REVIEW OF THE APPLICATION OF THE OPTIMA TB MODEL IN GAUTENG, SOUTH AFRICA

Undertaken by: Teresa Guthrie, M.PH (Health Econ.)
On behalf of the SA TB Think Tank
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1. INTRODUCTION AND APPROACH OF THE OPTIMA TB MODEL

The World Bank has supported the application of the Optima model for TB in Gauteng. The model was designed to support decision-makers in prioritization, resource allocation and planning, in order to maximize health impact, within the available budget envelope (Kerr et al, 2015[i]).

Optima TB is based on a dynamic compartmental population-based model, and specific sub-populations are divided into compartments based on age, location, risk-factors, health-status, co-morbidities, etc. For example, it can, in theory, accommodate special groups at risk, such as people living with HIV (PLHIV), miners, inmates of correctional facilities, health care workers etc. which are specifically targeted in the National TB Plan (NTP) and National Strategic Plan for HIV, TB and STIs, 2017-2022 (NSP[ii]). Hence this design aspect is a relevant value-add of the Optima model.

However, the challenge with the compartmental model is that it, obviously, requires data on every sub-population to parameterize the compartments. The province-specific data requirements can therefore be quite demanding, such as sub-population demographics, their TB disease characteristics (prevalence, infection and transmission rates within and between compartments), current programme coverage for the groups, as well as the effectiveness and costs of those programmes for those specific sub-populations. These data are often not available for the sub-groups at national level, and even less available at provincial level. In fact, the report notes that it was unable to undertake the modeling for miners and public health care workers, due to the unavailability of the necessary data for these groups in Gauteng.

2. REVIEW OF THE OPTIMA TB MODEL ASSUMPTIONS

Some key comments (from the full report) on the model's assumptions are as follows:

2.1. Epidemiological data and assumptions

2.1.1. The geospatial district mapping of TB and HIV epidemiological data presented in the Optima TB report are useful for the province to understand the burden of disease across its districts. Obviously, the maps are based on the data inputs, and any model is undermined by the availability of the required data and the applied assumptions.

2.1.2. A key challenge faced by the Optima modeling was the lack of TB prevalence survey data at the time of the study. This meant that routine

data on TB notifications formed the basis for estimating disease burden instead of active TB prevalence. This is a limitation that could not be remedied at that time, but if it is to be used in the other provinces, then the TB optima model should be populated with the new TB prevalence data, which will enhance the model's projection accuracy.

2.1.3. Regarding the data applied for the compartmentalized approach, a concern raised by a TB modeling expert was that if the Optima TB model is calibrated to the epidemic trends within each of the sub-groups, then attempting to fit it to the overall epidemic may result in some strange trends in specific risk groups such as inmates or miners, which could then translate into strange results when including the targeted interventions in the optimisation routine. Care is therefore required in the calibration process with rigorous review of the data and assumptions, and the resulting outputs.

2.1.4. Related to the sub-group compartment for the inmates in correctional facilities, the report noted that their TB notification data were 'not available', illustrating the earlier comment about the difficulty of getting sub-population specific data[1]. It has to be assumed therefore that where the provincial-level sub-group data were unavailable, the model applied the national-level data, if available, or where not available, reverted to default values. It is not clear to what degree this occurred, but if extensive, it could have undermined the model's ability to predict the provincial variation, and hence other provincial reports may have very similar findings to the Gauteng report.

2.1.5. HIV-TB co-infection is of great importance in the Gauteng co-epidemic setting, but the authors note the model was unable to capture inter-relation between the two. It appears that the Optima model has applied a constant rate of HIV infection to each compartment that does not change over time nor does it capture the reduced risk of latent TB infection (LTBI) and TB re-infection in relation to the scale-up of ART, which would cause a serious limitation during the optimization process. The Optima model did vary the diagnosis rate and/or ART coverage and estimated the impact on active TB cases and diagnosed DS-TB cases (see Figure 35, page 61), but a more sensitive transmission model might be better able to model the HIV-induced immune depletion and the effects of ART on LTBI activation.

[1] The implementing partners for the Global Fund support for HIV-TB interventions in correctional facilities may have been able to provide some specific data available for inmates in Gauteng.

2.2. Programmatic assumptions

2.2.1. Based on the detail provided in the Optima TB report, the model appears to have incorporated a comprehensive list of the most important TB interventions in South Africa, including interventions for the at-risk sub-populations of inmates of correctional facilities and miners. Also, the programmes' future coverage rates were calibrated to the NTP and the provincial Annual Performance Plan (APP) TB targets, which ensures its relevance to the provincial priorities. But the reviewer was unable to ascertain if the assumed current coverage rates for each intervention were correct.[2] If rolled out to other provinces, the TB programme managers and M&E persons must be fully involved in the populating of the model with their specific provincial data, preferably building their capacity to use the model themselves.

2.3. Cost effectiveness data and assumptions

2.3.1. The report and the tables in the appendixes provide limited detail on the modeled efficacy and cost-effectiveness of the interventions and the specific parameters applied in the model (only treatment outcomes and screening and testing yields were indicated). The authors note that they derived these estimates from a global systematic literature review, and that (obviously) country-specific factors, including quality and adherence, would influence the projected effectiveness of the interventions. The impact of these potential variations were not estimated in a sensitivity analysis, but they could be significant cost and outcome drivers. In addition, it appears that the model did not consider the synergistic effects of the combined package of interventions, rather than singular intervention effects.

2.3.2. The unit costs indicated in the appendix of the report appeared to be in the same ballpark as the unit costs applied by the TB Think Tank (LSHTM) for the costing of the NTP and also in the costing of the NSP, and some were taken from the Investment Case unit costs.

2.3.3. A number of unit costs were referenced as 'new, unpublished Aurum costs' or 'micro-costing using local secondary data' – the latter with no author referenced – making these cost estimates impossible to review and to determine their robustness. The assumptions applied to estimating the TB treatment costs for HIV-positive persons, inmates of correctional facilities and miners were not explained.

[2] Unfortunately, the Chief Director and the TB Director at the Gauteng DOH did not respond to an interview request, and hence it could not be ascertained if all GP's key interventions and coverage rates were correctly captured.

2.3.4. The report indicates that the TB diagnostic costs applied were from an NHLS costing conducted as part of this analysis (Pedro da Silva, Naseem Cassim). Since the laboratory test unit prices came from the NHLS it may be assumed that they are accurate – and could be easily updated with more recent NHLS prices if the model is to be applied in other provinces. There is one large amount indicated for 'other tests and monitoring' (R90,644,773), which seems to have been added as an annual fixed cost, but the reference of this figure and its calculation, are not explained. It seems a high (and possibly unnecessary) additional amount, if the majority of the other key tests have been costed separately.

2.3.5. In the absence of data to inform non-linear cost-coverage curves, linear cost-coverage curves were assumed. The report notes the limitation of assuming constant unit costs for interventions, rather than anticipating potential future reductions. A sensitivity analysis should have estimated the impact of such reductions or fluctuations. As the authors note *"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*." (Technical Summary document, WB, no date).

2.3.6. This also highlights the significant limitation of assuming a linear cost-coverage curve between the costs and available funding (based on past spending on each intervention) and their outcomes. Obviously, the assumptions made on cost functions are a critical driver of the optimization modelling and would have significant impact on the re-allocation recommendations of the model.

2.3.7. It seems that an inflation-related increase in future unit prices was not applied, and at the same time, the modeling appeared to have assumed constant available funding based on the reported spending in 2015/16. This is the correct approach if neither the costs nor the funding envelope have included inflation-adjustments.

2.3.8. In a brief about Optima HIV, the World Bank (no date[iii]) explained that Optima is not a costing or budgeting tool – it can inform investments but actual budgeting for implementation requires different tools. This is an important qualification/ caveat regarding the use of the Optima TB tool for Gauteng – that it should not be used for detail costing and budgeting, but rather to inform high level resource re-allocation between TB interventions, for the greatest impact.

2.4. Estimated spending on TB in 2016 and the optimzation results

2.4.1. In order to provide the budget ceiling within which to run the optimization, the Optima TB model used the provincial spending on TB in 2016/17, which was estimated by drawing on the GP DOH Basic Accounting System (BAS) and applying costings for certain aspects. Then, based on their calculated spending per person reached with an intervention, the cost-coverage-outcome relations were developed, assuming a linear relationship which has its uncertainties, as noted above. It was not clear what assumptions were applied to project the future TB funding trends in Gauteng, but it appears that the available funds were assumed to remain constant at 2016/17 levels, and since they also did not adjust their unit costs for inflation, only a stagnated snap-shot in time (2016/17) can only be provided by the model and which is applied to future years. This is a key limitation of the model.

2.4.2. In addition, Optima required the current spending by specific interventions, and a key challenge faced was the lack of such detail in the BAS records. A recently released analysis of South Africa's HIV and TB spending (Guthrie *et al*, 2018[iv]) found similar limitations with the BAS records[3], with key interventions' spending not specifically labeled. For this reason, the Optima team had to use additional costing techniques to estimate various costs, and an additional amount of R240 million was estimated as TB-related spending by Gauteng's health sector (shown in the Optima TB report, figure 18, page 46). This large additional amount was partly due to that additional fixed amount of R75 million for 'other diagnostic costs' (queried above), as well as an amount of R350 million which seems to have been some estimation of the human resources costs for DS and DR treatment. Thus the Optima model assumed a total of nearly R600 million for Gauteng's spending on TB, which has probably over-estimated the available envelope under which to run the optimization.

[3] Guthrie et al (2018) found that the TB-related transactions could not be easily extracted from BAS and had to be carefully searched for across several variables, including: 'responsibility' (for TB-hospitals), 'objective', 'sub-programme' and 'cost item' (the latter for TB medicines). No spending was found labeled as IPT, yet this is an important prevention intervention in most provinces for HIV-positive patients. The analysis also found that the spending labeled to 'MDR' or 'TB hospitals' probably included the DS-TB medication that was distributed to the clinics in the surrounding service areas, and which therefore should not be assumed to be all in-patient treatment costs. In Gauteng in particular, a large portion was labeled to MDR-TB. In addition, it appeared that the diagnostic costs were not consistently labeled as TB-related, which would have required the NHLS invoices to be separated by disease type (which was often not done as it was unnecessary because the finance officers who would usually capture the entire NHLS payments in one transaction). And finally, the BAS records would not have attributed a share of the time of the staff providing other services as well as TB-related intervention (apart from TB programme managers and any others clearly labeled as TB specifically), and thus would have under-captured the DOH's spending on personnel. As a result, using the BAS records to calculate the DOH spending per patient resulted in out-patient treatment costs being far lower than the LSHTM's unit cost, and the in-patient treatment spending per patient being far greater than the LSHTM (also because it would have been divided by the fewer numbers of DR-TB patients).

2.4.3. It is therefore important to acknowledge that the core function of the Optima model – to propose the optimal package of interventions and suggest any required re-allocations - is based upon an extremely weak and potentially flawed estimation of available funding in 2016/17, both the total and the split between interventions. A sensitivity analysis could run the potential variations in the available budget ceiling per intervention.

2.4.4. Finally the optimization findings and recommendations regarding re-allocations must be engaged with, and interrogated by, various stakeholders, and their assumptions and relevance 'ground-truthed'. For example, the three main changes implied (by figure 36, page 64) include:
- increasing the spending on new MDR-TB treatment regimens (noting the potential savings and benefits thereof) – *but with no modeled reduction in MDR-TB treatment costs, the model has probably over-estimated the resources needed.*
- increasing the DS-TB treatment spending, and;
- the need for *enhanced* mass screening at PHC level was noted, but concurrently the report suggested a reduction in spending on these activities*, seemingly to contradict the NDOH's campaign of 'finding the missing TB patients' through quality improvement at the PHC level.*

3. ALTERNATIVE TB MODEL OPTIONS

An alternative TB model to be considered in this discussion is the TIME Impact model, which was applied for the national cost estimates and projections for the South African NTP, along with efforts to capacitate the national and provincial departments of health to populate and run the model. Although the TIME model is user-friendly, is also heavy in its data demands (as would be any such TB model). Details on TIME are provided in Annex C.

Alternatively, the the actuary who developed the HIV Thembisa model, will be developing a local TB model that can be applied at provincial level. In addition, the Health Economics and Epidemiological Research Unit (HE^2RO) at WITS University, would be collaborating with the new TB Thembisa model to build the South African TB Investment Case[4]. This would be an important contribution to this field, and should involve the provincial policy and programme managers to capacitate them to parameterize and run the model themselves. This would enable the model's on-going application and accuracy.

[4] According to the senior South African health economist who led the development of the HIV Investment Case model.

4. SUMMARY

This summary of a full review focused on the **assumptions and the data used** to populate the Optima TB tool. It is important to note that the model faced the same key challenges, as does any model regarding limited available data with which to populate it, especially when operating at the provincial level. Although the model has the flexibility to add compartments for specific vulnerable populations, these increase its data demands. At the same time, although the model may be relatively simple, and more user-friendly that other more complex transmission models, it runs the risk of applying default generalized parameters when the detailed provincial and sub-group data are not available, which could result in limited variation between the provincial variation in the results. Hence the application of the model in the other provinces could result in very similar overall results and conclusions, if more nuanced provincial data are not available.

Unfortunately, there are limitations and gaps with the key pieces of data in the Optima TB model that significantly undermine its findings and recommendations. These limitations include:

4.1. The TB-HIV relationship, specifically with regards to LTBI activation and the effects of scaled-up ART, was not well accommodated in the model;

4.2. The programmatic coverage and effectiveness data – the assumed current coverage rates could not be validated and not all the interventions' effectiveness assumptions were provided in the report;

4.3. The unit costs – although most were in line with those applied in the NTP and NSP costing, some were not referenced and the additional cost of laboratory tests was not well justified. In addition, all unit costs were assumed to remain constant into the future, with no sensitivity analysis with possible changes in costs;

4.4. The cost-coverage and the coverage-outcome relationships were assumed to be linear which would have affected the model's calculation of the current and future coverage and impact, resulting in a simplistic, and probably not accurate, optimization process;

4.5. The available TB funding (using current spending) relied on the BAS data which are not always split correctly by intervention and which has thus undermined the model's assumed current split of spending. In addition, the modelers added a very high estimate of the health sector's contribution, which has probably over-estimated the available funding. These two aspects – available TB funding and how it is currently spent on interventions, form the basis of the optimization approach and hence may have skewed the re-allocation recommendations.

Each of these categories of data have significant impact and inherent uncertainty, but were not considered in a sensitivity analysis. In summary, given the limitations noted earlier regarding the model's cost and impact assumptions, as well as its calculation of the current spending upon which

the optimization results are based, it is suggested that even the high-level Optima resource re-allocation recommendations should be viewed with caution, and the model may therefore not be suitable for application in the other provinces.

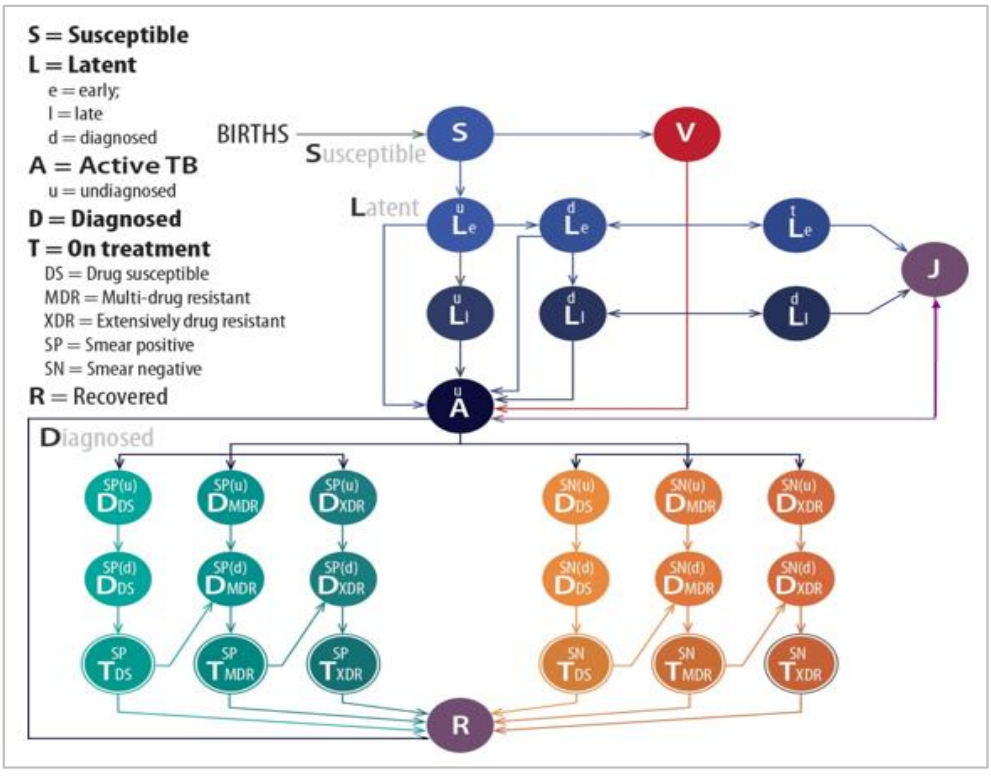
It is suggested that an alternative model, preferably a local 'Thembisa' version or the Time Impact model, could be applied more accurately in the other provinces. Whichever model is applied, the model should: include assumptions about reducing unit prices, especially for DR-TB treatment; improve and explain the cost-effectiveness assumptions; improve the estimation of current spending from provincial BAS records (which will continue to face challenges in some provinces until their capturing of BAS transactions improves); and apply a more nuanced input-outcome/coverage-impact relationship in the optimization approach.

> *"Finally, all epidemiological modelling results are uncertain and it is important to convey this uncertainty to policymakers. Development is ongoing for an automated framework to facilitate fitting the model to epidemiological data and generating uncertainty bounds around results introduced by assumptions regarding natural history, epidemiological data, the epidemiological effect of interventions and what happens in the future."*
> **(Houben *et al*, 2016).**

5. Annex A: Technical summary of the TB Optima model

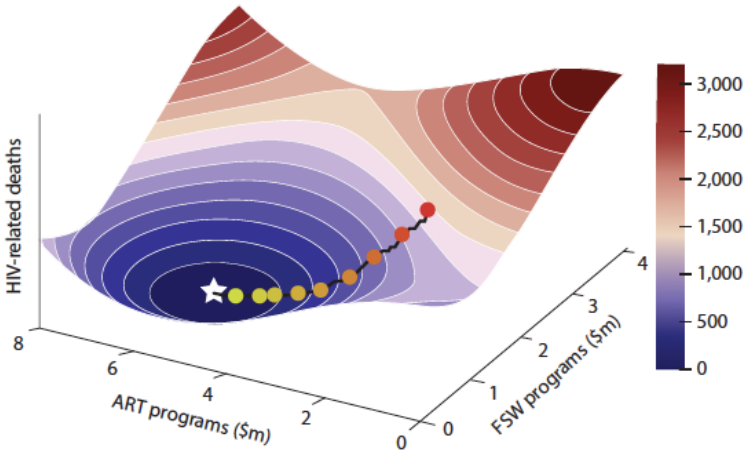
Technical Summary of Optima TB:
Optima TB is a mathematical model of TB transmission and disease progression integrated with an economic and programme analysis framework. Optima uses TB epidemic modeling techniques and incorporates evidence on biological transmission probabilities, detailed disease progression 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

6. Annex B: Schematic diagram of the health state structure of the model



Source: World Bank, Technical Summary of Optima TB (no date).

7. Annex C: Schematic diagram of Optima's approach to optimisation



Source: World Bank: www.optimamodel.com

8. Annex D: The TIME TB Impact Model

"TIME Impact is an epidemiological transmission model nested in TIME, a set of TB modelling tools available for free download within the widely-used Spectrum software. The TIME Impact model reflects key aspects of the natural history of TB, with additional structure for HIV/ART, drug resistance, treatment history and age. TIME Impact enables national TB programmes (NTPs) and other TB policymakers to better understand their own TB epidemic, plan their response, apply for funding and evaluate the implementation of the response. TIME Impact and TIME Estimates are linked to the OneHealth Tool, a comprehensive costing and budgeting tool developed by a group of UN agencies, including WHO, UNAIDS, UNDP, UNFPA, UNICEF and the World Bank. OneHealth provides a single framework for planning, costing, impact analysis, budgeting and financing of strategies for major diseases and health system components. OneHealth's TB costing module is designed to mimic the WHO TB Planning and Budgeting Tool, a detailed ingredients-based costing tool developed by the Global TB Programme. Users can control the coverages of diagnostic, treatment and patient support interventions over time, modify the population targeted to receive each intervention, cost the construction of new laboratories, and match budget lines to fit with national or international funder requirements. Development of a new TIME Economics module is currently underway. TIME Economics is intended to address TB-specific allocative efficiency and cost-effectiveness questions."

Source: Houben *et al,* 2016[v].

9. Annex E: Experts who provided their insights into the model

Anna Vassal, London School of Hygiene and Tropical Medicine
Gabriela Gomez, London School of Hygiene and Tropical Medicine
Gesine Meyer-Rath, Health Economics and Epidemiological Research Office (HE^{2}RO, WITS).
Liesl Page-Shipp, TB expert/ consultant.
Vusi Madi, Finance Manager, Gauteng Department of Health.

No response, as yet, from:
Ms Mmope, Chief Director, Gauteng Department of Health.
Ms Mlambo, Acting Director, Gauteng Department of Health.

REFERENCES

[i] Kerr CC et al. (2015). Optima: A Model for HIV Epidemic Analysis, Programme Prioritization, and Resource Optimization." JAIDS, 69(3):365-76.

[ii] South African National AIDS Council (SANAC), 2017. South Africa's National Strategic Plan for HIV, TB and STI's 2017-2022. http://sanac.org.za/wp-content/uploads/2017/05/NSP_FullDocument_FINAL.pdf

[iii] World Bank (no date). "Optima: an HIV optimization and analysis tool".

[iv] Guthrie T, Chaitkin M, Khoza N, Zulu N, Madisha V, Ndlovu N, Shezi S, Karume J, Motsoeneng P, Simelane S, Meyer-Rath G, Masuku S, Jamieson L, and Ghai K. (2018). *Consolidated Spending on HIV and TB in South Africa (2014/15–2016/17)*. Pretoria: National Department of Health; Washington, DC: Health Finance & Governance Project, Results for Development Institute. http://www.r4d.org/resources/analysis-consolidated-spending-hiv-tb-south-africa/

[v] Houben R, *et al.* 2016. TIME Impact – a new user-friendly tuberculosis (TB) model to inform TB policy decisions. BMC Medicine2016,14:56. https://doi.org/10.1186/s12916-016-0608-4