4 in 5 DR-TB cases.

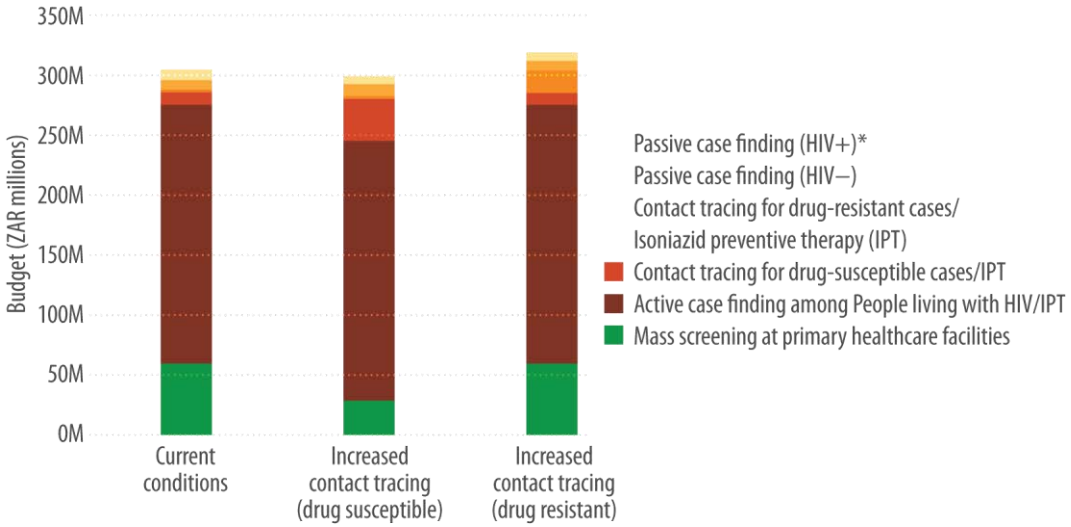
Table 3.10 Scenario: Alternative case finding interventions

Alternative case finding interventions*	Current conditions (2016)	Increased CT - DS	Increased CT - DR
Number of infections identified through active-case finding	45000	-	-
Of those, proportion identified through mass screening	13.7%	6.4%	13.6%
Of those, proportion identified through PLHIV-ACF (HIV+ only)	83.2%	83.2%	83.2%
Of those, proportion identified through contact tracing - DS	2.7%	10%	2.7%
Of those, proportion identified through contact tracing - DR	0.4%	0.4%	0.5%

Source: Prepared by authors in consultation with local experts
Notes: * = All remaining notified cases are assumed to be identified through passive case-finding where patients present with complaints and symptoms at primary health care (PHC); ACF = active case finding; CT-DR = contact tracing drug resistant; DS = drug susceptible; PLHIV = people living with HIV.

Figure 3.21 shows the estimated budget amounts needed to identify the same number of active cases using different case finding strategies. Accordingly, slightly less spending is required if the coverage of DS-TB contact tracing is increased. Slightly higher amounts of spending are required if the coverage of DR-TB contact tracing is increased.

Figure 3.21 Budgets required to maintain current numbers of active infections found with different interventions



Source: Populated Optima model for Gauteng.

Notes: * = Passive case finding: Assumes all remaining notified cases from a given year, which are not identified through active screening and finding measures, present with positive symptoms at PHCs in need only of an Xpert test for confirmation and following monitoring tests.

SCENARIO GROUP 3: Targeting high risk and key populations

This group of scenarios is about the impact of scaling up specific interventions for PLHIV and prisoners, which were found relevant by the stakeholders and are supported by Gauteng's strategies and plans.

TB and HIV interventions targeted at PLHIV

What is the impact of scaling up TB testing and treatment for TB and HIV in PLHIV? This scenario explores the projected impact of improving the overall PLHIV TB/HIV care cascade as detailed in **Table 3.11**. All values are sourced from the APP, with the exception of IPT and ART coverage, which are assumed due to lack of a data source.

Table 3.11 Scenario: Targets for improved HIV/TB care cascade in PLHIV

Testing and treatment scenarios for PLHIV (all interventions listed are for PLHIV)	Current conditions	Increased diagnosis	Improved treatment outcomes	Increased IPT	Increased ART	Increased testing + IPT + ART coverage
Case detection for DS-TB	67%	90%	67%	67%	67%	90%
Case detection for MDR-TB	67%	90%	67%	67%	67%	90%
Case detection for XDR-TB	67%	90%	67%	67%	67%	90%
Treatment initiation for DS-TB	90%	90%	95%	90%	90%	95%

Table 3.11 continued.

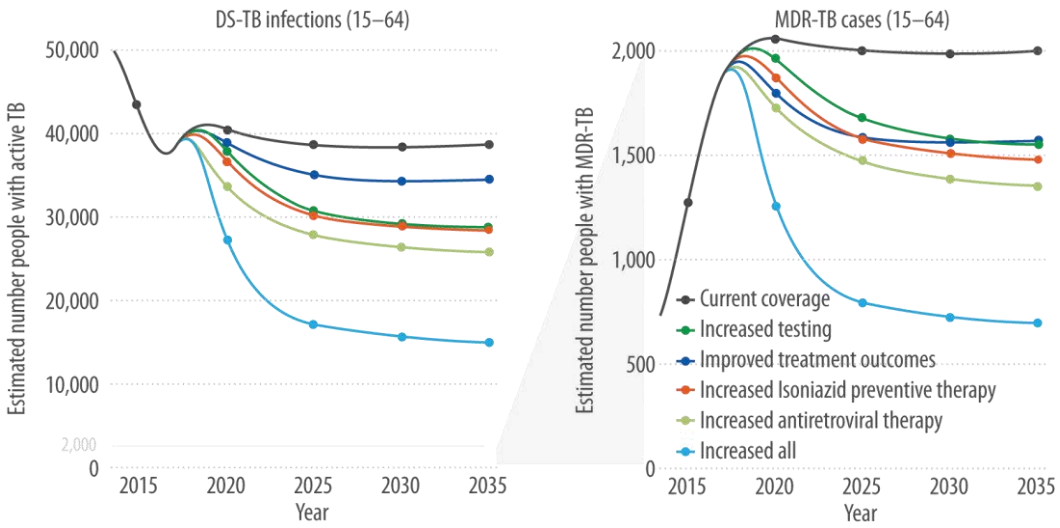
Table 3.11 Scenario: Targets for improved HIV/TB care cascade in PLHIV (continued)

Testing and treatment scenarios for PLHIV (all interventions listed are for PLHIV)	Current conditions	Increased diagnosis	Improved treatment outcomes	Increased IPT	Increased ART	Increased testing + IPT + ART coverage
Treatment initiation for MDR-TB	57%	57%	80%	57%	57%	80%
Treatment initiation for XDR-TB	100%	100%	100%	100%	100%	100%
Treatment success for DS-TB	86%	86%	90%	86%	86%	90%
Treatment success for DR-TB	54%	54%	65%	54%	54%	65%
IPT coverage of newly diagnosed PLHIV*	38%	38%	38%	65%	38%	65%
ART coverage across all PLHIV**	47%	47%	47%	47%	65%	65%

Source: Prepared by authors in consultation with local experts.
Notes: * = WHO South Africa Country Profile, 2016 for current IPT coverage among newly diagnosed PLHIV on ART; ** = Based on Thembisa Gauteng model 2.5; DR-TB = drug resistant tuberculosis; DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; PLHIV = people living with HIV; XDR-TB = extensively drug resistant tuberculosis.

Figure 3.22 shows that the largest observed decrease in PLHIV active TB prevalence is from independently scaling up ART coverage among diagnosed PLHIV, followed by TB diagnosis and IPT provision. The scaling up of ART, followed by IPT, also yields the most substantial decrease in the projected number of MDR cases. Simultaneously increasing the coverage of all programmes for PLHIV, reduces the number of DS-TB and MDR-TB infections by 65% by 2035.

Figure 3.22 Modelled number of active DS/MDR TB cases among PLHIV (2016–35)



Source: Populated Optima model for Gauteng.
Notes: PLHIV = people living with HIV; DS-TB = drug susceptible tuberculosis.

Targets for improved prisoner DS-TB care cascade

What is the impact of scaling up testing, treatment and IPT for Gauteng prisoners? This scenario explores the projected impact of improving the overall DS-TB prisoner care cascade as detailed in **Table 3.12**.

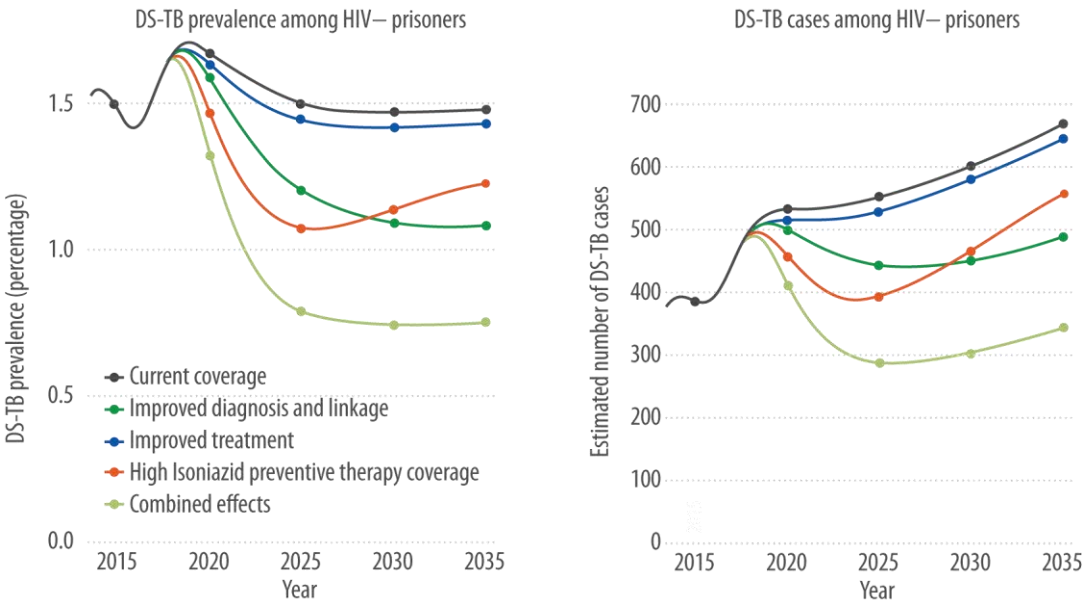
Table 3.12 Scenario: Targets for improved prisoner DS-TB care cascade

Testing and treatment scenarios for Prisoners	Current conditions	High IPT Coverage	Increase diagnosis + linkages	Increased treatment outcomes	Combined program scale up
IPT for prisoners	0.0%	30.0%	0.0%	0.0%	30%
Increased diagnosis rate - DS	65.6%	65.6%	85.0%	65.6%	85%
Linkage to care/initiating treatment - DS	90.3%	90.3%	95.0%	90.3%	95%
Treatment success - DS	83.0%	83%	83%	90.0%	90%
Treatment failure - DS	5.0%	5%	5%	5.0%	5%

Source: Prepared by authors in consultation with local experts.
Notes: DS = drug susceptible; IPT = Isoniazid preventive therapy.

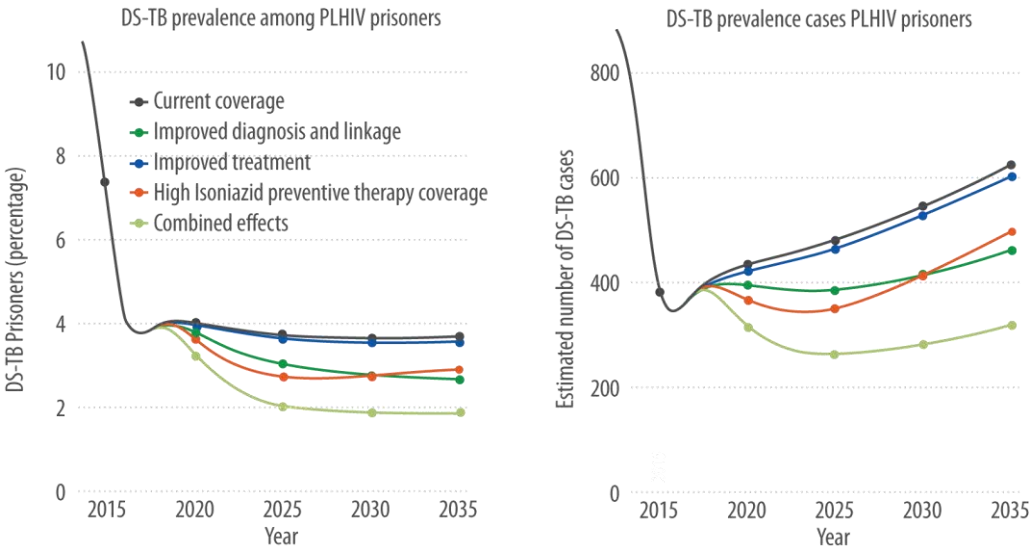
Figure 3.23 shows findings for HIV negative Gauteng prisoners. Improving diagnosis and linkage to treatment has the greatest impact on reducing the prevalence and number of DS-TB cases in these HIV negative prisoners. A simultaneous increase in the coverage of all interventions reduces DS-TB prevalence by almost 50% by 2035. Among HIV positive prisoners, IPT plays a bigger role—improving diagnosis and linkage to treatment, followed by an increase in IPT coverage, has the greatest impact (**Figure 3.24**). The impact of a simultaneous increase in the coverage of all interventions also reduces DS-TB prevalence by around 50% by 2035.

Figure 3.23 Modelled impact of improving the HIV negative prisoner care cascade (2016–35)



Source: Populated Optima model for Gauteng.
Notes: DS-TB = drug susceptible tuberculosis; IPT = Isoniazid preventive therapy.

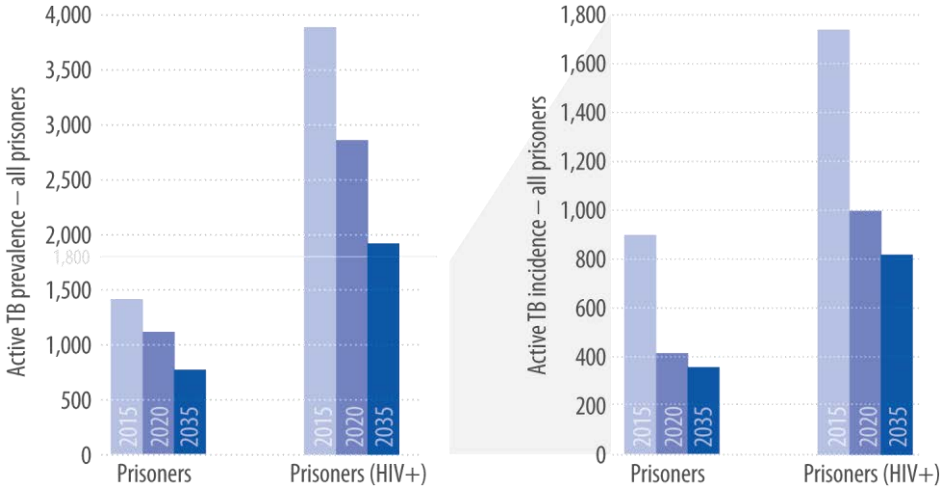
Figure 3.24 Modelled impact of improving the HIV positive prisoner care cascade (2016–35)



Source: Populated Optima model for Gauteng
Notes: DS-TB = drug susceptible tuberculosis; PLHIV = people living with HIV.

Finally, **Figure 3.25** shows the impact of an improved care cascade in all prisoners regardless of HIV status. As with active TB prevalence, a simultaneous improvement of all prisoner targeted interventions can yield significant decreases in the incidence of TB disease. A particularly sharp decrease in the incidence of TB infections in HIV negative prisoners is observed, of up to 60% by 2035.

Figure 3.25 Modelled impact of improving the prisoner care cascade on active TB prevalence and incidence (2020, 2035)



Source: Populated Optima model for Gauteng.
Note: TB = tuberculosis.

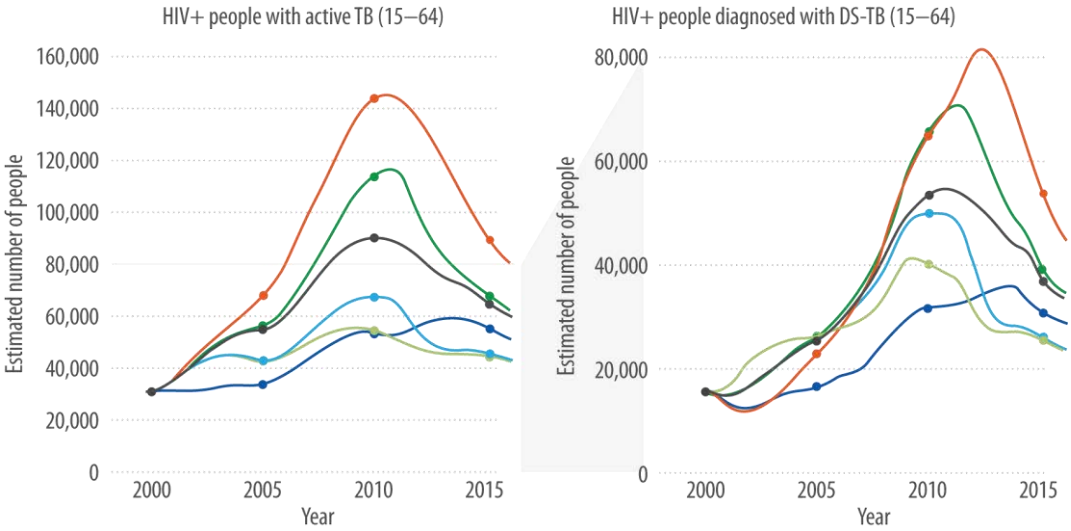
Effect of parameter variation on results

As mentioned under "Limitations of the analysis" in section 2.2, a formal sensitivity analysis was not carried out (see further considerations in Conclusions, section 4.4). The variation of just two parameters (the model's diagnosis rate and ART coverage among PLHIV) gave however some insight into the effect on the two model outputs 'active TB cases' and

'diagnosed DS-TB cases'. **Figure 3.26** shows the outputs when the diagnosis rate and/or ART coverage were varied by +/- 20%. As expected, a 20% reduction in the model's diagnosis rate and 20% increase in ART coverage both had large effects on the two outputs (pink and blue lines).

Other stages in the model application equally showed the importance of ART coverage in driving TB outputs. Sound estimation of PLHIV numbers and close monitoring of ART coverage will help in limiting the uncertainly attached to the 'ART coverage' parameter. The model's 'diagnosis rate' will likely remain uncertain and should be included in future sensitivity analyses.

Figure 3.26 Consequences of varying diagnosis rate and ART coverage in the model



Source: Populated Optima model for Gauteng.
Notes: DS-TB = drug susceptible tuberculosis; TB = tuberculosis.

3.4 WHAT MIGHT BE GAINED FROM OPTIMISED ALLOCATION OF CURRENTLY AVAILABLE FUNDING?

The analyses presented in this section responds to the core questions of this allocative efficiency study. Previous sections have identified the effects and costs of specific programmatic changes. Here, the TB response is looked at in its entirety and the question asked how resources should be allocated to maximise health outcomes. The results presented in this section were obtained through the use of Optima TB's optimisation algorithm mentioned earlier in this report and described in **Appendix A.**

As outlined in section 3.2 of this report, the "status quo" of keeping current TB spending and allocation patterns in Gauteng Province, is projected to lead to stable case numbers and deaths, and possibly a rise in MDR and the incidence of TB disease. The scope of this section is therefore to explore to what extent and how reductions in these key indicators could be achieved. Specifically, the section addresses the study questions on meeting Gauteng's strategic TB targets under current or projected funding, whether impact can be gained by allocating TB resources optimally, and whether reallocations would help in meeting the

strategic TB targets in the province. The analysis explored progress toward national and global targets related to:

- Case detection (NSP 2022)
- Loss to follow-up rates (APP 2020)
- Overall and MDR-TB treatment success rates (APP 2020)
- Reduction in TB-related death rate (APP 2020)
- Progress toward the 2035 END-TB targets
- Realism in optimisation: Introducing constraints

A useful approach to the mathematical optimisation analysis is the definition of constraints. Key points about constraining the analyses are:

- Constraints in the magnitude of reallocation can make scale-up of interventions more realistic, given the health sector capacity to increase service delivery over a short time period
- Adding constraints around treatment regimens can be important in order to reflect non-universal eligibility for a regimen
- There may be funding mechanisms and donor-based programme targeting policies which require constraining certain expenditure categories
- However, analyses should be as unconstrained as possible to allow the optimisation algorithm to run without too many restrictions and be able for the stated objective to find the global minimum

In consultation with the study team and participating experts, minimum and maximum funding amounts for specific interventions were defined (**Table 3.13**) to match constraints on intervention funding. As a general rule, to reflect the reality of programme implementation, changes in intervention funding between current and target funding levels were capped at either:

- a maximum of 30% per year, for existing interventions
- a maximum of ZAR 15M (equivalent to around USD 1 million), for new interventions for the first year, and 30% in subsequent years

…until the target level for the intervention funding was reached.

Table 3.13 Constraints in the optimisation analysis

Constraints	Lower bound	Higher bound	Justification
BCG vaccination	100%	–	
Mass Screening at PHC facilities (symptom screen, then Xpert)	50%	70%	30–50% scale-down per annum
Enhanced Mass Screening at PHC	30%	50%	30–50% scale-up per annum
Mass Screening/Outreach in High Risk Areas	20%	50%	20–50% scale-up per annum
Contact tracing for DS cases/IPT	100%	–	Minimum current funding
Contact tracing for DR cases/IPT	100%	–	Minimum current funding
ACF among PLHIV/IPT	100%	–	Minimum current funding

Table 3.13 continued.

Table 3.13 Constraints in the optimisation analysis(continued)

Constraints	Lower bound	Higher bound	Justification
DS TB Treatment	–	–	–
Old MDR regimen	10%	20%	Some still on treatment
Old MDR-with BDQ	10%	–	Some still on treatment
MDR-with BDQ shortened - modified extended regimen	–	90%	Cardiac problems: cannot be initiated
MDR-short course (KM)- modified short regimen	–	90%	Hearing problems: cannot be initiated
MDR-short course (BDQ)- short BDQ regimen	–	90%	Cardiac problems: cannot be initiated
XDR-current	20%	60%	Some still on treatment
XDR-new drug regimen shortened (BDQ and LZD)	–	90%	Cardiac problems: cannot be initiated
HIV+: DS TB	–	–	–
HIV+: Old MDR-TB	10%	20%	Some still on treatment
HIV+: Old MDR-TB/BDQ	–	90%	Cardiac problems: cannot be initiated
HIV+: New MDR TB	–	70%	Cardiac/hearing problems: cannot be initiated
HIV+: Old XDR-TB	20%	60%	Some still on treatment
HIV+: New XDR-TB	–	90%	Cardiac problems: cannot be initiated

Source: Prepared by authors in consultation with local experts.
Notes: BDQ = Bedaquiline; KM =kanamycin; DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; LZD = ; PLHIV = people living with HIV; XDR-TB = extensively drug resistant tuberculosis.

Optimised allocation of resources to minimise incidence, prevalence and deaths

In general, optimised allocations of resources are only optimal relative to a specific set of objectives and a given time frame. In other words, the optimised allocation to minimise TB disease incidence may differ from the optimised allocation to minimise TB prevalence or deaths. In order to reflect the different dimensions of the TB response, optimisation analysis was performed for a combination of three objectives with equal weighting:

- Minimise the incidence of TB
- Minimise the prevalence of active TB
- Minimise TB-related deaths

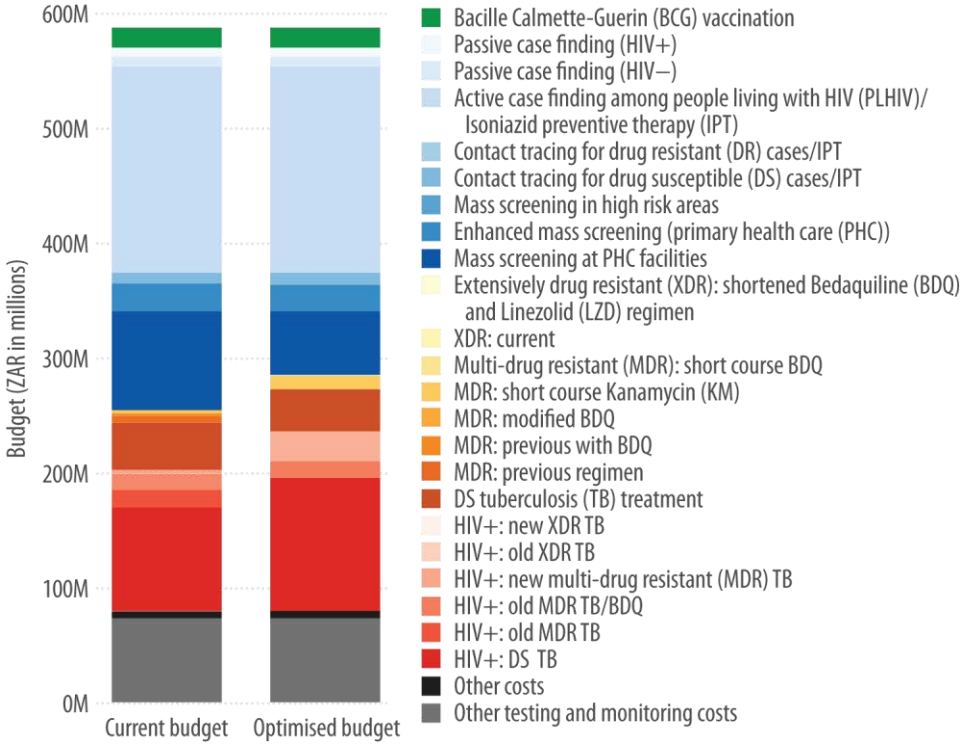
Figure 3.27 shows the overall optimised allocation of resources to minimise TB disease incidence, prevalence and deaths. In this analysis it was assumed that the same ZAR 590 million that were available for TB-related interventions in 2016 would remain available on an annual basis up to 2035. The optimised budget allocation differs from current allocations across several different areas, the main reductions being:

- Mass-screening at PHC level (as currently implemented)
- Old MDR and XDR treatment regimens

In the optimised allocation, funds are reallocated to

- Improved case finding – Enhanced mass-screening at PHC level (strengthened capacity) and outreach screening in high-risk areas
- Improved treatment regimens for better treatment outcomes – Various newer and BDQ-containing regimens, scaled-up DS-TB treatment

Figure 3.27 Current allocation of TB resources and optimised allocations to simultaneously minimise cumulative TB disease incidence, prevalence and deaths from 2017–35 in Gauteng Province



Source: Populated Optima model for Gauteng.

Notes: 2016=base year (current allocation); Optimised budget: It was assumed that the budget of ZAR 590 million that were available for TB-related programmes in 2016 would remain available on an annual basis up to 2035.

Table 3.14 lists all the interventions and current vs. optimised allocations, as well as the shifts in allocations.

Table 3.14 Current (2016) and optimal allocations of the 2016 budget, by intervention (in million ZAR)

Intervention	Current (2016) spending (million ZAR)	Optimised spending (million ZAR)	Difference (million ZAR)	% of optimised budget
BCG vaccination	18.793	18.793	–	3.7%
Mass-screening at PHC HIV-	111.012	55.506	- 55.506	10.9%
Enhanced mass-screening at PHC HIV-	0.000	23.940	23.940	4.7%
Outreach screening in high-risk areas	0.000	1.402	1.402	0.3%
Contact-tracing DS-TB	8.567	8.567	–	1.7%
Contact-tracing DR-TB	1.351	1.351	–	0.3%
Passive case finding HIV-	9.021	9.021	–	1.8%
Passive case finding PLHIV	7.956	7.956	–	1.6%

Table 3.14 continued.

Table 3.14 Current (2016) and optimal allocations of the 2016 budget, by intervention (in million ZAR) (continued)

Intervention	Current (2016) spending (million ZAR)	Optimised spending (million ZAR)	Difference (million ZAR)	% of optimised budget
Mass-screening at PHC PLHIV	178.657	178.657	–	35.1%
DS-TB treatment	41.512	47.905	6.393	9.4%
Old MDR treatment	4.192	0.419	- 3.773	0.1%
Old MDR/BDQ treatment	4.743	0.474	- 4.269	0.1%
MDR/BDQ treatment	0.000	1.602	1.602	0.3%
KM-SC treatment	0.000	3.582	3.582	0.7%
BDQ-SC treatment	0.000	8.420	8.420	1.7%
XDR-Current treatment	0.812	0.162	- 0.650	0.0%
XDR-new treatment	0.000	0.000	–	0.0%
PLHIV/DS-TB treatment	90.534	111.026	20.493	21.8%
PLHIV/Old MDR treatment	13.889	1.389	- 12.500	0.3%
PLHIV/Old MDR-BDQ treatment	15.713	14.134	- 1.579	2.8%
PLHIV/New MDR treatment	0.000	14.355	14.355	2.8%
PLHIV/Old XDR treatment	2.388	0.478	- 1.911	0.1%
PLHIV/New XDR treatment	0.000	0.000	–	0.0%
Total screening/diagnosis	335.356	305.192	- 30.164	59.9%
Total treatment	173.783	203.947	30.164	40.1%

Source: Populated Optima model for Gauteng.
Notes: BDQ = Bedaquiline; KM =kanamycin; DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; LZD = ; PLHIV = people living with HIV; XDR-TB = extensively drug resistant tuberculosis.

Shifts within diagnostic interventions

Gaps in diagnosis represent a major break point in the TB care cascade in most countries, and finding the "missing cases" is a chief challenge for TB programmes. Nevertheless, optimised allocation of resources would – according to the modelling results - require a shift of about ZAR 30 million from screening/diagnosis to treatment interventions (**Table 3.15**). Screening and diagnosis would then consume about 60% of the TB funding.

Figure 3.28 shows current and optimised allocation of the remaining ZAR 305 million for screening/diagnostic interventions. The optimal allocation would entail:

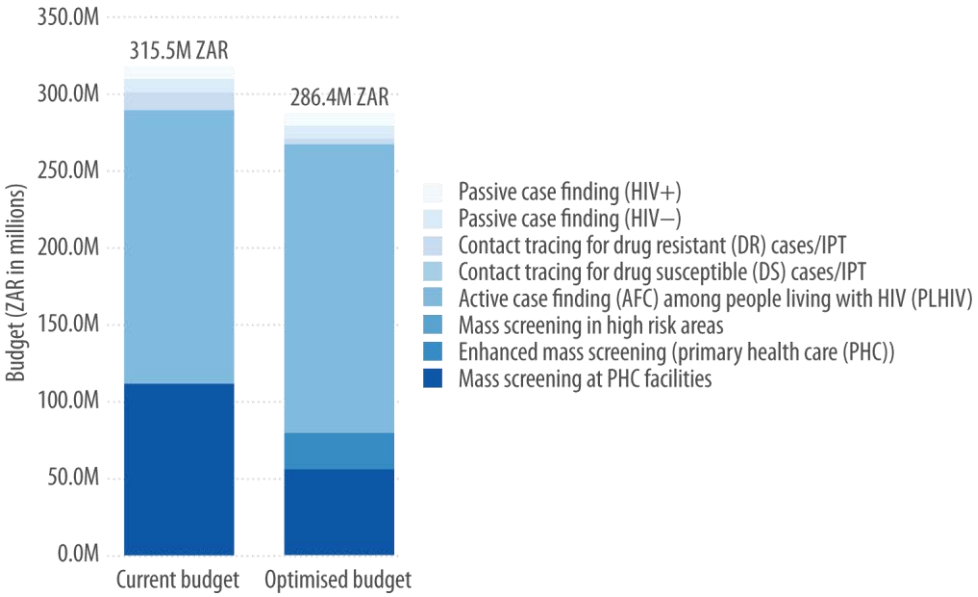
- Strengthening mass screening at PHC (toward "enhanced mass screening", asking all four symptom questions consistently), as well as investing in targeted outreach screening in high risk areas
- Sustaining the current amounts of funding for active case finding among PLHIV and contact-tracing interventions

Compared to the 2016 mix of case finding investments, the province would therefore prioritise allocations into case finding activities which are efficient at identifying TB cases—such as active case finding among PLHIV, and outreach screening in areas known to have high TB risk. The latter can be guided by the spatial analysis of TB notification data. Using 2015/16 demographic and TB surveillance data, this analysis found for instance that TB notification rates varied from below 150/100 000 (sub-districts Tshwane 4, Johannesburg C and B) to over 400/100 000 (Tshwane 1, Merafong City, Tshwane 5) (**Figure 1.3**). Exploiting the large differentials in local TB burden for targeted outreach screening would be one approach to identify cases in the community.

Considering that the actual prevalence and incidence of TB and thereby the size of the undiagnosed population are not known, strategies to increase case finding should be continuously monitored and carefully evaluated. This is required in order to assess whether the yield of newly identified cases is commensurate to the investments.

Considering that the actual prevalence and incidence of TB and thereby the size of the undiagnosed population are not known, strategies to increase case finding should be continuously monitored and carefully evaluated.

Figure 3.28 Current (2016) and optimised allocations of resources for TB diagnosis to minimise TB disease incidence, prevalence and deaths in Gauteng



Source: Populated Optima TB model for Gauteng.

Shifts within treatment interventions

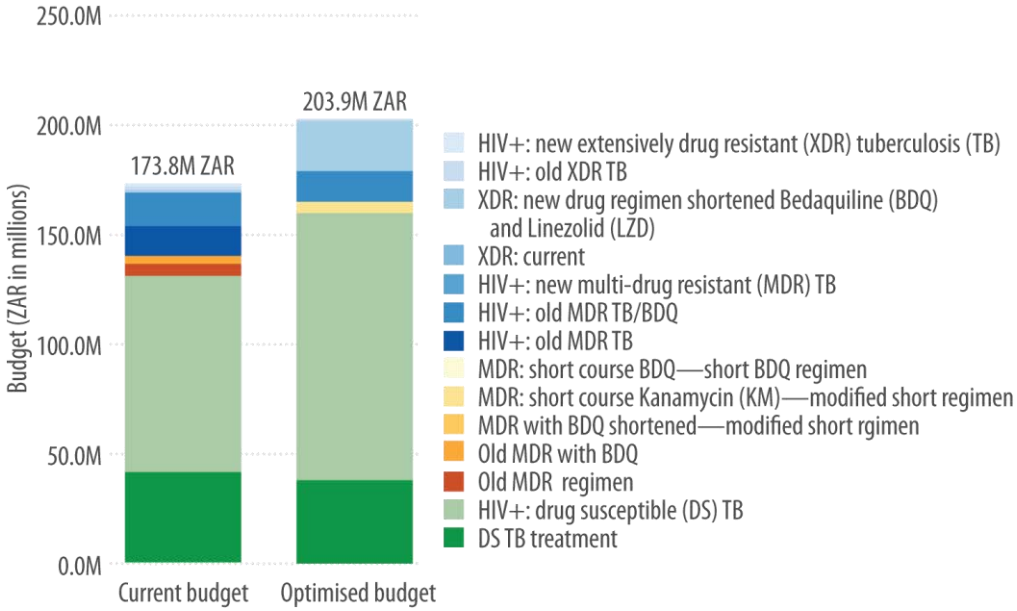
In an optimised intervention mix, TB treatment would receive slightly more funding (+ZAR 30 million) and would absorb approximately 40% of the total Gauteng TB spending.

Optimisation within the treatment component suggests increases in annual funding especially for (**Figure 3.29**):

- DS-TB treatment in co-infected patients (+ZAR 20.5 million)
- Shortened BDQ for HIV negative patients with MDR-TB (+ZAR 8.4 million)
- New MDR-TB regimens in co-infected patients (+ZAR 14.3 million)

These shifts in allocations take into account the constraints established for certain regimens in particular the limited eligibility for BDQ-containing regimens in patients with cardiac problems (**Table 3.14**).

Figure 3.29 Current (2016) and optimised allocations of resources for TB treatment to minimise TB disease incidence, prevalence and deaths in Gauteng

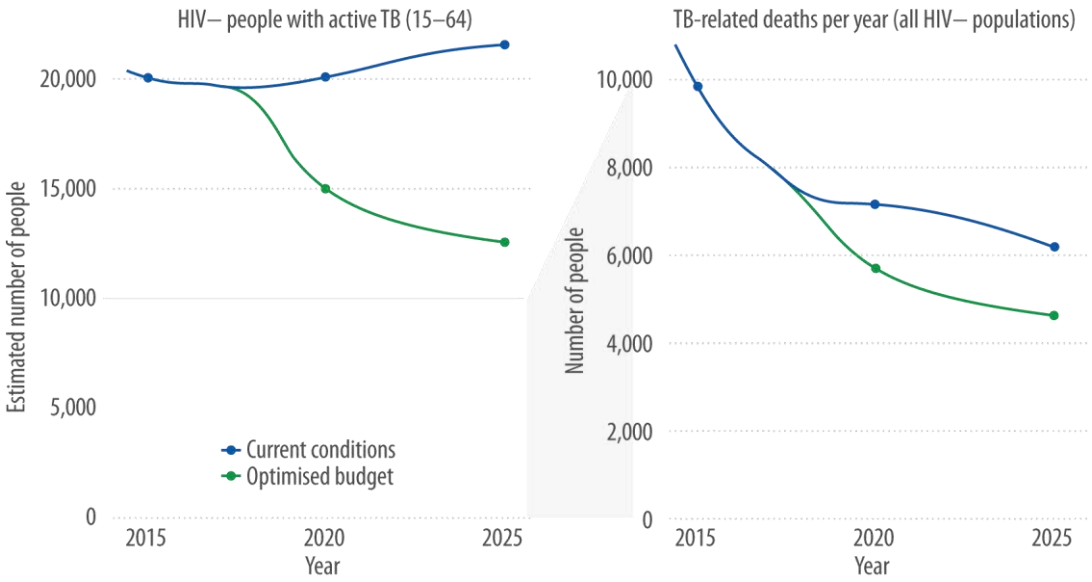


Source: Populated Optima model for Gauteng.

3.5 IMPROVED OUTCOMES WITH OPTIMISED ALLOCATIONS

The optimised allocation of resources as shown in **Figures 3.26–3.28** would have substantial effects. **Figure 3.30** describes trends in TB prevalence and TB-related deaths in HIV negative populations. Among adults aged 15–64 and HIV negative, an optimised budget allocation could reduce the number of active TB cases by 40% by 2022 i.e., within the current NSP, in comparison to current allocations (left chart). It could also reduce the number of annual TB-related deaths by 30% by 2022 in all HIV negative populations combined (right). TB disease incidence is however projected to remain unchanged despite reallocations.

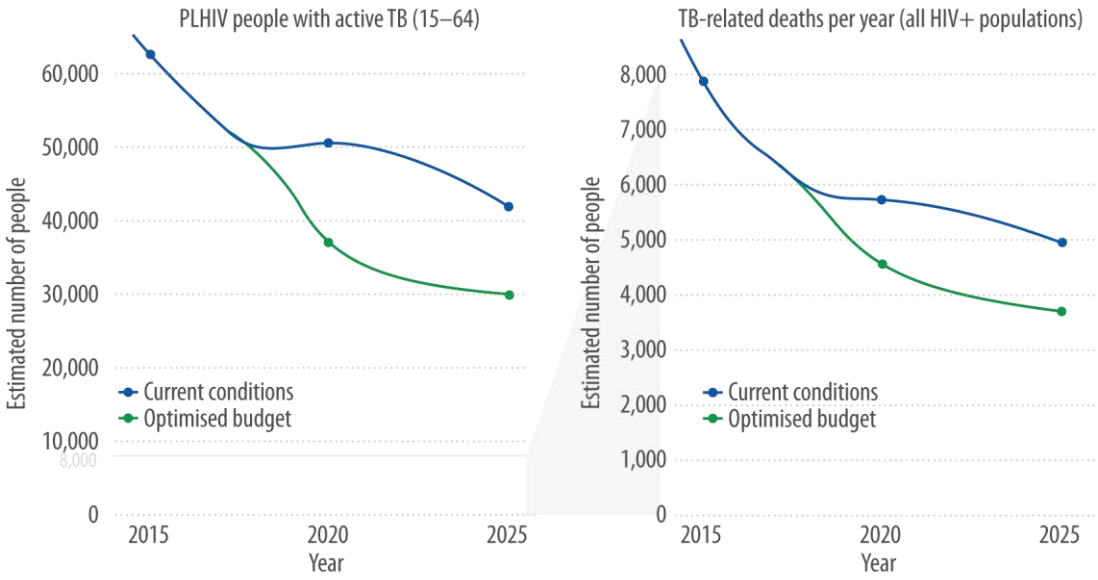
Figure 3.30 Epidemiological outcomes for the HIV negative populations with current and optimised allocations, Gauteng



Source: Populated Optima TB model for Gauteng.
Note: The annual budget is assumed constant at ZAR 590 million until 2025; TB = tuberculosis.

Figure 3.31 shows key outcomes of optimised allocations for PLHIV for the NSP time frame up to 2022. The optimised allocation could reduce the number of active TB cases by about 40% by 2022 (left chart). It could also reduce the number of annual TB-related deaths by approximately 30% in 2022 (right). Incidence of TB infections is projected to remain unchanged.

Figure 3.31 Epidemiological outcomes for PLHIV with current and optimised allocations, Gauteng



Source: Populated Optima TB model for Gauteng.
Note: The annual budget is assumed constant at ZAR 590 million until 2025; PLHIV = people living with HIV; TB = tuberculosis.

Other areas for optimizing the TB response, which were not analysed in the model

The analyses represented in the optimised allocation do not include all possible dimensions of optimisation in the TB response. A number of other areas could be considered in strengthening the TB response. For example:

Comprehensive infection control in health care facilitates - an area, in which additional investments could be made, particularly considering the rising prevalence of MDR-TB in Gauteng Province. This analysis included element of the infection control programme (IPT, cough screening of health facility clients), but many other elements of such a programme were not represented (e.g., personal risk reduction measures like N95 masks, environmental controls like room ventilation interventions and ultraviolet germicidal irradiation (UVGI) devices, and administrative controls such as triage of coughing clients, safe environment for sputum collection, etc.). The package of interventions within comprehensive infection control was too complex to model with insufficient data on expenditure, cost components and impact.

Medical surveillance programme – a related programme for the protection of health workers. Available survey data suggest that implementation is incomplete in Gauteng: Not all HCWs have an annual HIV test, 26% of HCWs having an annual chest x-ray.[34] HCWs personal protection is inadequate, only 20% make use of ventilation, and UVGI was only installed at 1% of GP facilities at the time of the survey. Of all HCWs interviewed, 77% would use a N95 mask for personal protection. Despite attempts to include HCWs as a key population (see "Limitations" in section 2.2), it was not possible to model a programme targeted at this highly exposed population.

TB programmes in gold mine and prison settings – the analysis made efforts to include the intervention packages targeted at gold mine employees and prison inmates, but it was not possible to obtain sufficient data to which would have been required to assess the extent of possible efficiency gains in these areas.

3.6 OPTIMISED ALLOCATION OF RESOURCES TO IMPROVE TB CARE CASCADES

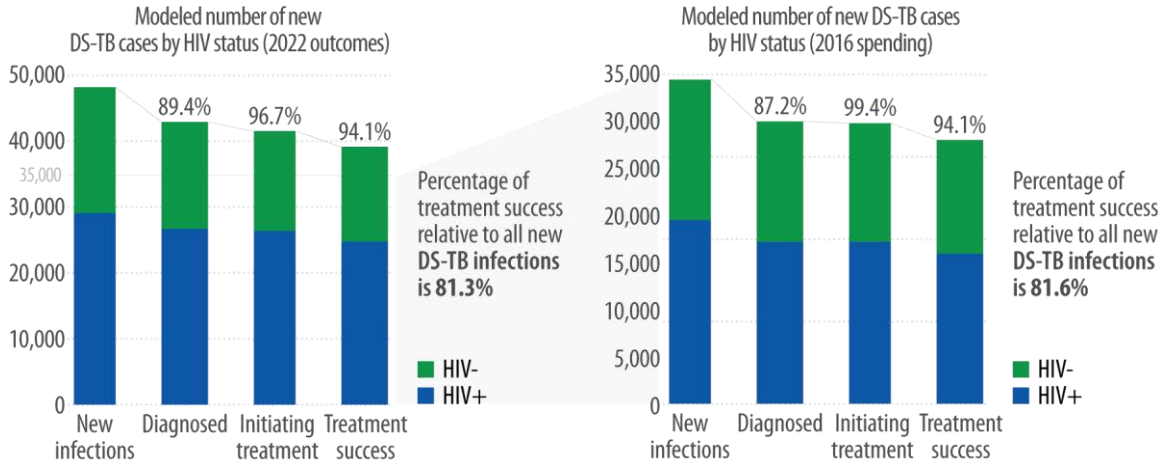
The historical focus of the TB Programme has been on treatment success rates, which fail to reflect pre-treatment, upstream losses contributed by cases who are not diagnosed or linked to treatment. Therefore, in addition to the overall optimisation described in the previous section, optimisations were run to determine best allocations for maximizing DS-TB and DR-TB treatment success, a key measure for the TB response. This section summarises the findings from these optimisations.

The historical focus of the TB Programme has been on treatment success rates, which fail to reflect pre-treatment, upstream losses contributed by cases who are not diagnosed or linked to treatment.

Figure 3.32 shows the modelled number of DS-TB cases by stage of care cascade and HIV status, using a cross-sectional approach to the cascades based on estimated new active TB

infections in one year. The number of active infections passing through the active infection junction in one year included relapse and re-infection cases. It was estimated that under 2016 spending allocations, treatment success relative to all new DS-TB infections was at 81.3% (left chart). It was also estimated that 37000 TB cases were undiagnosed of which approximately 23000 PLHIV and 14000 HIV negative. Among notified DS-TB cases, about 60% were co-infected with HIV. Under optimised allocation conditions of the 2016 budget, a very marginal improvement could be made to yield 81.6% treatment success relative to all new DS-TB infections (right). For the DS-TB care cascade, the optimised budget improved linkage to treatment by 2.7%, but decreases the percentage of diagnosed new DS-TB infections by 2.2%. This indicates the high importance of preventing pre-treatment loss once the investment has been made into finding and diagnosing TB cases.

Figure 3.32 Care cascade outcomes for DS-TB cases with current and optimised allocations, Gauteng

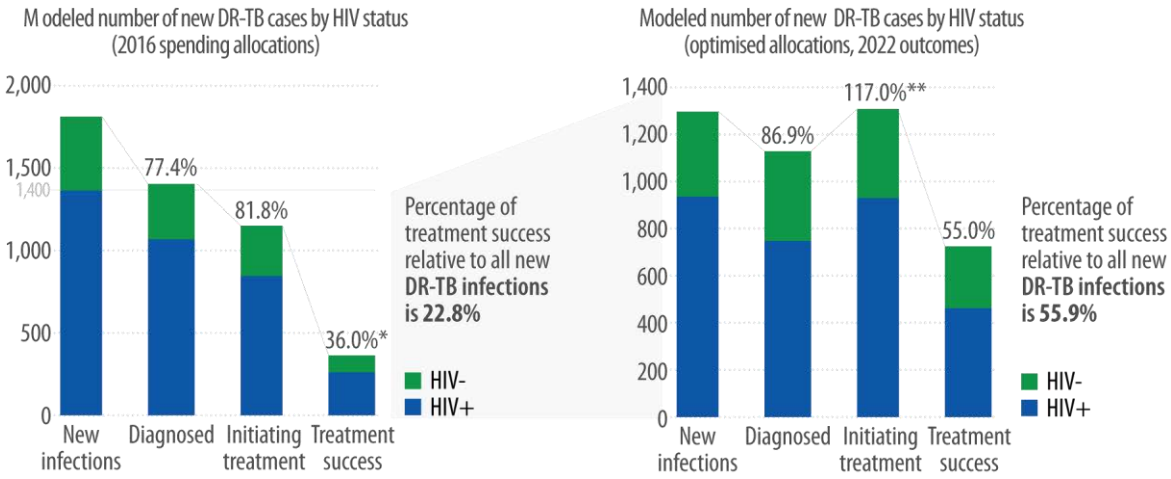


Source: Populated Optima TB model for Gauteng.

Note: Treatment success includes cure and treatment completion and uses the modelled number of all new DS-TB infections as the denominator; DS-TB = drug susceptible tuberculosis.

Figure 3.33 presents the modelled number of DR-TB cases by stage of care cascade and HIV status. It was estimated that under 2016 spending allocations, treatment success relative to all new DR-TB infections was at 22.8% (left chart). A large proportion of DR-TB cases were co-infected with HIV (~75%). The estimated losses along the DR-TB care continuum suggest that improvements could address initial diagnosis rate and pre-treatment loss to follow-up, but also increasing the number of patients completing treatment. Under optimised allocation conditions of the 2016 budget, a substantial improvement could be made to yield 55.9% treatment success relative to all new DR-TB infections (right). For the DR-TB care cascade, the optimised budget increased the proportion of diagnosed new DR-TB infections by 9.5%, significantly improved treatment coverage for both new and retreated cases by around a third while maintaining treatment success rates. The cascade includes additional DR-TB patients who have been re-engaged in care, and re-started treatment following failure. This is because the optimised budget has increased access to high quality DR-TB management.

Figure 3.33 Care cascade outcomes for DR-TB cases with current and optimised allocations, Gauteng



Source: Populated Optima TB model for Gauteng.

Note: Treatment success includes cure and treatment completion and uses the modelled number of all new DS-TB infections as the denominator; * = The 36% treatment success rate is informed by 2014 MDR-TB outcomes data. This was only used in the historical calibration and not to inform future projections after optimization modeling; ** = Includes additional DR-TB patients who have been re-engaged in care, and re-started treatment following failure (the optimised budget increased access to high quality DR-TB management); DR-TB = drug resistant tuberculosis.

3.7 OPTIMISED ALLOCATIONS UNDER DIFFERENT BUDGET ENVELOPES AND THEIR IMPACT

Optimal allocations change as a function of the available budget. An "investment staircase" analysis was carried out in order to illustrate which investments remain "best buys" even under severe funding constraints and which interventions become part of the recommended intervention mix at higher budget availability.

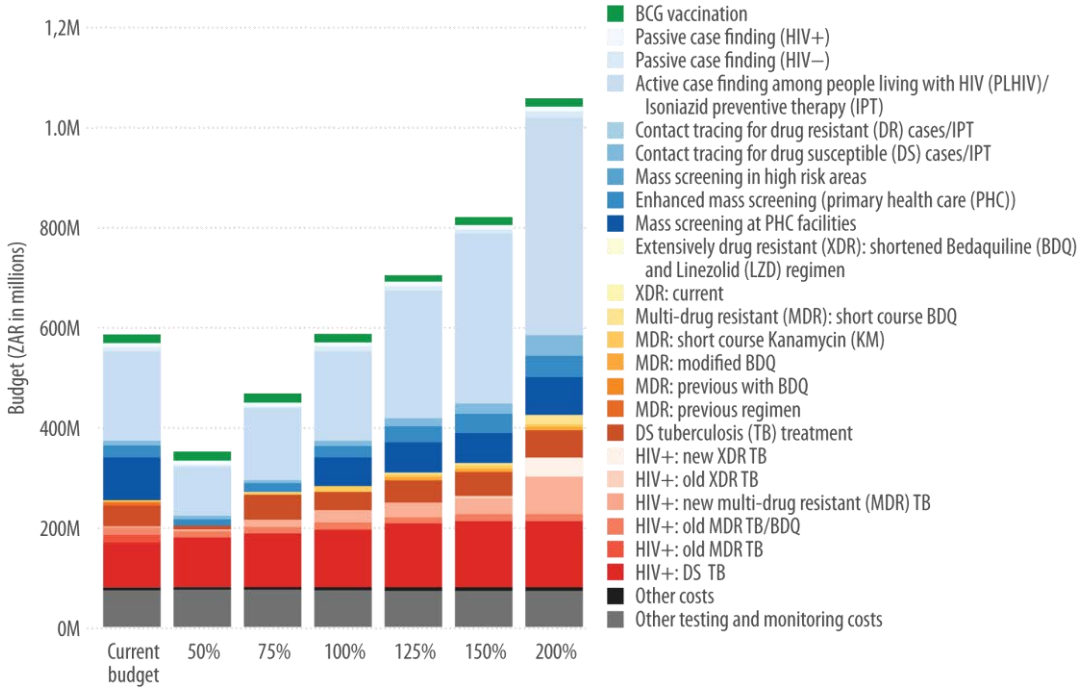
Figure 3.34 shows the allocation pattern by budget level. Under conditions of increased budget availability (as should be the case if historical budget increases continue to apply) the following interventions are continuously prioritised:

- Active case finding in patients in HIV care, as well as enhanced mass screening at PHC, and outreach screening in high-risk areas
- New MDR-TB regimens in PLHIV
- At 200% of budget: new XDR-TB regimens

Figure 3.35 shows the impact of optimised allocations of different budget envelopes on TB outcomes. Optimised allocation brings major reductions in active and new active TB infections and TB deaths. The projections suggest that the gains are however not sustained beyond 2025 if the optimised budgets stays at 100%, as funding gets too tight to deliver the interventions.

- Reducing the current budget by 50% would lead to dramatic increases in the numbers of active TB infections and deaths, and some increase in new active TB infections
- Budget increases buy additional impact, however, large increases beyond 150% of current budget have diminishing returns

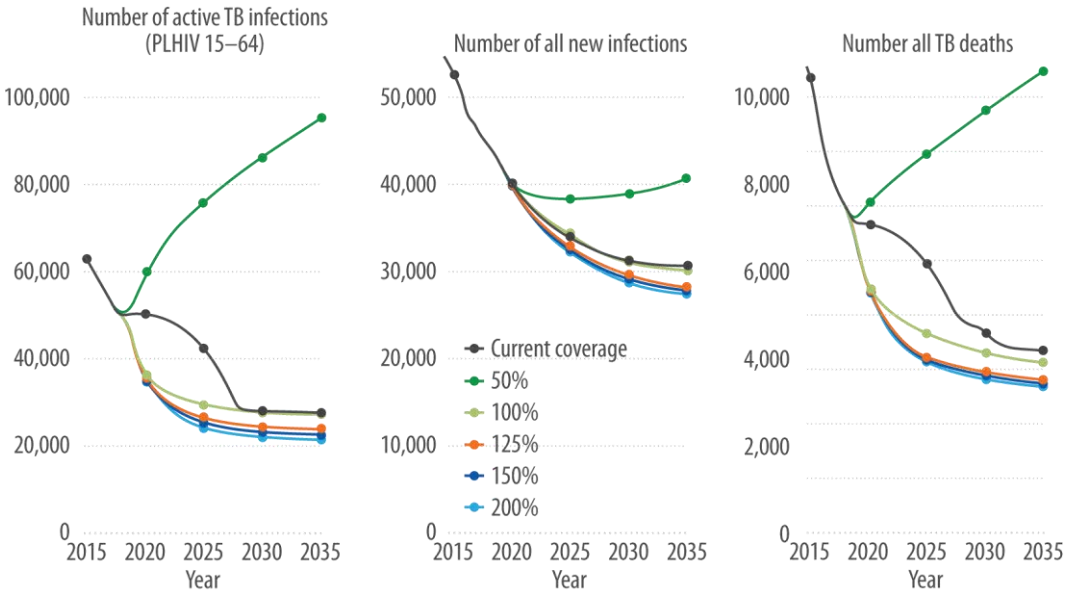
Figure 3.34 Optimised spending allocations under different budget envelopes, Gauteng



Source: Populated Optima TB model for Gauteng.

Notes: Current budget: 2016 spending allocation of ZAR 590 million; 100%: Optimised 2016 spending allocation of ZAR 590 million; 50–200%: Optimised 2016 spending allocation of 50-200% of the 2016 budget of ZAR 590 million.

Figure 3.35 Modelled impact of optimised allocations at under different budget envelopes, Gauteng (2015–35)



Source: Populated Optima TB model for Gauteng.

Notes: Current budget: 2016 spending allocation of ZAR 590 million; 100%: Optimised 2016 spending allocation of ZAR 590 million; 50–200%: Optimised 2016 spending allocation of 50–200% of the 2016 budget of ZAR 590 million; PLHIV = people living with HIV; TB = tuberculosis.

3.8 OPTIMISED ALLOCATIONS OF RESOURCES FOR MEETING STRATEGIC TB TARGETS

This final results section explores to what extent the optimised allocations shown in previous sections could help Gauteng to achieve national and global TB targets (**Table 1.3** and Section 2.2). This includes again different budget levels of 50–200% of the ZAR 590 million available in 2016, and these budgets are optimised for the combined objective of minimising TB disease incidence, prevalence and deaths as before.

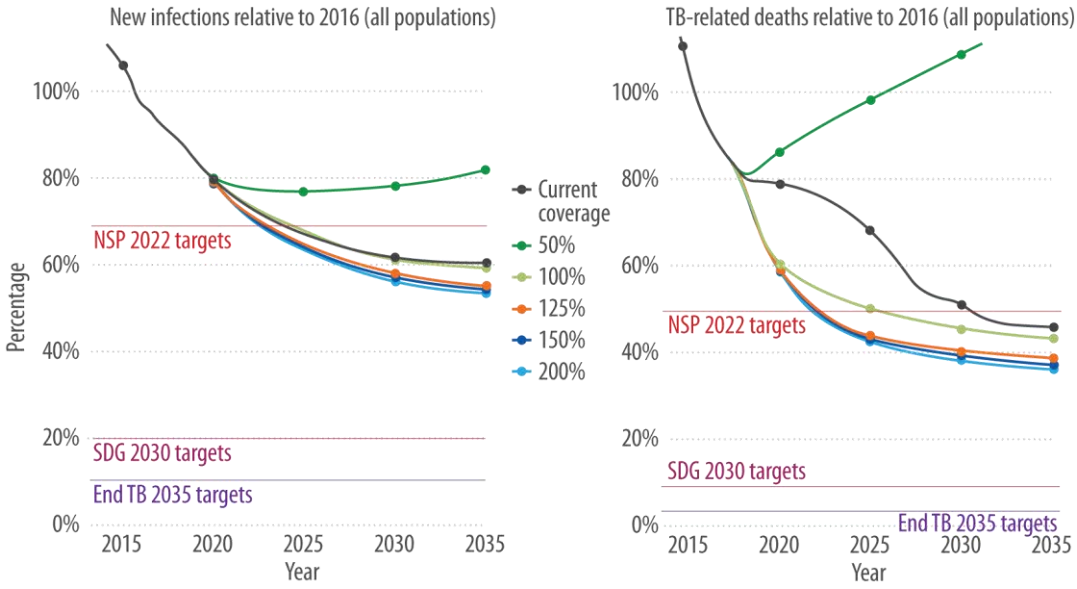
Figure 3.36 shows the model projections by using 2016 as the base year for new TB infections (left chart) and TB deaths (right), and showing relative proportions against the base year. Different key targets and milestones are represented by the dotted lines.

The model outputs suggest that NSP 2022 targets feasible, but in order to meet 2030 and 2035 targets, new approaches and significant budget increases are required. Rapid attainment of universal ART coverage for PLHIV would also accelerate progress in TB.

To reach NSP targets:

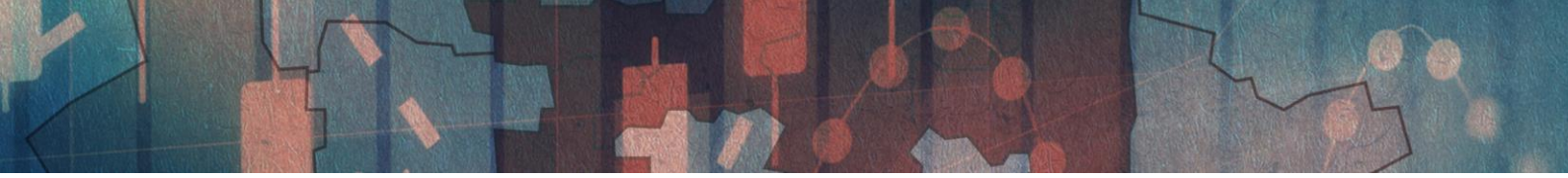
- 150% of the current budget will **reduce TB disease incidence by 30% by 2022**
- 125% of the current budget will **reduce TB-related mortality by 50% by 2022**
- With current budget optimally allocated, these **targets will be reached in 2025**
- Without optimal allocation, the **NSP target for TB related deaths will be reached after 2030**

Figure 3.36 Optimised allocation in relation to 2022, SDG 2030 and End-TB 2035 targets, Gauteng



Source: Populated Optima TB model for Gauteng.

Notes: Current budget: 2016 spending allocation of ZAR 590 million; 100%: Optimised 2016 spending allocation of ZAR 590 million; 50–200%: Optimised 2016 spending allocation of 50–200% of the 2016 budget of ZAR 590 million; NSP = National Strategic Plan; SDG = Sustainable Development Goals; TB = tuberculosis.



4. CONCLUSIONS

4.1 LEARNING FROM MODELLING SCENARIOS

The scenarios conducted in this Optima TB pilot application highlight significant opportunities to reduce TB deaths and avert infections in HIV- populations by improving the care cascade (scenarios 1–4), in particular:

- Improving the diagnosis rate and linkage to treatment of active TB cases
- Improving the treatment outcomes of MDR-TB cases

A transition to shorter MDR-TB regimens significantly improves treatment outcomes, and requires around 10% in additional funding

When combined with other interventions, scaling-up DS-TB contact tracing requires less overall spending to sustain the same number of actively identified TB cases, compared to the current funding of screening interventions.

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An increase in the coverage of interventions targeted at PLHIV and prisoner populations yields significant reductions in the number of active-TB infections, in particular:

- PLHIV: Increasing testing, treatment initiation, and ART coverage
- Prisoners: improving the diagnosis rate and linkage to treatment

4.2 SHIFTING FUNDING TOWARDS OPTIMAL ALLOCATION

TB testing programmes: There is currently high coverage of symptom-screening and Xpert testing has been rolled out. Consistently asking the full set of four symptom screening questions rather than only the cough question would increase screening sensitivity and yield. Strengthening processes around mass-screening can improve the number of TB suspects receiving diagnostic confirmation with Xpert. A saving on the mass-screening as currently practiced would allow for investment in improved quality mass screening (up to ZAR 24 million) as well as a ZAR 2 million investment in outreach screening in areas identified as high-risk zones.

Contact tracing remains important and funding of about ZAR 8.6 million for DS-TB and ZAR 1.4 million for DR-TB should be sustained.

TB treatment programmes: Shifting resources from older regimens would allow scaling-up new DR-TB regimens, and in particular enable DOH to roll out MDR-TB short-course treatments (approximately ZAR 12 million). At the same time, DS-TB treatment would benefit from additional funding to ensure near-universal DS-TB treatment (approximately ZAR 21 million).

4.3 GAINING IMPACT THROUGH RE-ALLOCATIONS

The same budget **allocated differently** could, by 2022:

- Reduce the number of active TB infections in the general population by up to 40%
- Reduce the number of active TB infections among PLHIV by up to 40%
- Reduce the total number of TB deaths by up to 30% (ca. 2000)
- Reduce the number of TB deaths among PLHIV by up to 30%

The 2016 budget amount, allocated optimally is unlikely to achieve all APP 2020 targets in the short intervening period. However, the target for success rates for all TB cases can be met (improvement from 83% to 85% by 2020), as well as the MDR-TB initiation rate (117%) by 2020, at 2016 funding levels and optimally allocated.

To reduce TB disease incidence by 30% by 2022 as per NSP 2017-2022 will require 150% of the 2016 spend on TB, and to reduce TB-related mortality by 50% by the same year will require 125% of the 2016 spend. The case detection for all TB cases is 3% away from the NSP 2022 targets by 2022.

The additional scale-up of DS-TB and DR-TB treatments (including the prioritisation of more effective DR-TB regimens) among diagnosed cases through re-allocations will shorten the average time until treatment success is achieved. With a shorter duration of disease, the number of active TB cases is in turn expected to decrease. A similar reduction in the incidence of TB disease would however be unlikely given the high proportion of new active cases that come from the large pool of people with long-term latent TB infections. To observe a reduction in the number of people progressing from late latent-TB to active-TB, and thus incidence of disease, other interventions that affect that transition rate - i.e. social protection, nutrition - are needed.

The additional scale-up of DS-TB and DR-TB treatments (including the prioritisation of more effective DR-TB regimens) among diagnosed cases through re-allocations will shorten the average time until treatment success is achieved.

4.4 TB ANALYTICS FOR DECISION-MAKING

This analysis represents a continuation of the work accomplished in South Africa's National HIV and TB Investment Case, and other key analytical and modelling studies on TB in South Africa, in this case just focusing on one province. In the course of implementation of the allocative efficiency analysis, several intermediate analytics products had value for the stakeholders:

- TB expenditure breakdown by intervention (summarised in **Figure 3.9**)
- Unit cost estimates (presented in **Tables B8–B10**)
- A revised costing assessment of TB tests run by the NHLS[35]
- Geospatial maps on TB notification indicators (**Figure 1.3** and **Figure 1.4**)
- Geospatial maps on TB outcomes and HIV/TB integration (**Figures D.1–D3**)

The Optima TB parametrisation was drawing on the extensive published literature from South Africa and elsewhere. The study team compared assumptions and values with individual studies where appropriate, including from studies published after completion of the allocative efficiency analysis such as the South African Tuberculosis Drug Resistance Survey

2012–14.[36] Other studies were equally used including any studies on technical efficiency which is often closely associated with allocative efficiency. For instance, one study on adherence to TB screening protocols and best practices confirmed the importance of further quality improvement of the PHC-level mass screening, the investigation of contacts, and improved linkage to care.[37]

4.5 LESSONS LEARNT FROM THE MODEL APPLICATION

The pilot application of Optima TB in Gauteng Province provided important lessons, especially in the areas of integrating the effects of the HIV epidemic into the analysis of TB resource allocations, and the accounting for uncertainty in the modelling process. The lessons were then used to refine the Optima TB model and its Graphic User Interface (tb.optimamodel.com).

We learnt that in the co-epidemic setting, model inputs on future targets and attainable coverage of the ART programme require broad consultation with TB and HIV experts, and agreement on the assumptions taken, so that stakeholders see their collective understanding of the ART scale-up reflected in the TB modelling study. Albeit limited, the Optima TB model did capture aspects of HIV-TB comorbidity and effects of ART on TB. The study team also used available local ETR and EDR data disaggregated by HIV-status to capture heterogeneity of TB outcomes and care (despite data limitations). Projecting forward from 2016, the modelling team used fix HIV incidence and ART coverage rates. This was based on a conservative assumption that the status quo would hold true moving forward in the short-term to 2022, and was also rooted in the fact that the analysis addressed resource allocation to TB interventions only. Keeping ART coverage constant for the projected PLHIV population may not have been an ideal choice, given NDOH's commitment to roll-out ART to all diagnosed PLHIV within the universal treatment policy. The 'higher ART' scenario demonstrated the large effect the ART scale-up has on TB dynamics (in scenario 8, ART was the most important intervention to reduce active TB infections—the 65% ART coverage tested in this scenario happened to match the 65% ART coverage target in Gauteng Thembisa version 4.1). Given the optimisation analysis focused on medium-term resource allocation within the APP and NSP periods, the results were not rendered invalid with the conservative ART coverage assumptions to 2022. Thanks to the learning from the Gauteng application:

- Optima TB analyses now explicitly include ART as a TB-sensitive programmatic intervention rather than as a background assumption, which allows greater flexibility in defining more appropriate scenarios and optimisations to provide the most relevant policy recommendations.

- The Graphic User Interface of the Optima TB app includes a scalable ART intervention within its list of programmes which is parametrised to affect TB dynamics while being funded outside of TB financing streams.
- While these are useful improvements to make ART effects more explicit, the impact of HIV with and without ART on different parameters was already present in the Gauteng model version and used in the application, as described in the "Methodology" section.

As in most complex modelling analyses, there were multiple layers of uncertainty in the outputs of the model. While comprehensive considerations of uncertainty were not possible at the time, two epidemiological variables were considered key and explored further in univariate analyses—ART coverage and diagnosis rates. Because of the team's experience from Gauteng, the tool could subsequently be strengthened:

- In the current version of Optima TB, users are able to have uncertainty bounds represented for every input parameter by entering standard deviation values from the best available data or estimate, assuming a normal distribution.
- Uncertainty relating to programme costs and efficacies can also be included and used to inform the model, allowing a more rigorous comparison between alternate allocations.
- Uncertainty bounds for results can then be generated by sampling from this parameter distribution.

While some of the above-mentioned functionalities were not yet fully available in the model version piloted in Gauteng, the study team was pleased that the peer reviewers confirmed that the recommendations emanating from the results are in line with recommendations from the WHO and other published findings. Overall, the application team concluded that the model structure is well-suited and appropriate to address the typical policy questions TB programmes encounter around priority interventions, costs to meet TB coverage and impact targets and the impacts of changes in TB resource allocations.

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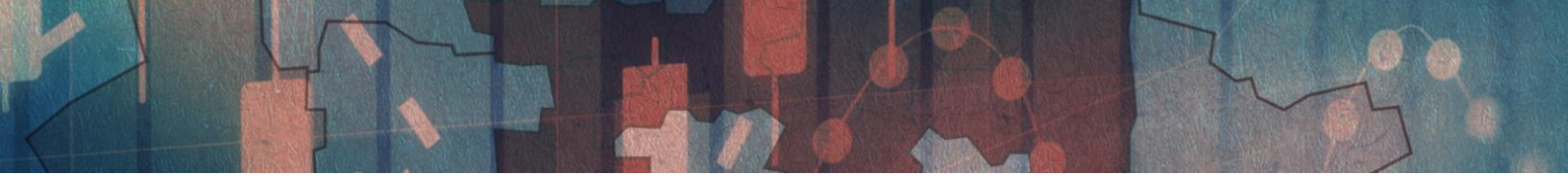
The adaptations of Optima TB thanks to the learning from the Gauteng, Belarus and Peru pilot applications will further strengthen the robustness of the results and the reliability of conclusions of such analyses. The Gauteng analysis has specifically helped to further develop and refine the Optima TB model for the TB setting with generalised HIV epidemics. Like all modelling tools, there are always additional improvements to be made, so the decision support models can provide is continuously enhanced for its policy-relevance.



5. RECOMMENDATIONS

Based on the pilot application of Optima TB, important health impact could be gained (35% reduction in active TB cases and 28% reduction in TB deaths by 2022) by sustaining 2016 TB financing of ZAR ~590 million and making specific changes/ reallocations towards optimal allocations:

REDUCE PRE-TREATMENT LOSS-TO FOLLOW-UP AND INCREASE LINKAGE TO CARE, PARTICULARLY FOR MDR-TB

- Facilitate treatment initiation by further integrating point of care, and strengthening de-centralization with healthcare staff and treatment capacity
- Fit-for-purpose patient monitoring systems including integration of systems between health facilities and laboratories
- High-quality treatment initiation counselling is likely to make a positive contribution to treatment initiation and adherence
- Focused efforts can significantly improve treatment initiation in diagnosed MDR-TB cases

USE PHC MASS-SCREENING FUNDING TO STRENGTHEN ITS CORRECT IMPLEMENTATION

- Enhance population screening at PHC facilities, by consistently asking all four questions in the symptomatic screening protocol (approximate investment of ZAR 24 million into quality-enhanced PHC mass-screening replacing low-quality mass-screening services)This can nearly double screening sensitivity (from about 21% to 38%) and address the decreasing yield

TRANSITION TO SHORTER DRUG-REGIMENS FOR DRUG-RESISTANT TB

- Investment in newer MDR-TB regimens can significantly improve treatment success rates (from 23% treatment success among the estimated new DR-TB infections to as high as 56% treatment success), and accelerate smear-conversionEstimated spending shifts are ZAR 8 million less for older MDR regimen types, and approximately ZAR 14 million more for new MDR regimens including short-course.

MAINTAIN CONTACT-TRACING FOR DRUG-RESISTANT TB CASES

- Continued investment of approximately ZAR 1.4 million into DR-TB contact tracing is expected to identify about 144 MDR-TB infections annually

REALLOCATE SOME FUNDING FROM MASS-SCREENING TO OUTREACH IN HIGH RISK AREAS

- Large investments in outreach programmes are not advisable if current diagnosis coverage levels are to be sustained and budgets remain at similar levels
- Modest amounts of funding into outreach (approx. 0.3% of 2016 budget or ZAR 1.4 million), however, can be beneficial and increase TB diagnoses among hard to reach populations
- Outreach needs to draw on spatial TB epidemic analysis

ADDITIONAL SCALE-UP OF IPT

- In prisons, IPT scale-up to 30% coverage will yield significant short-term gains in reducing active cases in prison populations (especially in HIV-positive prisoners where a 20-30% reduction in future DS-TB cases was projected)
- IPT scale-up in the PLHIV population will yield moderate to small short-term gains in reducing active cases among adult PLHIVs (estimated gains through further ART scale-up to 65% of PLHIV were considerably larger)

IMPROVE LINKAGE TO TB CARE IN CORRECTIONAL SERVICES

- Significant improvements have been achieved in screening practices, treatment initiation and outcomes for prisoners
- Additional improvements in diagnosis rates (to 85% for DS-TB) and treatment outcomes (to 90% treatment success for DS-TB), however, could yield up to a 50% reduction in DS-TB prevalence

MAINTAIN ACTIVE CASE FINDING COVERAGE LEVELS IN PLHIV

- Maintaining current spending of ZAR 178M on active case finding during HIV/ART routine consultations at PHC are projected to have identified almost 30,000 TB cases among PLHIV, or 75% of all TB/HIV notified cases, in 2017

INSTITUTIONALISE DR-TB REPORTING FROM ALL CORRECTIONAL FACILITIES

- All Gauteng prison facilities should report into the national TB surveillance system for DS and DR-TB to track TB in these high-risk settings (and enable analyses like the present one)

ENHANCE TB INFECTION PREVENTION AND CONTROL FOR THE APPROX. 55,000 PUBLIC HEALTH CARE WORKERS IN GAUTENG

- There is a lack of epidemiological and programmatic data on TB in HCWs in Gauteng (this analysis was not able to include HCWs as a sub-population due to lack of critical data for modelling)
- A concerted effort is needed to appropriately monitor and analyse the disease burden in this population, ensure that all personal TB protection measures are taken, and that the TB medical surveillance programme is fully implemented

- MAXIMISE THE INTEGRATION AND USE OF TB ROUTINE DATA TO STRENGTHEN PROGRAMME IMPLEMENTATION, AND ENSURE SPECIFIC M&E ACTIVITIES SUCH AS:
  - Tracking of TB-specific expenditures within the health sector
  - Reporting of how TB cases are identified (by intervention modality)
  - Systematic analysis of TB treatment outcome data in mining sector (by commodity, TB drug sensitivity and HIV status)
  - Geospatial analysis of key indicators to target TB interventions
  - Patient perspectives on TB prevention, treatment and care services are known
- FURTHER SCALE-UP OF ART IN THE GENERAL POPULATION.
  - Increasing ART coverage to 65% of all PLHIV would have a significant positive impact on the TB burden in PLHIV by decreasing active TB prevalence and the number of MDR-TB cases by around 30%

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APPENDICES

Appendix A OPTIMA HIV MODEL

The Optima mathematical modelling suite was designed to support decision-makers in prioritization, resource allocation and planning to maximise health impact. Optima-HIV was the most widely used component of the Optima modelling suite. A more detailed summary of the model and methods is provided elsewhere.[38]

Optima TB is a mathematical model of TB transmission and disease progression integrated with an economic and programme analysis framework. Optima uses TB epidemic modeling techniques and incorporates evidence on biological transmission probabilities, detailed disease progression and population mixing patterns. Optima TB is a compartmental model, which disaggregates populations into different model compartments including susceptible, vaccinated, undiagnosed early or late latent-TB, diagnosed early or late latent-TB, on treatment early or late latent-TB, undiagnosed active TB, diagnosed active TB, on treatment and recovered active-TB populations. In addition, active-TB compartments are further disaggregated by drug resistance type into drug susceptible (DS), multi-drug resistant (MDR) and extensively drug resistant (XDR). **Box A.1** summarises the main features of Optima TB.

Box A.1 Optima TB model features and key definitions at a glance

Disaggregation by smear-status and drug-resistance

- Both smear positive and negative; DS-TB, MDR-TB, XDR-TB

New vs. relapse cases

The WHO definition for incident TB cases includes both new and relapse cases. In the model, incident TB cases correspond to the following transitions between compartments:

- New cases: these are represented by the number of progressions to active TB from early and late latent-TB compartments. 'New' also includes recurring episodes of TB from the recovered compartment following re-infection
- Relapse cases: these correspond to all unsuccessful treatments in the model, which include failure, relapse, LTFU and re-treatments

Latent TB

- Multiple compartments for latent TB infection (LTBI)
- Cannot skip latent state for disease progression
- States include undiagnosed, on treatment, and completed treatment
- Accounts for re-infection and latent care-status using a secondary latent TB pathway. Cases previously treated for LTBI, or vaccinated individuals, can transition to the active TB pathway in the case of reinfection

Box A.1 continued.

Box A.1 Optima TB model features and key definitions at a glance (continued)

Vaccination, immunity and resistance

- Vaccination explicitly included in model
- Patients that spontaneously clear from infection

Treatment

- States for undiagnosed, diagnosed, diagnosed but not on-treatment, on-treatment, and recovered patients for different types of drug-resistance
- Failed or defaulted treatment can acquire drug resistance

Treatment outcomes

- Treatment *success* includes 'cured' and 'treatment completion', as per the WHO
- Treatment *failure* in the model includes 'loss to follow-up' during treatment, 'treatment failure', and 'not evaluated'
- *Death* during TB treatment is not included in treatment failure, but is considered separately

Population structure and key populations

- Age-structured populations: can be user defined
- Ability specify additional key populations with defined transition rates to/from general population groups
- HIV positive populations can be represented as separate key population

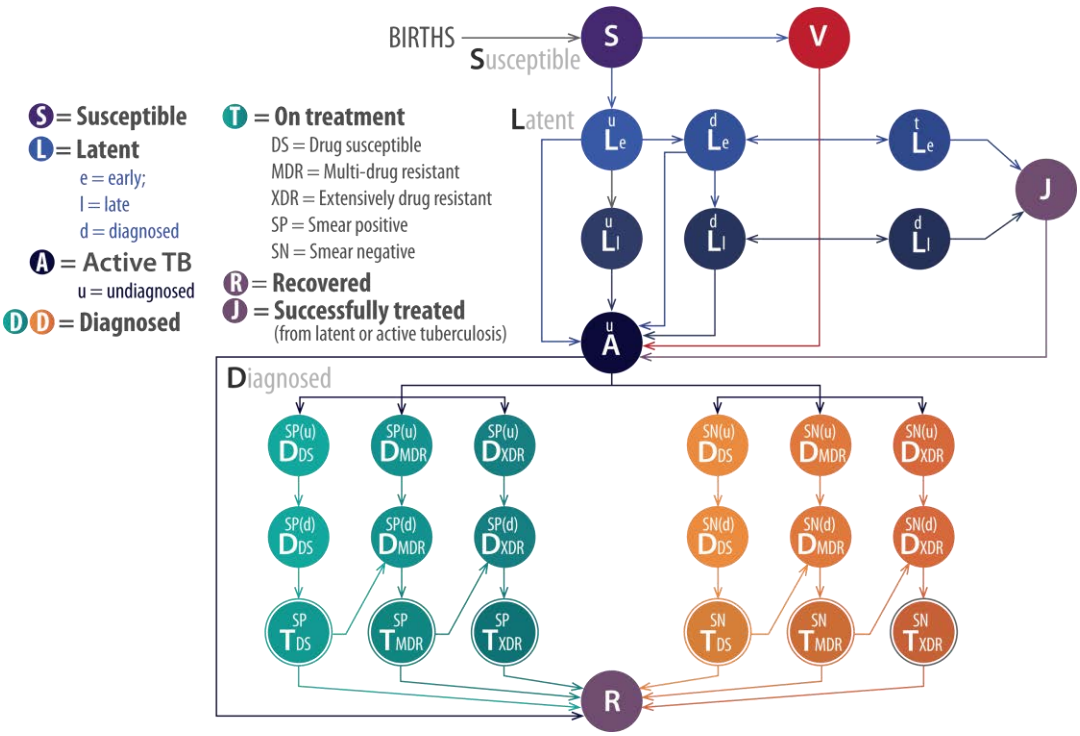
Accounting for the TB/HIV co-epidemic setting

- Several model parameters directly affected by HIV: Mortality rates (excluding TB-related deaths), Mortality rates (including TB-related deaths), Susceptibility to TB infection, TB infectiousness, Departure rate from early TB latency (rate of progression from a recently acquired latent TB infection), Probability of latent TB infection versus active TB infection, Proportion of new active TB cases with different smear/strain combinations, Rate of TB diagnosis (by population which may be targeted differently), and Proportion of TB treatment outcomes for each smear/strain combination
- Each of these parameters influenced to a different extent, depending on both the proportion of population co-infected with HIV and ART coverage
- Model handles treatment for PLHIV known to be infected (or diagnosed) with active TB, whereby PLHIV can be initiated on ART, given that ART coverage is applied every timestep (of 0.25 of a year) across all PLHIV assuming equal coverage of those with and without notified TB.
- In the updated Optima TB model, it is possible to include a targeted TB-sensitive intervention that increased ART coverage specifically among PLHIV with a diagnosed TB co-infection.

Optima TB is based on a dynamic, population-based TB model (**Figure A.1**). The model uses a linked system of ordinary differential equations to track the movement of people among health states. The overall population is partitioned in two ways: by population group and by TB health state. TB infections occur through the interactions among different populations. The main effect of HIV (and diabetes/other co-morbidities on which data is available) is to increase the probability of progression from latent-TB (esp. early latent) to active-TB in the model. ART (or insulin in the case of diabetes) coverage then applies to the specified proportion of co-infected populations, and would revert their probability of progression back towards its original value.

Each compartment (Figure, disks) corresponds to a single differential equation in the model, and each rate (Figure, arrows) corresponds to a single term in that equation. **Table A.1** lists the parameters used in Optima; most of these are used to calculate the force of infection. The analysts interpret empirical estimates for model parameter values in Bayesian terms as previous distributions. The model then must be calibrated: finding posterior distributions of the model parameter values so that the model generates accurate estimates of TB prevalence, the number of people on treatment, and any other epidemiological data that are available (such as TB-related deaths). Model calibration and validation normally should be performed in consultation with governments in the countries, in which the model is being applied.

Figure A.1 Compartmental HIV health states and transmission-related interactions across the care cascade as represented in Optima HIV



Source: Based on model structure at the time of analysis.

Notes: Each compartment represents a single population group with the specified health state or care status. Each arrow represents the movement of individuals between health states or care status. All compartments except for "susceptible" and "vaccinated" represent individuals with either latent or active TB. Death can occur for any compartment, and TB-related mortality varies between active TB compartments. The possibility of relapse and reinfection is also included in the model. Individuals who complete active TB treatment move into compartment R where they remain one year unless they experience relapse and move back to the D compartment. Otherwise they move to compartment J where they can get reinfected.

Relapse and re-infection are important considerations in TB epidemics, and these are represented by the arrow from recovered to active in **Figure A.1**. The transition rates from the treatment compartments to the recovered compartment are informed by the treatment success rates. The progression rate from recovered to the active compartment is increased, skipping the latent pathway.

TB RESOURCE OPTIMISATION AND PROGRAMME COVERAGE TARGETS

Optima is able to calculate allocations of resources that optimally address one or more TB-related objectives (for example, impact-level targets in a country's TB national strategic plan). Because this model also calculates the coverage levels required to achieve these targets, Optima can be used to inform TB strategic planning and the determination of programme coverage levels.

The key assumptions of resource optimisation are the relationships among (1) the cost of TB programmes for specific target populations, (2) the resulting coverage levels of targeted populations with these TB programmes, and (3) how these coverage levels of TB programmes for targeted populations influence clinical outcomes. Such relationships are required to understand how incremental changes in spending (marginal costs) affect TB epidemics.[a]

To perform the optimisation, Optima uses a global parameter search algorithm, which is an adaptive stochastic descent algorithm. The algorithm is similar to simulated annealing in that it makes stochastic downhill steps in parameter space from an initial starting point. However, unlike simulated annealing, the algorithm chooses future step sizes and directions based on the outcome of previous steps. For certain classes of optimisation problems, the team has shown that the algorithm can determine optimised solutions with fewer function evaluations than traditional optimisation methods, including gradient descent and simulated annealing.

UNCERTAINTY ANALYSES

Optima uses a Markov chain Monte Carlo algorithm for performing automatic calibration and for computing uncertainties in the model fit to epidemiological data. With this algorithm, the model is run many times (typically, 1,000–10,000) to generate a range of epidemic projections. Their differences represent uncertainty in the expected epidemiological trajectories. The most important assumptions in the optimisation analysis are associated with the cost-coverage and coverage-outcome curves.[b]

[a] A traditional approach is to apply unit cost values to inform a linear relationship between money spent and coverage attained. This assumption is reasonable for programmes such as an established treatment programme that no longer incurs start-up or initiation costs. However, the assumption is less appropriate for diagnostic programmes. Most programmes typically have initial setup costs, followed by a more effective scale-up with increased funding. However, very high coverage levels have saturation effects because these high levels require increased incremental costs due to the difficulty of diagnosing more people as the yield of diagnostic interventions declines.

[b] All available historical spending data and achieved outcomes of spending, data from comparable settings, experience, and extensive discussion with stakeholders in the country of application can be used to inform these ranges. All logistic curves within these ranges then are allowable and are incorporated in Optima uncertainty analyses. These cost-coverage and coverage-outcome curves thus are reconciled with the epidemiological, and biological data in a Bayesian optimal way, thereby enabling the calculation of unified uncertainty estimates.

Appendix B DATA INPUTS INTO THE MODEL

DEMOGRAPHIC INPUTS

Table B.1 Population sizes

Population name	Value	Year	Source or Assumption
General population, 0–4 years old	1,389,893	2016	Extrapolated from Gauteng population census data 2001, 2007 and 2011. 2011 report "Census 2011 Provinces at a glance by Statistics SA, Report No. 03-01-43"
General population, 5–14 years old	1,773,428	2016	
General population, 15–64 years old	8,320,712	2016	
General population, 65+ years old	580,980	2016	
People living with HIV (PLHIV), 15–64 years old	2,047,858	2016	Derived from: Shisana O, Rehle T, Simbayi LC, Zuma K, Jooste S, Zungu N, Labadarios D, Onoya D et al. (2014) South African National HIV Prevalence, Incidence and Behaviour Survey, 2012. Cape Town: HSRC Press
People living with HIV (PLHIV), 65+ years old	17,968	2016	
Prisoners, 15–64 years old	27,399	2016	Derived from the "Dep. Correctional Services Annual Report 2014/15", using HIV prevalence data from: a) Mutingh L. The prevalence of HIV in South Africa's prison system: some, but not all the facts, at last. Civil Society Prison Reform Initiative. Newsletter No. 26 (May), 2008. and b) Telisinghe et al. 2014 PLoS ONE 9(1): e87262
PLHIV prisoners, 15–64 years old	9,280	2016	
Health care workers, 15–64 years old*	41,705	2016	Using Vusi Madi's estimated population size (2016): 54,875 (Clinical staff 46831, CHWs: 8044, WBOTs: 711) and using general population HIV prevalence data , taking into account ¾ of HCWs are female.
PLHIV health care workers, 15–64 years old*	13,170	2016	
Miners, 15–64 years old*	49,900	2016	Using data from Gauteng's 6 gold mines (Anglo Gold, Harmony, Driefontein Sibanye, South Deep, Kloof Sibanye and Cooke Sibanye) with a total of 57,813 permanent and contract employees.
PLHIV miners, 15–64 years old*	5,917	2016	

Notes: * = While demographics data was provided for these populations, not enough epidemiological data was available to include them in the analysis; Historical data used in the analysis are provided at *Gauteng Historical Epi Data for Report*).

Table B. 2 Births, net immigration and background (non-TB) mortality

Population name	Value	Year	Source or Assumption
Annual number of births	279,791	2016	Derived from report "Census 2011: Fertility in South Africa by Statistics SA, no. 03-01-63"
Annual number of net immigration, 15–64 years old	300,000	2015	Sourced from the report "Census 2011: Migration dynamics in South Africa" published by Statistics South Africa
Annual number of net immigration, 65+ years old	39,147	2015	Sourced from the report "Census 2011: Migration dynamics in South Africa" published by Statistics South Africa
Annual non-TB death rate, 0–4 years old	0.6%	2016	Institute for Health Metrics and Evaluation, Global Burden of Disease study 2016.

Table B.2 continued.

Table B.2 Births, net immigration and background (non-TB) mortality (continued)

Population name	Value	Year	Source or Assumption
Annual non-TB death rate, 5–14 years old	0.1%	2016	Institute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, 15–64 years old	0.8%	2016	Institute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, 65+ years old	5.5%	2016	Institute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, PLHIV 15–64 years old	5.2%	2016	Spectrum model data
Annual non-TB death rate, PLHIV 65+ years old	10.3%	2016	Spectrum model data
Annual non-TB death rate, Prisoners	0.8%	2016	In the absence of data to inform this, assumed equal to the 15–64 population non-TB death rate
Annual non-TB death rate, PLHIV prisoners	5.2%	2016	In the absence of data to inform this, assumed equal to the 15–64 PLHIV population non-TB death rate
Annual non-TB death rate, Health care workers*	0.8%	2016	In the absence of data to inform this, assumed equal to the 15–64 population non-TB death rate
Annual non-TB death rate, PLHIV health care workers*	5.2%	2016	In the absence of data to inform this, assumed equal to the 15–64 PLHIV population non-TB death rate
Annual non-TB death rate, Miners*	0.8%	2016	In the absence of data to inform this, assumed equal to the 15–64 population non-TB death rate
Annual non-TB death rate, PLHIV miners*	5.2%	2016	In the absence of data to inform this, assumed equal to the 15–64 PLHIV population non-TB death rate

Note: * = While demographics data was provided for these populations, not enough epidemiological data was available to include them in the analysis.

Table B.3 ART coverage

Population name	Value	Year	Source or Assumption
ART coverage of PLHIV, excluding prisoners	47.4%	2016	Thembisa model. Johnson and Dorrington, 2017
ART coverage of PLHIV, prisoners	98.0%	2016	Department of correctional services annual report, 2014–15

TB EPIDEMIOLOGICAL PARAMETERS

Table B.4 TB epidemiological parameters

Full Name	Population	Latest year or default value	Source or Assumption
Vaccination Rate	Annual number of births	100%	According to the Gauteng District Health Barometer, the province has continuously achieved full BCG vaccination coverage since 2007.
Latency Treatment Initiation Rate	0–4, PLHIV	0	Due to the lack of data, latent-TB treatment could not be included in the analysis
Latency Treatment Abandonment Rate	0–4, PLHIV	0	Due to the lack of data, latent-TB treatment could not be included in the analysis

Table B.4 continued.

Table B.4 TB epidemiological parameters (continued)

Full Name	Population	Latest year or default value	Source or Assumption
Latency Treatment Success Rate	0–4, PLHIV	0	Due to the lack of data, latent-TB treatment could not be included in the analysis
Early Latency Departure Rate (Off ART)	PLHIV off-ART	0.99	Assumed that early-latent TB status for PLHIV is only a year, after which they progress either to active TB or late-latent TB.
Early Latency Departure Rate (On ART)	All populations incl PLHIV on ART	0.2001	Houben et al. 2016 (appendix of TIME model)—0.1%/year reactivation rate (0.01–0.25).
Late Latency Departure Rate*	All populations	0.003	Andrews et al. 2012—risk of progression to active. The values used in calibration were either 0.00185 or 0.0037, with the higher values used for the PLHIV populations
Probability of Early-Active vs. Early-Late LTBI Progression*	All populations	0.177	Andrews et al. 2012—risk of progression to active. The values used in calibration were either 0.177 or 0.354, with the higher value used for the PLHIV populations
Infection Vulnerability Factor (Vaccinated vs. Susceptible)	All populations	0.5	Mantgani et al., 2013 (protective efficacy of BCG found to range from 0–80%). A value of 0.5 was used for populations aged 0–14, and no protection (i.e. 1) was used for all populations older than 14 years old.
Infection Vulnerability Factor (Latent Treated vs. Susceptible)	All populations	0.5	Samandari et al., 2011
Smear positive (SP) TB Infectiousness*	All populations	1	Values between 1–30 in calibrations were used (highest being prisoners and lowest 5–14 years old)
Smear negative (SN) TB Infectiousness (Compared to SP-TB)	All populations	0.22	Behr et al.1999
Active Infection Rate (Active Recovered)*	All populations	0.02	This value is representative of a global average. In Gauteng, this parameter was not used for calibrations partly due to the fact that data was insufficient to inform this.
Smear positive TB natural recovery rate, excluding PLHIV off-ART	All populations incl PLHIV on ART	0.03	Tiemersma et al. 2011
Smear positive TB natural recovery rate, PLHIV off-ART	PLHIV off-ART	0	Assumed that PLHIV populations off-ART will not recover from TB without undergoing active TB treatment
Smear negative TB natural recovery rate, excluding PLHIV off-ART	All populations incl PLHIV on ART	0.16	Tiemersma et al. 2011
Smear negative TB natural recovery rate, PLHIV off-ART	PLHIV off-ART	0	Assumed that PLHIV populations off-ART will not recover from TB without undergoing active TB treatment
Smear positive untreated-TB death rate, all non-PLHIV	All populations, except PLHIV	0.12	Tiemersma et al. 2011

Table B.4 continued.

Table B.4 TB epidemiological parameters (continued)

Full Name	Population	Latest year or default value	Source or Assumption
Smear positive untreated-TB death rate, all PLHIV	PLHIV populations	0.17	Assumed this is equivalent to the general TB-untreated death rate added to the PLHIV general non-TB death rate
Smear negative untreated-TB death rate, all non-PLHIV	All populations, except PLHIV	0.02	Tiemersma et al. 2011
Smear negative untreated-TB death rate, all PLHIV	PLHIV populations	0.07	Assumed this is equivalent to the general TB-untreated death rate added to the PLHIV general non-TB death rate

Notes: * = Parameters with the least confidence/available literature, and chosen across different studies to be adjusted to calibrate the model. Not all of these apply to the calibration process in Gauteng. The underlying epidemiological parameters adjusted when calibrating for Gauteng, were: "Late Latency Departure Rate"; "Probability of Early-Active vs. Early-Late LTBI Progression"; "Smear positive (SP) TB Infectiousness".

NOTIFICATION DATA

Historical data used in the analysis are provided on Gauteng historical Epi Data for Report

Notified cases provided from the ETR and EDR systems were disaggregated by smear-status and resistance-type by WAMTechnology on behalf of the DOH. In the 15-64 age-group however, certain TB cases were assigned to a "HIV-status unknown" group. The TB cases in the "HIV-status unknown group" were assigned to a HIV status using the ratio of PLHIV to non-HIV TB cases informed by the rest of the dataset. In terms of numbers, for year 2015, there were:

- 31,134 notified active TB cases with HIV–positive status
- 14,137 notified active TB cases with HIV–negative status
- 1,263 active TB cases with unknown HIV status (2.7% of all notified cases), split by us into 32,003 HIV-positive and 14,531 HIV–negative.

Table B.5 Number of notified cases by age, smear status and drug resistance type

Population	Smear-status and drug resistance-type	Number of notified cases	Latest year available	Source
General population, 0–4 years	Smear positive DS-TB	443	2016	ETR.Net
General population, 5–14 years	Smear positive DS-TB	267	2016	ETR.Net
General population, 15–64 years	Smear positive DS-TB	4,912	2016	ETR.Net
General population, 65+ years	Smear positive DS-TB	295	2016	ETR.Net
People living with HIV (PLHIV), 15–64 years	Smear positive DS-TB	10,229	2016	ETR.Net
People living with HIV (PLHIV), 65+ years	Smear positive DS-TB	88	2016	ETR.Net
Prisoners, 15–64 years	Smear positive DS-TB	60	2016	ETR.Net
PLHIV prisoners, 15–64 years	Smear positive DS-TB	11	2016	ETR.Net
General population, 0–4 years	Smear positive MDR-TB	3	2015	EDR.Web
General population, 5–14 years	Smear positive MDR-TB	14	2015	EDR.Web
General population, 15–64 years	Smear positive MDR-TB	207	2015	EDR.Web

Table B.5 continued.

Table B.5 Number of notified cases by age, smear status and drug resistance type (continued)

Population	Smear-status and drug resistance-type	Number of notified cases	Latest year available	Source
General population, 65+ years	Smear positive MDR-TB	10	2015	EDR.Web
People living with HIV (PLHIV), 15–64 years	Smear positive MDR-TB	858	2015	EDR.Web
People living with HIV (PLHIV), 65+ years	Smear positive MDR-TB	3	2015	EDR.Web
Prisoners, 15–64 years	Smear positive MDR-TB	N/A	N/A	EDR.Web
PLHIV prisoners, 15–64 years	Smear positive MDR-TB	N/A	N/A	EDR.Web
General population, 0–4 years	Smear positive XDR-TB	–	2015	EDR.Web
General population, 5–14 years	Smear positive XDR-TB	–	2015	EDR.Web
General population, 15–64 years	Smear positive XDR-TB	5	2015	EDR.Web
General population, 65+ years	Smear positive XDR-TB	–	2015	EDR.Web
People living with HIV (PLHIV), 15–64 years	Smear positive XDR-TB	39	2015	EDR.Web
People living with HIV (PLHIV), 65+ years	Smear positive XDR-TB	–	N/A	EDR.Web
Prisoners, 15–64 years	Smear positive XDR-TB	N/A	N/A	EDR.Web
PLHIV prisoners, 15–64 years	Smear positive XDR-TB	N/A	N/A	EDR.Web
General population, 0–4 years	Smear negative DS-TB	1,738	2016	ETR.Net
General population, 5–14 years	Smear negative DS-TB	729	2016	ETR.Net
General population, 15–64 years	Smear negative DS-TB	3,770	2016	ETR.Net
General population, 65+ years	Smear negative DS-TB	492	2016	ETR.Net
People living with HIV (PLHIV), 15–64 years	Smear negative DS-TB	17,549	2016	ETR.Net
People living with HIV (PLHIV), 65+ years	Smear negative DS-TB	217	2016	ETR.Net
Prisoners, 15–64 years old	Smear negative DS-TB	83	2016	ETR.Net
PLHIV prisoners, 15–64 years	Smear negative DS-TB	205	2016	ETR.Net
General population, 0–4 years	Smear negative MDR-TB	10	2015	EDR.Web
General population, 5–14 years	Smear negative MDR-TB	11	2015	EDR.Web
General population, 15–64 years	Smear negative MDR-TB	110	2015	EDR.Web
General population, 65+ years	Smear negative MDR-TB	7	2015	EDR.Web
People living with HIV (PLHIV), 15–64 years	Smear negative MDR-TB	670	2015	EDR.Web
People living with HIV (PLHIV), 65+ years	Smear negative MDR-TB	3	2015	EDR.Web
Prisoners, 15–64 years	Smear negative MDR-TB	N/A	N/A	EDR.Web
PLHIV prisoners, 15–64 years	Smear negative MDR-TB	N/A	N/A	EDR.Web
General population, 0–4 years	Smear negative XDR-TB	–	2015	EDR.Web
General population, 5–14 years	Smear negative XDR-TB	–	2015	EDR.Web
General population, 15–64 years	Smear negative XDR-TB	2	2015	EDR.Web
General population, 65+ years	Smear negative XDR-TB	–	2015	EDR.Web
People living with HIV (PLHIV), 15–64 years	Smear negative XDR-TB	17	2015	EDR.Web
People living with HIV (PLHIV), 65+ years	Smear negative XDR-TB	–	N/A	EDR.Web
Prisoners, 15–64 years	Smear negative XDR-TB	N/A	N/A	EDR.Web
PLHIV prisoners, 15–64 years	Smear negative XDR-TB	N/A	N/A	EDR.Web

DIAGNOSIS-TREATMENT OUTCOMES

Table B.6 Values used for various rates, by population

	HIV –				HIV +		HIV –	HIV +		
Parameter	0–4 years	5–14 years	15–64 years	65+ years	15–64 years	65+ years	Prisoners, 15–64 years	Prisoners, 15–64 years	Latest year available	Source / assumption
SP DS Diagnosis Rate*	66%	66%	66%	66%	66%	67%	66%	66%	2014	Based on notified cases, incidence, and prevalence
SP DS Treatment Uptake Rate	90%	90%	90%	90%	90%	90%	90%	90%	2015	ETR.Net
SP DS Treatment Abandonment Rate	4%	4%	7%	4%	7%	5%	3%	5%	2015	ETR.Net
SP DS Treatment Success Rate	95%	94%	89%	79%	86%	71%	95%	91%	2015	ETR.Net
SP MDR Diagnosis Rate*	66%	66%	66%	66%	66%	66%	N/A	N/A	2014	Based on notified cases, incidence, and prevalence
SP MDR Treatment Uptake Rate	57%	57%	57%	57%	57%	57%	N/A	N/A	2013	EDR.Web
SP MDR Treatment Abandonment Rate	11%	25%	48%	57%	40%	27%	N/A	N/A	2014	EDR.Web
SP MDR Treatment Success Rate	89%	55%	43%	20%	41%	40%	N/A	N/A	2014	EDR.Web
SP XDR Diagnosis Rate*	66%	66%	66%	66%	66%	66%	N/A	N/A	2014	Based on notified cases, incidence, and prevalence
SP XDR Treatment Uptake Rate	100%	100%	100%	100%	100%	100 %	N/A	N/A	2013	EDR.Web
SP XDR Treatment Abandonment Rate	N/A	N/A	80%	26%	83%	N/A	N/A	N/A	2011	EDR.Web
SP XDR Treatment Success Rate	N/A	N/A	63%	N/A	41%	N/A	N/A	N/A	2014	EDR.Web
SN DS Diagnosis Rate*	66%	66%	66%	66%	66%	67%	66%	66%	2014	Based on notified cases, incidence, and prevalence
SN DS Treatment Uptake Rate	90%	90%	90%	90%	90%	90%	90%	90%	2015	ETR.Net
SN DS Treatment Abandonment Rate	4%	4%	7%	4%	7%	5%	3%	5%	2015	ETR.Net
SN DS Treatment Success Rate	95%	94%	89%	79%	86%	71%	95%	91%	2015	ETR.Net
SN MDR Diagnosis Rate*	66%	66%	66%	66%	66%	66%	N/A	N/A	2014	Based on notified cases, incidence, and prevalence

Table B.6 continued

Table B.6 Values used for various rates, by population (continued)

	HIV –				HIV +		HIV –	HIV +		
Parameter	0–4 years	5–14 years	15–64 years	65+ years	15–64 years	65+ years	Prisoners, 15–64 years	Prisoners, 15–64 years	Latest year available	Source / assumption
SN MDR Treatment Uptake Rate	57%	57%	57%	57%	57%	57%	N/A	N/A	2013	EDR.Web
SN MDR Treatment Abandonment Rate	11%	25%	48%	57%	40%	27%	N/A	N/A	2014	EDR.Web
SN MDR Treatment Success Rate	89%	55%	43%	20%	41%	40%	N/A	N/A	2014	EDR.Web
SN XDR Diagnosis Rate*	66%	66%	66%	66%	66%	66%	N/A	N/A	2014	Based on notified cases, incidence, and prevalence
SN XDR Treatment Uptake Rate	100%	100%	100%	100%	100%	100%	N/A	N/A	2013	EDR.Web
SN XDR Treatment Abandonment Rate	N/A	N/A	80%	26%	83%	N/A	N/A	N/A	2011	EDR.Web
SN XDR Treatment Success Rate	N/A	N/A	63%	N/A	41%	N/A	N/A	N/A	2014	EDR.Web
SP DS Death Rate (On Treatment)	1%	3%	4%	17%	8%	24%	1%	5%	2015	ETR.Net
SP MDR Death Rate (On Treatment)	14%	20%	10%	23%	20%	33%	N/A	N/A	2014	EDR.Web
SP XDR Death Rate (On Treatment)	N/A	N/A	21%	N/A	25%	N/A	N/A	N/A	2014	EDR.Web
SN DS Death Rate (On Treatment)	1%	3%	4%	17%	8%	24%	1%	5%	2015	ETR.Net
SN MDR Death Rate (On Treatment)	14%	20%	10%	23%	20%	33%	N/A	N/A	2014	EDR.Web
SN XDR Death Rate (On Treatment)	N/A	N/A	21%	N/A	25%	N/A	N/A	N/A	2014	EDR.Web

*Notes: * = The model "diagnosis rate" is the annual transition of people from the undiagnosed compartments to the diagnosed compartments. It is calculated taking into consideration the number of notified cases, estimated incidence and prevalence.*

Table B.7 Screening interventions: Target groups, unit costs, volume, total spend and yield

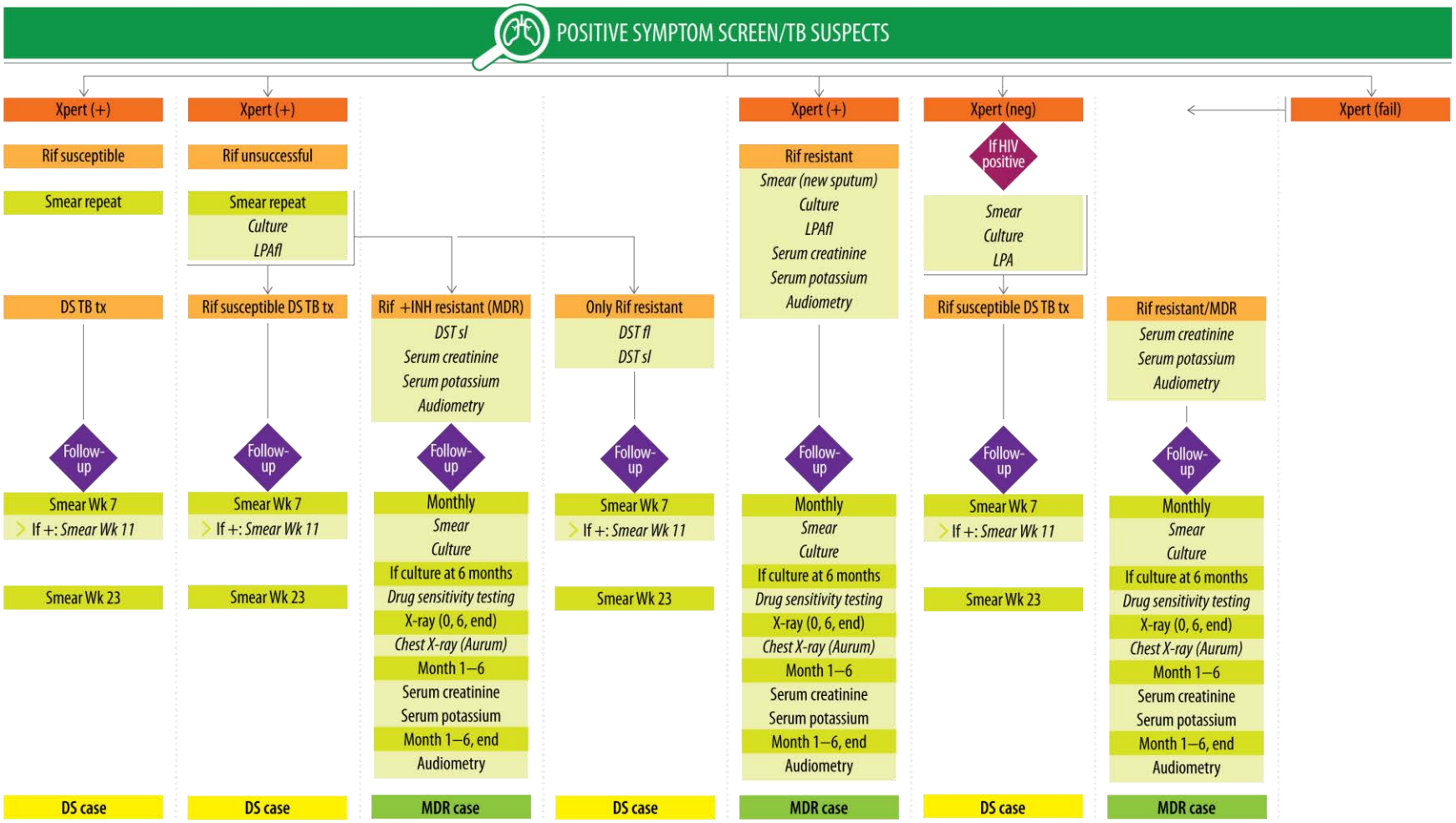
Intervention	Target Population	Unit cost (ZAR), 2016	Source or assumption	Number of screens, 2016	Source or assumption	Total estimated spending (ZAR)	Yield	Source or assumption	Initial screening and tests received
Mass Screening at PHC facilities (include Symptom screening and then Xpert)	All populations, including PLHJV off-ART	7	South African HIV and TB investment case, 2016	11,192,172	Annual number of symptom screens carried out informed by ETR.Net	73,308,727	0.4%	Van Rie, 2014	Symptom screening which involves only asking the cough question; Gene Xpert
Enhanced-Mass Screening at PHC facilities	All populations, including PLHJV off-ART	13	Assumed double the current cost of asking 1 screening questions, to reflect cost of additional staff time/ training to ask the 4 symptom screen questions	–	Not currently implemented	–	0.5%	Assumed small improvement in yield due to higher sensitivity and more cases going forward to full diagnosis	Symptom screening which involves asking all four questions; Gene Xpert
Mass Screening-mobile unit/outreach in high risk area (include symptom screen, sputum collection)	All populations	1,089	Gilbert, 2016	–	Not currently implemented	–	2.2%	Kranzer, 2012	Symptom screening which involves asking all four questions; Gene Xpert
Contact tracing for DR cases (using symptom screening)	All DR-TB cases	129	New Aurum unit costs, unpublished document	5,330	Assumed contacts of 80% of notified index DR-TB cases traced and screened for active TB. Average number of close contacts per active TB case assumed to be 3.3.	689,078	2.7%	Lebina, 2016	Symptom screening which involves asking all four questions; Gene Xpert

Table B.7 continued.

Table B.7 Screening interventions: Target groups, unit costs, volume, total spend and yield (continued)

Intervention	Target Population	Unit cost (ZAR), 2016	Source or assumption	Number of screens, 2016	Source or assumption	Total estimated spending (ZAR)	Yield	Source or assumption	Initial screening and tests received
Contact tracing for DS cases (using symptom screening)	All DS-TB cases	129	New Aurum unit costs, unpublished document	34,020	Assumed contacts of 20% of notified index DS-TB cases traced and screened for active TB. The average number of close contacts per active TB case assumed to be 3.3.	4,398,071	2.7%	Lebina, 2016	Symptom screening which involves asking all four questions; Gene Xpert
ACF among PLHIV in care	PLHIV on ART	79	Assumed additional costs 6x greater than enhanced mass screening to reflect full check-up as per PHC101	707,613	Assumed monthly symptom screening of 80% of all PLHIV on ART	55,618,394	4.0%	Used average of yields reported in Kranzer, 2010 and Kranzer, 2012	Symptom screening which involves asking all four questions; Gene Xpert

Figure B.1 Diagnostic and monitoring "pathways" based on initial Xpert result (used in costings)



Sources: 2016/17 unit costing, NHLS price lists for biochemistry.

Note: Some lesser used diagnostic tests were not included, such as thyroid stimulating hormone and liver serum enzymes.

Table B.8 Sensitivity of screening /testing methods

Screening or testing method	Target population	Sensitivity	Source or assumption
Only cough question asked	All individuals, regardless of HIV status	21%	Claassens et al., 2017
All four WHO symptom screen questions asked	All individuals, regardless of HIV status	38%	Claassens et al., 2017
Only cough question asked	Individuals known to be HIV negative	24%	Claassens et al., 2017
All four WHO symptom screen questions asked	Individuals known to be HIV negative	42%	Claassens et al., 2017
Gene Xpert	Pooled sensitivity	88%	Steingart et al., 2014

PROGRAMMATIC DATA: TB TREATMENT

Table B.9 Treatment interventions: Target groups, unit costs, volume, total spend and outcome

Treatment programme	Target Population	Unit cost/Course of treatment, ZAR	Source or assumption	Patients covered, 2016	Source or assumption	Total estimated spending (ZAR)	Treatment success	Adherence to treatment	Source or assumption
DS-TB Treatment	Non-PLHIV, excluding key populations	2,807	Micro-costing using local secondary data and local studies (*see supplementary information Gauteng Treatment Cost Calculations for Report*)	14,789	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	41,512,361	79.2%	93.8%	Current treatment outcomes
Standardised MDR-TB regimen	Non-PLHIV, excluding key populations	62,054	Micro-costing using local secondary data and local studies	113	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	3,493,313	63.8%	44.8%	Current treatment outcomes
Standardised MDR-TB regimen with BDQ	Non-PLHIV, excluding key populations	70,210	Micro-costing using local secondary data and local studies	113	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	3,952,490	69.3%	89.1%	WHO Review of the evidence on Bedaquiline, 2016

Table B.9 continued.

Table B.9 Treatment interventions: Target groups, unit costs, volume, total spend and outcome (continued)

Treatment programme	Target Population	Unit cost/Course of treatment, ZAR	Source or assumption	Patients covered, 2016	Source or assumption	Total estimated spending (ZAR)	Treatment success	Adherence to treatment	Source or assumption
Modified extended MDR-TB regimen with BDQ	Non-PLHIV, excluding key populations	62,364	Micro-costing using local secondary data and local studies	–	Not currently implemented	–	69.3%	89.1%	WHO Review of the evidence on Bedaquiline, 2016
MDR-TB short course with kanamycin	Non-PLHIV, excluding key populations	31,411	Micro-costing using local secondary data and local studies	–	Not currently implemented	–	65.4%	68.8%	Kibret et al., 2017
MDR-TB short course with BDQ	Non-PLHIV, excluding key populations	37,258	Micro-costing using local secondary data and local studies	–	Not currently implemented	–	69.3%	89.1%	WHO Review of the evidence on Bedaquiline, 2016
XDR-TB current treatment regimen	Non-PLHIV, excluding key populations	194,351	Micro-costing using local secondary data and local studies	10	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	944,544	62.7%	20.2%	Current treatment outcomes
XDR-TB new drug regimen with BDQ and LZD	Non-PLHIV, excluding key populations	226,255	Micro-costing using local secondary data and local studies	–	Not currently implemented	–	66.4%	89.1%	Pym et al., 2016; WHO report on Bedaquiline, 2016
PLHIV: DS-TB Treatment	PLHIV	2,865	Micro-costing using local secondary data and local studies	31,601	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	90,533,507	78.2%	92.5%	Current treatment outcomes

Table B.9 continued.

Table B.9 Treatment interventions: Target groups, unit costs, volume, total spend and outcome (continued)

Treatment programme	Target Population	Unit cost/Course of treatment, ZAR	Source or assumption	Patients covered, 2016	Source or assumption	Total estimated spending (ZAR)	Treatment success	Adherence to treatment	Source or assumption
PLHIV: Standardised MDR-TB regimen	PLHIV	62,112	Micro-costing using local secondary data and local studies	447	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	13,888,870	55.7%	55.3%	Current treatment outcomes
PLHIV: Standardised MDR-TB regimen with BDQ	PLHIV	70,268	Micro-costing using local secondary data and local studies	447	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	15,712,783	69.3%	89.1%	Assumed same outcomes as HIV–
PLHIV: New MDR-TB regimens	PLHIV	45,703	Micro-costing using local secondary data and local studies. Average cost of the 3 new DR-TB drug regimens that are not currently implemented	–	Not currently implemented	–	67.4%	85.5%	Assumed same outcomes as HIV-, average of the 3 new DR-TB drug regimens that are not currently implemented
PLHIV: XDR-TB current treatment regimen	PLHIV	194,409	Micro-costing using local secondary data and local studies	59	Number of notified cases, disaggregated using % coverage of different regimens informed by expert opinion	5,707,834	41.4%	16.9%	Current treatment outcomes
PLHIV: XDR-TB new drug regimen with BDQ and LZD	PLHIV	226,313	Micro-costing using local secondary data and local studies	–	Not currently implemented	–	66.4%	89.1%	Assumed same outcomes as HIV–

COST DATA

In addition to the cost data shown in **Tables B.6 and B.8,** the following unit costs were used.

Table B.10 Summary table of unit costs for TB prevention and diagnosis

Diagnosis & preventive interventions	Unit cost (per test or person-year), 2016, ZAR	Source
BCG vaccination	56	Master Procurement Catalogue, 2017
X-ray	172	New Aurum Institute unit costs.
LPAfl testing	464	NHLS World Bank TB Market analysis costing
Liquid culture testing	258	NHLS World Bank TB Market analysis costing
Microscopy	121	NHLS World Bank TB Market analysis costing
Xpert testing	355	NHLS World Bank TB Market analysis costing
First Line DST	645	NHLS World Bank TB Market analysis costing
Second Line DST	836	NHLS World Bank TB Market analysis costing
IPT for 0-4, key-population (miners, prisoners)	177	'South Africa Provincial TB Budget Tool' (Version 1.5)
IPT/ART for HIV positive individuals	177	'South Africa Provincial TB Budget Tool' (Version 1.5)
BACTEC	183	NHLS World Bank TB Market analysis costing
Mass screening at PHC	6.55	Schnippel et al. 2015 (Investment case)
Enhanced mass screening at PHC	13.10	Assumed requires double staff and training time involved in current mass screening at PHC
ACF for PLHIV at PHC	78.60	Assumed same cost as current mass screening at PHC, multiplied by twelve to account for PLHIV undergoing monthly screening
Screening outreach in high-risk areas	1089.03	Gilbert et al. 2016. Unit cost used following removal of HIV testing cost included in the original study
Contact tracing DS/DR-TB	129.28	Aurum Institute unit costs

Notes: Main source for diagnostic unit cost data: NHLS costing conducted as part of this analysis (Pedro da Silva, Naseem Cassim).

Table B.11 Component costs of TB treatment regimens

Regimen	Inpatient costs*, 2016 ZAR	Outpatient costs*, 2016 ZAR	Drug costs, 2016 ZAR	Other costs*, 2016 ZAR	Total treatment cost, 2016 ZAR	Annualised treatment cost used in model, 2016 ZAR	Diagnosis and monitoring costs, 2016 ZAR	Total treatment cost with diagnosis*, 2016 ZAR
DS TB	737	1,020	448	602	2,807	2,807	744	3,551
Old MDR regimen	7,374	12,522	10,280	11,983	62,054	31,027	4,397	35,424
Old MDR-with BDQ	7,374	12,522	16,133	14,287	70,210	35,105	4,397	39,502
MDR-with BDQ shortened - modified extended regimen	8,848	14,869	9,133	13,702	62,364	37,418	5,276	42,694
MDR-short course (KM)—modified short regimen	8,427	6,771	5,364	10,849	31,411	31,411	8,793	40,204
MDR-short course (BDQ)—short BDQ regimen	8,427	6,771	8,907	13,153	37,258	37,258	8,793	46,051
XDR-current	31,601	12,506	94,152	11,983	194,351	97,175	4,397	101,572
XDR-new drug regimen shortened (BDQ and LZD)	36,116	14,181	124,169	14,066	226,255	129,289	5,025	134,313
HIV+: DS TB	737	1,020	506	602	2,865	2,865	744	3,609
HIV+: Old MDR regimen	7,374	12,522	10,338	11,983	62,112	31,056	4,397	35,453
HIV+: Old MDR-with BDQ	7,374	12,522	16,191	14,287	70,268	35,134	4,397	39,531
HIV+: New MDR regimens	10,174	11,216	7,860	13,483	45,703	40,130	7,721	47,851
HIV+: Old XDR	31,601	12,506	94,210	11,983	194,409	97,204	4,397	101,601
HIV+: New XDR	36,116	14,181	124,227	14,066	226,313	129,322	5,025	134,346
Prisoners: DS TB	737	1,020	448	602	2,807	2,807	744	3,551
Prisoners: MDR	10,174	11,216	7,802	13,483	45,645	40,079	7,721	47,800
Prisoners: XDR	36,116	14,181	124,169	14,066	226,255	129,289	5,025	134,313
Miners: DS TB	737	1,022	448	602	2,808	2,808	744	3,552
Miners: MDR	10,174	11,247	7,802	13,483	45,680	40,110	7,721	47,831
Miners: XDR	36,116	14,181	124,169	14,066	226,255	129,289	5,025	134,313

Notes: Full details are provided at *Gauteng Treatment Cost Calculations for Report*; * = Compared to Schnippel et al., 2012 for inpatient/MDR-TB costs, Cox et al., 2015 for outpatient costs, as a benchmark to ensure they are sensible

Appendix C CALIBRATION PROCESS

The Optima TB model calibration was performed by first matching to the population size for each population, including to the population size for people living with HIV ('demographic calibration').

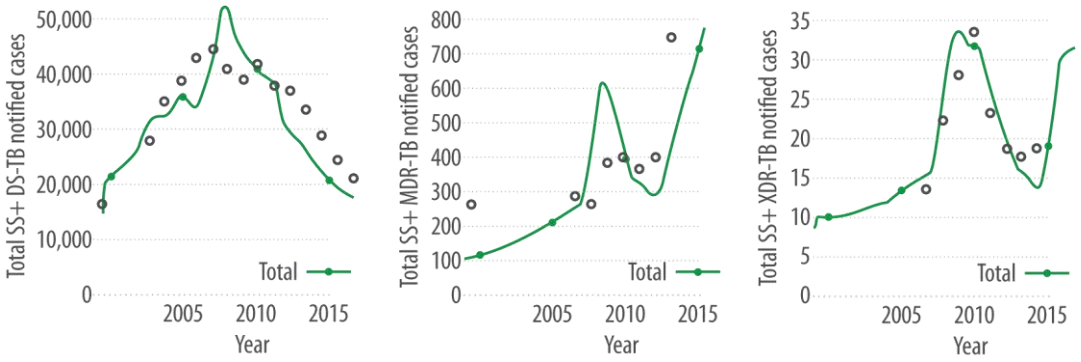
This was followed by calibrating against TB case notification data ('epidemiological calibration'). To initiate the model, the estimated prevalence of TB (all people with active TB) in the year 2000 was used as an input, as well as the number of people known to be living with active TB and the number on TB treatment. From then on, the model considered only parameter rates, and the incidence of active TB is therefore an output of the model.

The following parameters were investigated during the epidemiological calibration process:

- Smear positive TB infectiousness
- Late latency departure rate
- Probability of early-active vs. early-late LTBI progression

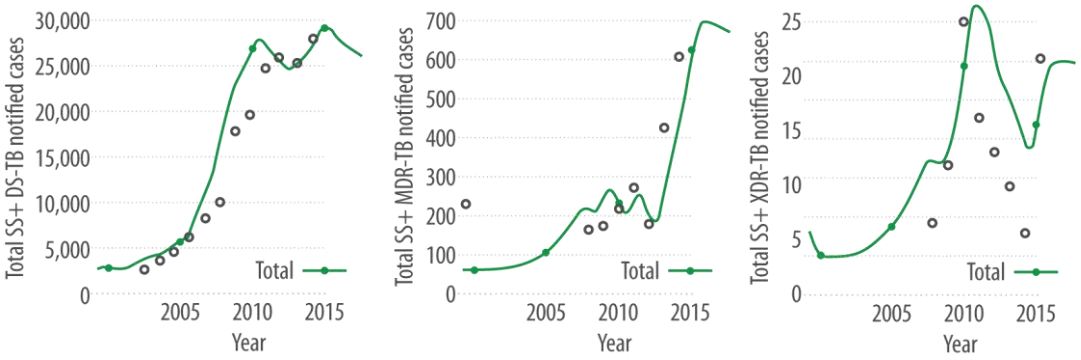
Ranges within which the above three parameters were manually varied are mentioned in the 'Source or Assumption' column in **Table B.5**. The three parameters were varied separately within bounds deemed reasonable, until a fit to reported data was achieved. The order in which they were adjusted, was determined by the level of uncertainty surrounding them. The first parameter to be adjusted was therefore SP-TB infectiousness. This was done in within bounds of 1–30. This parameter averaged at 30 for prisoners, and at between 1–10 for HIV-negative and HIV-positive populations. Given that this is not a known value for Gauteng, the bounds around this parameter are reasonably wide and might have been adjusted to a similar extent through an automatic calibration. The second parameter adjusted was the late-latency departure rate (annual probability of transitioning to active TB junction for individuals with LTBI for more than 5 years), for which an initial value of 0.003 was sourced from Andrews et al. 2012. A final value of 0.00185 was used for HIV-negative populations and doubled (0.0037) for PLHIV. Last, the probability of early-active vs. early-late LTBI progression was doubled for PLHIV (0.354) from the value (0.177) sourced from Andrews et al. 2012 used for all other populations. Therefore, the main parameter that was varied was SP-TB infectiousness, with far less variation/adjustment required for the two other calibration parameters.

Figure C.1 Overall calibration for sputum smear positive TB case notifications (DS, MDR, XDR)



Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; SS = sputum smear; XDR-TB = extensively drug resistant tuberculosis.

Figure C.2 Overall calibration for sputum smear negative TB case notifications (DS, MDR, XDR)



Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; SS = sputum smear; XDR-TB = extensively drug resistant tuberculosis.

Figure C.3 Population-specific calibrations for sputum smear positive TB notifications

a. DS-TB case notifications (SS+)

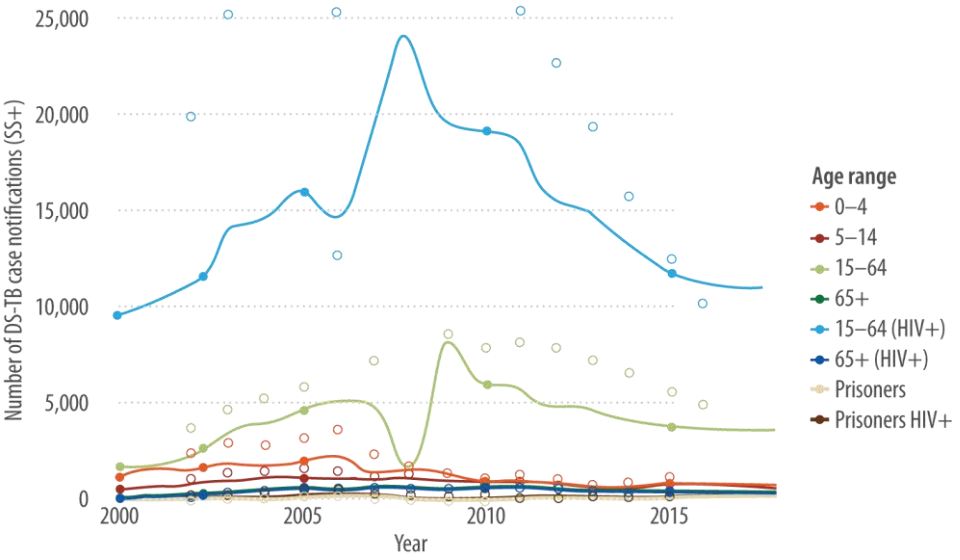
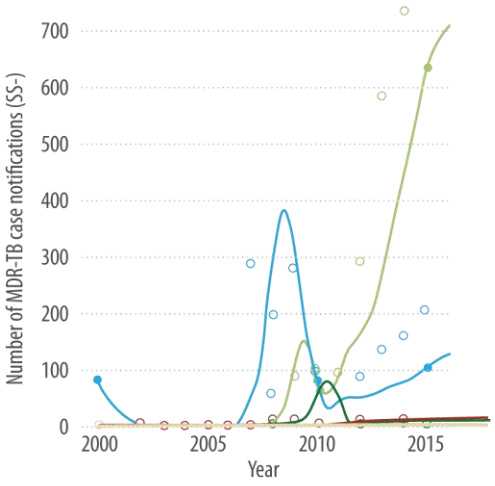
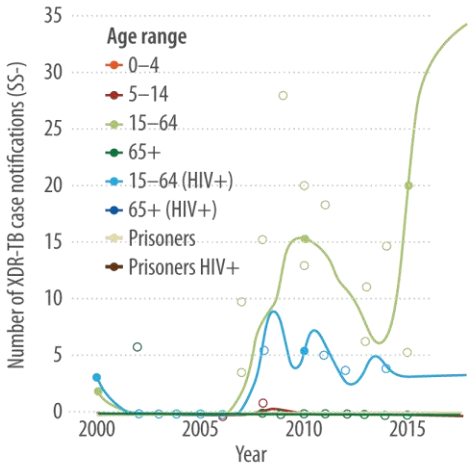


Figure C.3 Population-specific calibrations for sputum smear positive TB notifications (continued)

b. MDR-TB case notifications (SS+)



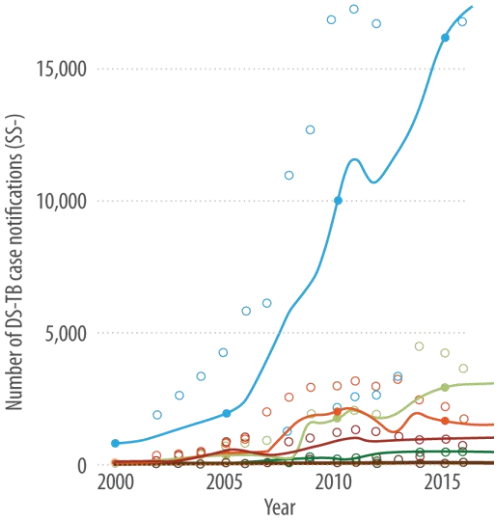
c. XDR-TB case notifications (SS+)



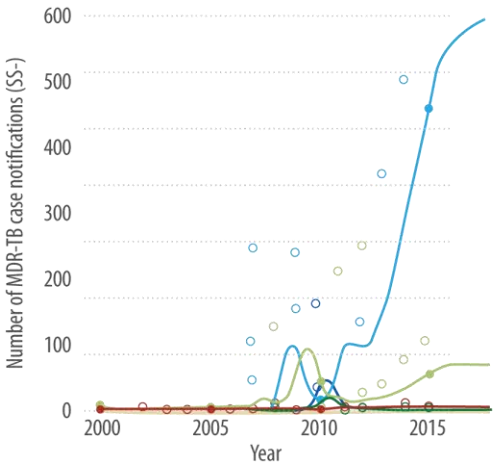
Notes: DS-TB = drug susceptible tuberculosis; MDR-TB = multi-drug resistant tuberculosis; SS = sputum smear; XDR-TB = extensively drug resistant tuberculosis.

Figure C.4 Population-specific calibrations for sputum smear negative TB notifications

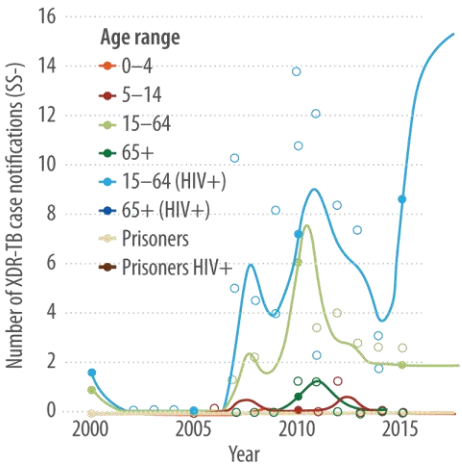
a. DS-TB case notifications (SS–)



b. MDR-TB case notifications (SS-)



c. XDR-TB case notifications (SS-)

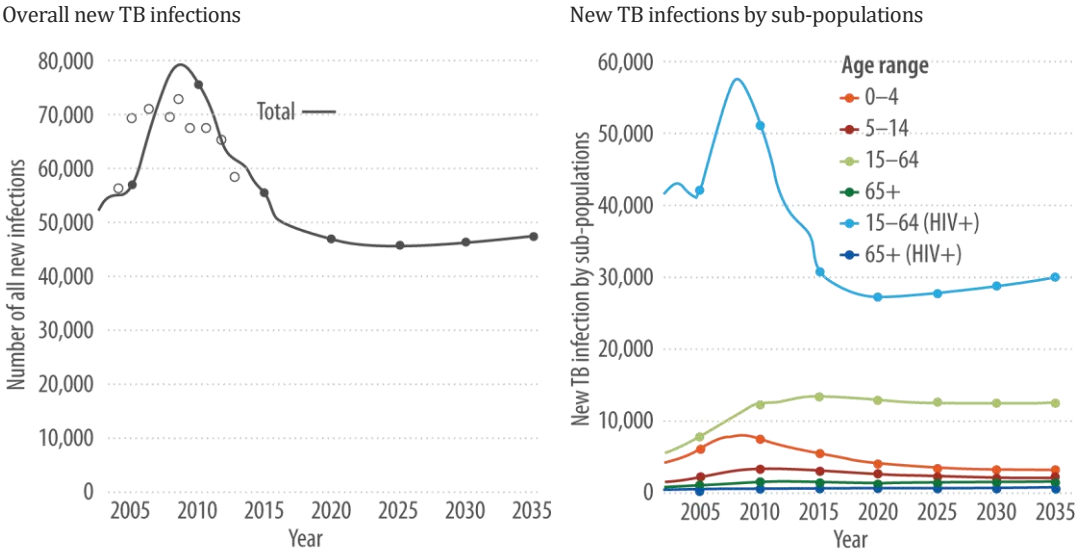


The historical notification data were plotted against model estimates of incidence and active TB prevalence:

NEW TB INFECTIONS

Figure C.5 shows new TB infections modelled by the calibrated Optima TB model. Note that the peaks of modelled incidence around 2010 are driven by gaps in TB notifications in Gauteng's surveillance system (as described in the NDOH Joint Review of HIV, TB & PMTCT Programmes in South Africa, 2014). For calibration purposes, constant TB and ART program coverage and outcomes to 2035 were assumed.

Figure C.5 Optima-TB modelled new TB infections against available data



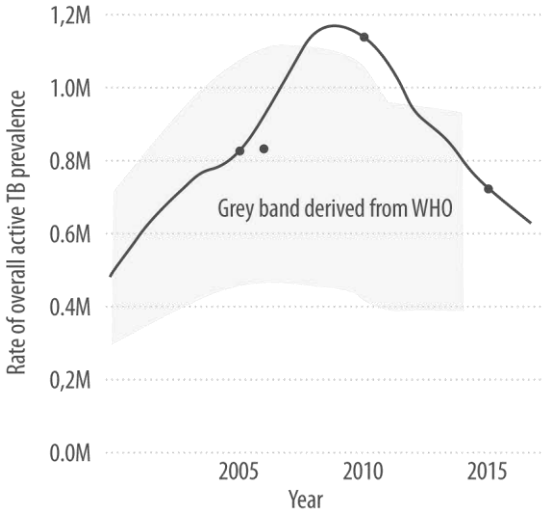
Note: o = Published TB incidence estimates for Gauteng, Nanoo et al. 2015.

ACTIVE TB PREVALENCE

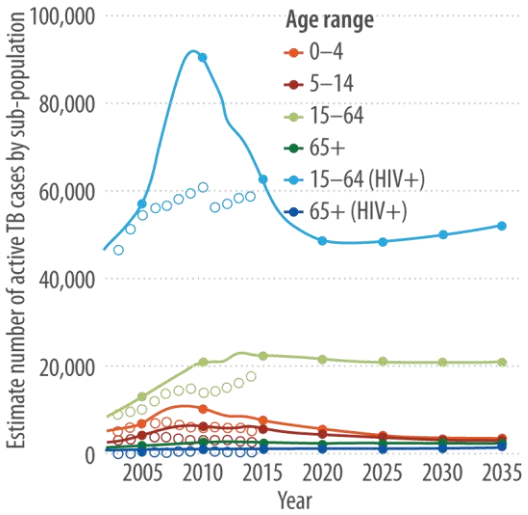
Figure C.6 shows active TB prevalence in comparison with values for Gauteng derived from national WHO estimates. The peaks of modelled prevalence around 2010 are likewise driven by gaps in TB notifications in Gauteng's surveillance system. TB and ART program coverage and outcomes to 2035 were again held constant.

Figure C.6 Optima-TB modelled active TB prevalence against available data

Overall active TB prevalence rate



Active TB cases by sub-populations

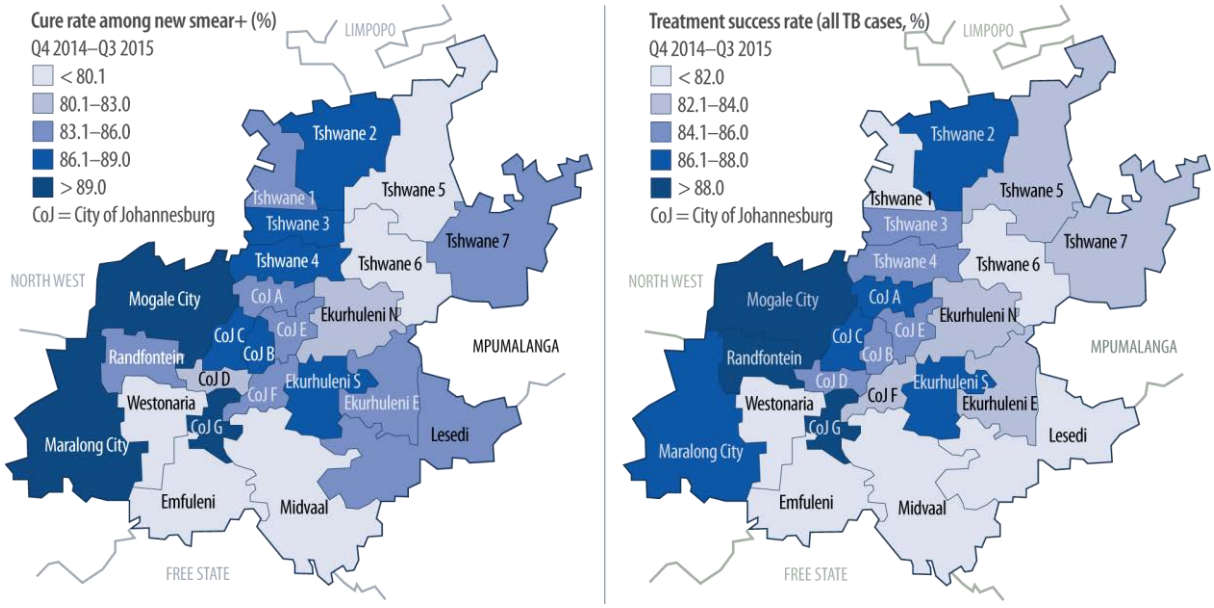


Notes: Data points: Derived from WHO; figures scaled to Gauteng Province.

Appendix D SPATIAL MAPPING OF PROGRAMMATIC TB DATA

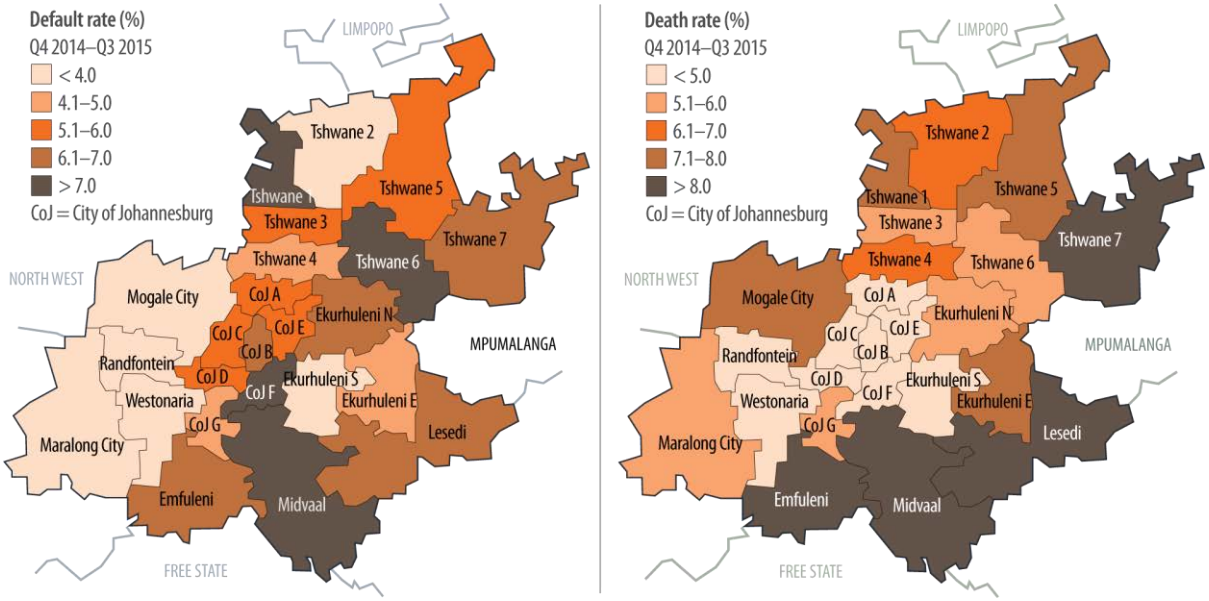
TB OUTCOMES

Figure D.1 Geospatial mapping of TB cure and treatment success rates, Gauteng (2014/15)



Sources: SA Surveillance System; Routine TB surveillance data from October 2014 to September 2015.

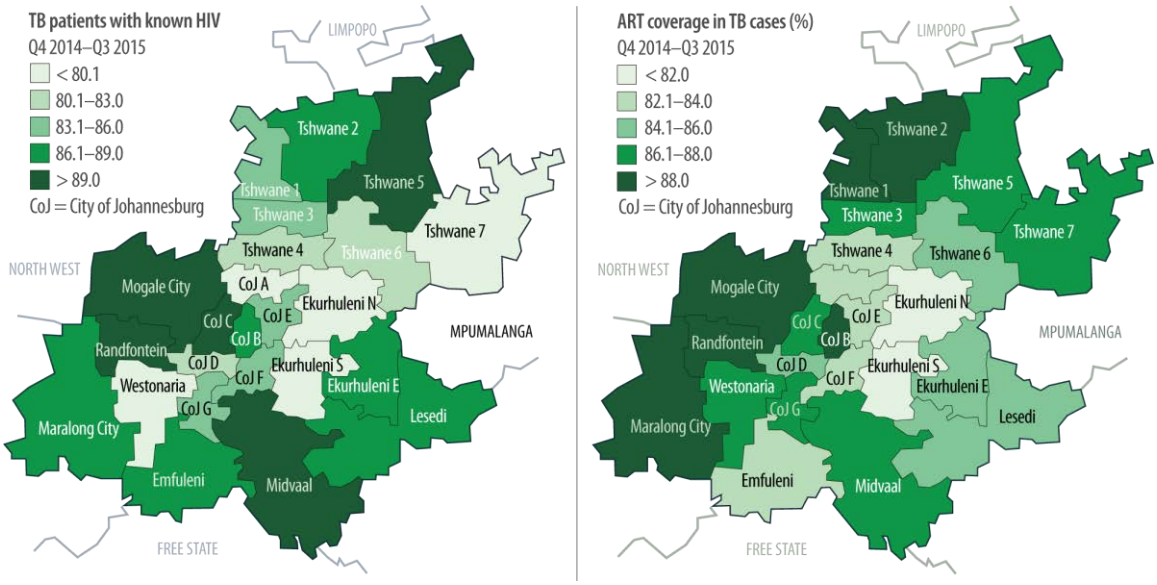
Figure D.2 Geospatial mapping of default and death rates, Gauteng (2014/15)



Sources: SA Surveillance System; Routine TB surveillance data from October 2014 to September 2015.

HIV/TB PROGRAMME INTEGRATION

Figure D. 3 Geospatial mapping of HIV testing and ART coverage in TB cases, Gauteng (2014/15)



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