Highlights

- Mathematical and economic modelling is being used to inform how disease control resources are allocated and what policies are adopted. These models specify complex non-linear relationships between service coverage and impact. However, functions describing the relationship between costs and service volume have typically been less sophisticated, assuming constant marginal costs of expanding service coverage. This approach runs counter to the theoretical understanding of the way costs behave when scaling up.
- We propose an alternative approach. We developed a mechanistic framework to estimate total costs for inclusion in model-based economic evaluations using a combination of secondary data from small-scale costing studies and routine reporting systems. We provide a pragmatic, mechanistic framework rooted in economic theory for others facing similar data constraints to improve resource allocation models used to define packages of interventions within LMIC settings.
- Using a case study of tuberculosis case detection in South Africa, we show that the functional form chosen to estimate total costs will determine the magnitude of total costs when increasing the outputs and coverage. In turn, these differences can impact policy choice and resource allocation decisions. The framework presented here is a first step towards a more transparent and empirically based cost modelling approach to better inform resource allocation processes.

1 Introduction

In the context of Universal Health Coverage (UHC), increased attention is being placed on priority setting both across and within disease-specific programs, to ensure funds are allocated efficiently to maximize impact. Supported by development funders, mathematical (disease transmission) and economic modelling are being increasingly used to inform prioritisation processes and evaluate strategies for achieving target coverage levels for infectious disease programmes (some recent examples include [1]–[3]). These models typically predict the impact and cost-effectiveness of combinations of coverage of a range of disease-specific interventions. They are either used to optimise cost-effectiveness under a budget constraint (constrained optimisation) or to report incremental cost-effectiveness ratios that compare competing policy portfolios.

Disease transmission models explore complex and sophisticated non-linear relationships between service coverage and epidemiological impact (health benefits). However, they have often assumed constant marginal costs when modelling expanding service coverage, with exceptions being [4]–[6]. A linear approach runs counter to economic theory describing how costs behave under changes in the production process, overlooking economies of scale and scope. These economies are the conditions under which long-run unit costs decrease as output increases or as the range of services expands, respectively. Economies of scale and scope are due because fixed costs such as buildings or utilities are spread over larger patient volumes, facilities become more efficient through specialisation and shared inputs such as human resources are utilised over a larger number of services. In recent years, several large-scale empirical costing studies have been conducted, particularly in the area of HIV and immunization. These studies have suggested that the relationship between marginal costs, scale and population-level coverage is likely to be non-linear (for example [7]–[10]). This evidence undermines the assumption of linear marginal costs typically used in disease transmission models, and suggests that other functional forms for cost calculation should be considered [4]. However, identifying and characterising cost functions has been a challenge in practice, as both cost accounting identities and flexible cost functions have proven difficult to parameterise [4]. Empirically deriving cost functions using econometric methods is a substantial and costly undertaking, particularly where comprehensive multi-site cost

data is not available through routine systems. In addition, cross-sectional surveys of costs may not well predict longitudinal variation in costs due to an increase in scale. Theoretically-defined cost functions linking longitudinal expenditure data to coverage levels can also be used. However, expenditures may be partial estimates of cost and available data on service outputs may be insufficient to fit these functions in many low- and middle-income country (LMIC) settings [11].

As an alternative approach, we propose a mechanistic mathematical framework to estimate total costs for inclusion in transmission model-based economic evaluations. We use a combination of secondary data from small scale costing studies and routine reporting systems. Our approach aims to disaggregate both site-level (costs incurred at point of service) and above-site-level (costs incurred at a higher organisational level – at district or national) costs. It allows for scope and scale effects in the estimation of total incremental costs of different interventions. We applied this framework to a model previously used to inform resource allocation in tuberculosis (TB) [12], to illustrate both the data requirements and assumptions. We aim to provide a pragmatic, mechanistic framework rooted in economic theory. The purpose of such a framework is to improve resource allocation models used by analysts facing time and data constraints and aiming to define packages of interventions within disease-specific programs.

2 Conceptual framework

Economic theory posits that technologies and production processes can have varying returns to scale. The variation in returns to scale will be different whether we analyse production costs in the short run (the period where some of the factors of production are fixed) or the long run (when all factors of production are variable). For example, in the short run, it may not be possible to change the size or numbers of health facilities in each area. But the level of service coverage may be increased by increasing variable factors such as number of staff within the existing facilities. Typically, disease-specific program expansion (such as in vertical HIV and TB programs) is characterised using a short run cost function. This is motivated by (a) a payer perspective that is often focused on the single disease, limiting the decision space to varying only those factors of

production that are under the control of the vertical program; and (b) relatively short planning cycles of three to five years.

The (short-run) average cost function is commonly assumed to have a u-shape. With increasing scale, average costs decrease. This is because the fixed component is divided among increasing units of production until the point where operating at high levels of capacity starts to constrain the efficiency of the production process, for example because no additional patients can be screened without opening new laboratories to process diagnostic tests. After this point, average costs begin to rise. In this case, a short run cost function for each provider will have the following form:

$$C_s(y, x_2) = w_1 x_1 + w_2 x_2; \text{ such that } f(x_1, x_2) = y \text{ (equation 1)}$$

Where y is the unit of output, w_1 and w_2 are prices, x_1 are the variable factors of production, and $x_2$is the fixed factor of production.

However, interventions are expanded by disease programmes across a fixed network of service providers. The field of transportation economics provides a relevant approach to understanding the form of cost function that is appropriate for a disease programme[13]. Here *economies of scale* are determined by *economies of capacity utilisation*, the relationship between cost and the capacity of each vehicle, i.e. how full is each plane (or health service provider); and *economies of density*, the relationship between cost and density of use of the network structure, i.e. how many planes (or health service providers) are used to provide the service, keeping the capacity of planes constant.

We postulate that a cost function, in the case of scale-up of disease-specific services, should be derived both by considering the relationship between the number and type of facilities (density of provision), and the number of people serviced at each facility (capacity utilisation). The pattern of programme expansion through the health service network has been shown to have an impact on the distribution of costs over time [4]. Local knowledge and input will help framing the calculations, whether programme expansion is through stand-alone campaigns or facility-based; whether large facilities join the scale-up first, followed by smaller facilities; or whether there is a

regional variation in scale-up strategies. Additionally, strategies within disease areas may exhibit *economies of scope* between service areas that de facto expand capacity at the facility level in reducing costs from joint production of services.

Following these principles, we start by proposing a simple cost function in the form of an adapted accounting identity that captures density (number of facilities expanding services linked to the pattern of program expansion) and capacity (number of people receiving the service in each facility) across levels of outputs. In this model, we assume a centrally-coordinated disease control programme, where services are provided by many service outlets (e.g. clinics and hospitals). The form of total costs (TC) per strategy considered in the short run should be as follows:

$$TC = FP + \sum_{i \in I} FF_i + \sum_{i \in I} (VF \text{ x } n\_output)_i \text{ (equation 2)}$$

Where FP= fixed programme cost; FF_i=fixed facility cost for facility i; VF_i=variable facility cost for facility i; n_output_i=number of outputs for facility i, i = total number of facilities.

We define fixed programme cost as an investment at a national level by the programme to manage the intervention or its continuous service delivery. Facility-level fixed costs (in the short run) differ by facility, but are variable at national level (as a function of the number of facilities). These facility-level fixed costs include building costs or management costs. They can also include 'programme' costs that are incurred above the site level, but are fixed by facility, such as supervision and training. Facility-level variable costs are all those costs that change as output levels change, for example consumables (such as HIV test kits and sputum tests).

When programmes expand, they can also produce economies of scope due to integration of services or the use of same inputs to produce joint outputs. There are various sources of economies of scope, we focus on influence of joint production on fixed costs. Here we postulate that some fixed costs can be incurred to deliver simultaneously more than one output. We only consider economies of scope operating from the intervention standpoint and only considered incremental costs for those activities delivered jointly with other programmes (for example, TB screening of antiretroviral treatment patients during monitoring visits for HIV care). To reflect

these joint costs, we defined fixed and variable costs at facility-level in intervention-facility pairs, if only fixed costs are influenced by scope expanding equation 2 to:

$$TC = FP_j + \sum_{j\in J}\sum_{i\in I} FF_{ij} - \sum_{i\in 1} FF_{shared\,i} + \sum_{j\in J}\sum_{i\in I}(VF \text{ x } n\_outputs)_{ij} \text{ (equation 3)}$$

Where FP= fixed programme cost for intervention j; FF_{ij}=fixed facility cost for facility i and intervention j; FF_shared_i = fixed facility costs shared between 2 or more interventions; VF_i = variable facility cost for facility i and intervention j; n_output_{ij}=number of outputs for facility i and intervention j; I = total number of facilities; J = total number of interventions.

Equation 3 allows fixed costs at the programmatic and site level to be distinguished and allows for densities of scale across multiple service providers.

3 Case Study

We conducted a case study to illustrate the empirical application and data requirements for disease transmission models (epidemiological mathematical models of infectious diseases commonly used in economic evaluations). Using existing empirical work to support National Strategic Plans for tuberculosis in South Africa, we compare three scenarios: 1) linear cost function (conventional approach): average costs remain the same during scale-up; 2) uniform facility-level cost function, including economies of capacity and scope, assuming a uniform scale-up across facilities; and 3) density cost function, including economies of capacity, scope and density where larger facilities increase service outputs in the first instance, then they are followed by smaller facilities joining programme expansion.

Our case study was provided by the TB Modelling and Analysis Consortium (TB MAC)[14], as part of an analysis examining the feasibility of achieving the 2025 goals of the WHO 'End TB strategy 2016-2035' in three countries: China, India, and South Africa [12]. This analysis compared several interventions along the TB care cascade (prevention, case finding, diagnosis and treatment). Cost functions were defined as linear relationships, with a constant marginal cost per additional unit of output. In South Africa, it was found that while no single intervention scenario was sufficient to reach the epidemiological targets by 2025, a combination of all

interventions could potentially be [15]. From a societal perspective, expanded TB control substantially reduced patient-incurred costs and helped avert household catastrophic costs [16]. From a healthcare payer perspective, most interventions appeared highly cost-effective compared to conventional willingness-to-pay thresholds, yet considerable budget increases would be needed to achieve the ambitious scale up [12].

In this study, we expand the previous analysis to compare three proposed approaches to cost functions. We examine the scale up of TB symptom screening for all patients attending primary care clinics, followed by current diagnosis algorithm for those found to be symptomatic. We focused on a case finding intervention because this intervention was the main driver of total costs in the previous analysis [12].

3.1 Specification of joint production functions for intervention and services

First, we defined outputs from the disease transmission model for each intervention and service. Outputs were defined as all the units that will have costs attached to them – for example, number of people tested, number of person-months on treatment. These outputs are related to the intervention examined in that they are expected to change directly as a result of the intervention (i.e. number of people screened and number of people tested), but also consequential outputs along the TB care cascade (i.e. number of people treated if more people are diagnosed following an expansion of screening activities).

In consultation with local policy makers, we defined the production process for each output, in terms of activities directly related to the intervention, supporting services needed to achieve implementation coverage targets, and health system level where these activities take place. Intervention activities include, for example, nurse time for TB symptom screening and test costs for TB diagnosis; supporting services will be outreach activities, staff training at facilities being recruited into the programme, and health system level activities considered could include information technology systems for tracking diagnoses. In order to do this, we looked at the main factors of production for each output and the resources required by the facilities to start offering or expand current services.

We then estimated total costs as a function of disaggregated average costs into the following components: programme costs (assumed fixed each year), facility-level fixed costs, and variable costs at facility level as per equations above. All data on unit costs were sourced from the literature (Table I).

[TABLE I]

3.2 Specification of programme expansion patterns

To illustrate the difference in total costs estimations, we calculated and compared incremental costs (compared to a base case of no screening intervention) under three assumption scenarios:

- Linear assumption of costs: scenario 1
- Cost functions applying economies of capacity utilisation: scenario 2
- Cost functions applying economies of capacity utilisation and density: scenario 3

In figure 1, we present a step-by-step description of the link between the conceptual framework and the calculation of costs for each scenario. Data on the primary health care facility sizes in South Africa were obtained from the National Department of Health, specifically from the National Health Information System [17]. The database included number of patients attending outpatient services per facility. For scenario 2, we modelled programme expansion across facilities by assuming service volume would be increased proportionally to the site size within each site (defined as the number of patients attending outpatient services). This scenario reflects the intrinsic assumption in the previous analysis [12], which is that the TB program is facing partially exogenous fixed costs, in that the total number of facilities available nationally remains fixed while the size of facilities changes, without limiting the ability of facilities to absorb the additional demand for services. However, we include economies of scale and scope at facility level. In a third scenario, we varied the pattern of recruitment into the programme for facilities and assumed that the programme started expanding from larger facilities (as these are assumed to be recruited earlier in a new programme or programme expansion) to smaller ones. All facilities achieved the same number of patients per facility as in the initial scenario.

[Figure 1]

We present total costs and the difference between scenario 1 and 2, and then 2 and 3.

4 Discussion

In figure 2a, we present the incremental costs under three cost assumption scenarios. We observe reductions in incremental costs due to the inclusion of economies of capacity (over 20% reduction); however, the addition of economies of density did not show major impact in comparison (less than 5% reduction). In figure 2b, we present the difference between these scenarios. The differences between scenarios are due to the assumptions in economies of scale (and scope). The small differences between scenarios reflect the impact of sharing fixed site costs, when human resources are considered variable inputs.

[FIGURE 2]

Cost data availability and quality was an issue when parameterising costs functions. Detailed cost data to fit cost functions empirically exists but these are rare as detailed cost estimates at different stages of implementation and time points are needed for a large sample size. Cost data requirements for the proposed approach were less onerous than those for parameterising cost functions empirically, see table II. Comprehensive, standardised and disaggregated unit costs (for a limited number of outputs) are a pre-requisite. Information on the network of facilities available to the programme (including type and size of the facility) is usually available centrally at country-level. Finally, descriptive and detailed information on services, intervention and ancillary activities needed to expand coverage as well as planned programme scale up should be sought from policy makers.

[Table II]

The assumption of a linear relationship between costs, scale and pattern of programme expansion can change the total predicted costs in the presence of economies of density and/or capacity utilization. The extent to which all these should be considered and whether they will matter for priority setting depends on the intervention considered and services evaluated. While economies

of capacity (or scale at facility level) and scope can substantially change the total cost estimates over time, assumptions on how the program expands within the network of facilities (economies of density) did not seem to have a major impact on cost estimates over time in our case example. Consideration on whether to include economies of density will depend on the intervention evaluated. In our case study, delivery of intensified case finding for TB is an intervention with (relatively) low fixed costs, both at facility and programme levels, particularly in a setting such as South Africa where facilities have low spare capacity. The relative proportion of fixed costs that are incurred at programme level compared to facility level could help explain the difference in our results compared to previous studies. Indeed, previous studies have shown that the inclusion of economies of scale has an impact on the resulting prioritisation [4]–[6]. In addition, these studies highlighted that assumptions on the proportion of fixed costs or pattern of programme expansion does influence the total costs estimates. These two assumptions are made explicit in this framework.

Our case study presents the introduction of one intervention in South Africa and illustrates the impact of several assumptions of programme scale-up. We expect results to vary in other cases and with other assumptions. Whether to use more complex cost functions including economies of capacity or density would be then a decision based on whether the intervention considered has high fixed costs or other reasons to expect strongly non-linear cost functions.

This framework has the advantage of being transparent and based on available, routinely collected data. However, there are intrinsic differences between transport and health economics. Three areas for consideration in cost formation are supply and demand constraints, as well as quality of care. Firstly, health system-wide constraints could be better defined. For example, more information is needed to characterise the distribution of spare human resource capacity and how this capacity can be reallocated. Supply-side constraints may be heterogeneously distributed across the care cascade. This differential distribution can be accounted within the joint production function by limiting the overall scale to the capacity of the service that is constrained. This would be one approach among several that could be applied in economic evaluations, an example could be found here [18]. Furthermore, our framework does not investigate the variation of costs due to quality of services. We recognise that quality of care can vary both between levels

of the health system and between different facilities at the same level (e.g. rural vs urban, new vs old). These differences become central to efficiency analyses across unit costs. However, if data on how unit costs varied in a specific setting because of differences in operational environment such as quality, uptake and accessibility of care, then these could be accommodated within our framework by including additional terms for facility-level fixed and variable costs.

By disaggregating fixed costs at the programme and facility level, we allow for different densities of scale across multiple service providers, thus extending previous approaches where programme and facility level costs are aggregated into 'platform' costs [19]. Another limitation of this framework is that it focuses on predicting total costs in the short run. Depending on the decision-maker perspective, it can be argued that long run cost functions (where all inputs are considered variable) would be more appropriate when looking at scaling up interventions. Decisions within disease-specific programmes tend not to include changes in infrastructure such as building additional facilities. In this context, short run cost functions would reflect this perspective.

This framework is based on two key sources of data: 1) empirical cost data reported in a disaggregated manner, both by inputs and activities; and 2) facility size data available on the network of facilities that will be scaling up the intervention of interest. These data are generally available from cross sectional studies, and an implicit assumption in this framework is that observed behaviour of costs in a cross-sectional sample of facilities of different sizes can be extrapolated to predict behaviour of costs in facilities expanding services longitudinally. Our approach reflects a limitation of current data availability. Furthermore, not all disease-specific programmes will have cross sectional data available and standardised at facility level. There are several ongoing initiatives to improve availability of cost data in a variety of diseases and, in particular, the Global Health Cost Consortium (GHCC) has led efforts to standardise HIV- and TB-specific costs with additional guidance for reporting standards (including a framework for standardisation of interventions, units, activities, and inputs). These reporting standards are part of the GHCC's reference case for costing activities, which is a set of 'acceptable' principles and methodological guidance on how to achieve those principles, and includes both theory and evidence-based guidance [20].

Finally, further research will be needed to expand this framework to include explicit budget constraints. This becomes essential when considering equity and efficiency trade-offs, for example when a programme can only afford partial scale-up. Our results will then show that gains in efficiency could be contrasted with a more equitable scale-up (if we understand smaller facilities to be more remote/ serving poorer populations on average).

5 Conclusions

The functional form an analyst uses to estimate total costs during priority setting exercises will determine the magnitude of total costs when increasing outputs and coverage. This, in turn, will impact the results of any optimisation routine. Yet, data availability in low- and middle-income countries can limit the analysis of costs in economic evaluations. Ultimately, infectious diseases modellers and economists should aim to choose rationally the functional form and include more transparent and empirically-based cost models into their analyses, as put forward in recently published guidance for country-level modelling in tuberculosis [21]. This framework describes a general approach for describing and developing these models.

6 References

[1] S.-J. Anderson, P. D. Ghys, R. Ombam, and T. B. Hallett, "Frontloading HIV financing maximizes the achievable impact of HIV prevention," *J. Int. AIDS Soc.*, vol. 21, no. 3, p. e25087, 2018, doi: 10.1002/jia2.25087.

[2] J. F. Vesga, T. B. Hallett, M. J. A. Reid *et al.*, "Assessing tuberculosis control priorities in high-burden settings: a modelling approach," *Lancet Glob. Health*, vol. 7, no. 5, pp. e585–e595, 2019, doi: 10.1016/S2214-109X(19)30037-3.

[3] O. J. Celhay, S. P. Silal, R. J. Maude, C. E. Gran Mercado, R. Shretta, and L. J. White, "An interactive application for malaria elimination transmission and costing in the Asia-Pacific," *Wellcome Open Res.*, vol. 4, p. 61, 2019, doi: 10.12688/wellcomeopenres.14770.2.

[4] G. Meyer-Rath and M. Over, "HIV treatment as prevention: modelling the cost of antiretroviral treatment--state of the art and future directions," *PLoS Med.*, vol. 9, no. 7, p. e1001247, 2012, doi: 10.1371/journal.pmed.1001247.

[5] P. Winskill, P. G. Walker, R. E. Cibulskis, and A. C. Ghani, "Prioritizing the scale-up of interventions for malaria control and elimination," *Malar. J.*, vol. 18, no. 1, p. 122, Apr. 2019, doi: 10.1186/s12936-019-2755-5.

[6] H. C. Turner, J. E. Truscott, F. M. Fleming, T. D. Hollingsworth, S. J. Brooker, and R. M. Anderson, "Cost-effectiveness of scaling up mass drug administration for the control of soil-transmitted helminths: a comparison of cost function and constant costs analyses," *Lancet Infect. Dis.*, vol. 16, no. 7, pp. 838–846, 2016, doi: 10.1016/S1473-3099(15)00268-6.

[7] A. Lépine, S. Chandrashekar, G. Shetty *et al.*, "What Determines HIV Prevention Costs at Scale? Evidence from the Avahan Programme in India," *Health Econ.*, vol. 25 Suppl 1, pp. 67–82, Feb. 2016, doi: 10.1002/hec.3296.

[8] E. Marseille, L. Dandona, N. Marshall *et al.*, "HIV prevention costs and program scale: data from the PANCEA project in five low and middle-income countries," *BMC Health Serv. Res.*, vol. 7, p. 108, Jul. 2007, doi: 10.1186/1472-6963-7-108.

[9] O. Galárraga, R. G. Wamai, S. G. Sosa-Rubí *et al.*, "HIV prevention costs and their predictors: evidence from the ORPHEA Project in Kenya," *Health Policy Plan.*, vol. 32, no. 10, pp. 1407–1416, Dec. 2017, doi: 10.1093/heapol/czx121.

[10] N. A. Menzies, A. A. Berruti, and J. M. Blandford, "The determinants of HIV treatment costs in resource limited settings," *PloS One*, vol. 7, no. 11, p. e48726, 2012, doi: 10.1371/journal.pone.0048726.

[11] R. M. Stuart, L. Grobicki, H. Haghparast-Bidgoli *et al.*, "How should HIV resources be allocated? Lessons learnt from applying Optima HIV in 23 countries," *J. Int. AIDS Soc.*, vol. 21, no. 4, p. e25097, 2018, doi: 10.1002/jia2.25097.

[12] N. A. Menzies, G. B. Gomez, F. Bozzani *et al.*, "Cost-effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa: a combined analysis of nine models," *Lancet Glob. Health*, vol. 4, no. 11, pp. e816–e826, 2016, doi: 10.1016/S2214-109X(16)30265-0.

[13] T. Hoon Oum, J. S. Dodgson, D. A. Hensher *et al.*, *Transport economics: selected readings*. London and New York: Routledge, 2014.

[14] TB MAC, "TB modeling and analysis consortium." http://tb-mac.org/ (accessed Jun. 13, 2020).

[15] R. M. G. J. Houben, N. A. Menzies, T. Sumner *et al.*, "Feasibility of achieving the 2025 WHO global tuberculosis targets in South Africa, China, and India: a combined analysis of 11 mathematical models," *Lancet Glob. Health*, vol. 4, no. 11, pp. e806–e815, 2016, doi: 10.1016/S2214-109X(16)30199-1.

[16] S. Verguet, C. Riumallo-Herl, G. B. Gomez *et al.*, "Catastrophic costs potentially averted by tuberculosis control in India and South Africa: a modelling study," *Lancet Glob. Health*, vol. 5, no. 11, pp. e1123–e1132, 2017, doi: 10.1016/S2214-109X(17)30341-8.

[17] Directorate: National Health Information System. National Department of Health, Republic of South Africa, "Health Information Research Monitoring and Evaluation: National Health Information System." http://www.hisp.org/index.php/sa-projects/.
[18] F. M. Bozzani, D. Mudzengi, T. Sumner *et al.*, "Empirical estimation of resource constraints for use in model-based economic evaluation: an example of TB services in South Africa," *Cost Eff. Resour. Alloc. CE*, vol. 16, p. 27, 2018, doi: 10.1186/s12962-018-0113-z.
[19] K. Hauck, A. Morton, K. Chalkidou *et al.*, "How can we evaluate the cost-effectiveness of health system strengthening? A typology and illustrations," *Soc. Sci. Med. 1982*, vol. 220, pp. 141–149, 2019, doi: 10.1016/j.socscimed.2018.10.030.
[20] Global Health Costing Consortium, "Reference Case for Estimating the Costs of Global Health Services and Interventions," 2017. https://ghcosting.org/pages/standards/reference_case.
[21] N. A. Menzies, C. F. McQuaid, G. B. Gomez *et al.*, "Improving the quality of modelling evidence used for tuberculosis policy evaluation," *Int. J. Tuberc. Lung Dis. Off. J. Int. Union Tuberc. Lung Dis.*, vol. 23, no. 4, pp. 387–395, 01 2019, doi: 10.5588/ijtld.18.0660.
[22] A. Vassall, M. Siapka, N. Foster *et al.*, "Cost-effectiveness of Xpert MTB/RIF for tuberculosis diagnosis in South Africa: a real-world cost analysis and economic evaluation," *Lancet Glob. Health*, vol. 5, no. 7, pp. e710–e719, 2017, doi: 10.1016/S2214-109X(17)30205-X.
[23] L. Cunnama, E. Sinanovic, L. Ramma *et al.*, "Using Top-down and Bottom-up Costing Approaches in LMICs: The Case for Using Both to Assess the Incremental Costs of New Technologies at Scale," *Health Econ.*, vol. 25 Suppl 1, pp. 53–66, Feb. 2016, doi: 10.1002/hec.3295.
[24] E. Sinanovic, L. Ramma, A. Vassall *et al.*, "Impact of reduced hospitalisation on the cost of treatment for drug-resistant tuberculosis in South Africa," *Int. J. Tuberc. Lung Dis. Off. J. Int. Union Tuberc. Lung Dis.*, vol. 19, no. 2, pp. 172–178, Feb. 2015, doi: 10.5588/ijtld.14.0421.
[25] Republic of South Africa, Department of Health, "Master Procurement Catalogue," 2018. http://www.health.gov.za/index.php/component/phocadownload/category/196.
[26] Global Health Costing Consortium, "Unit Cost Study Repository (UCSR)," 2018. https://ghcosting.org/pages/data/ucsr/app/ (accessed Jun. 13, 2020).
[27] ImmunizationEconomics.org, "EPIC data repository," 2018. http://immunizationeconomics.org/data-repository (accessed Jun. 13, 2020).

7 Legends and Figure

Figure 1. Step by step method and equivalent scenario calculation

Figure 2. Incremental costs by cost estimation scenario (USD 2016)

Legend

Panel 2a. Total costs per year in scenario 1 (linear assumption of costs) are shown in columns, while scenarios 2 (cost functions applying economies of capacity utilisation) and 3 (cost functions applying economies of capacity utilisation and density) are shown in lines (green and red, respectively). There is a reduction observed when adding economies of capacity utilisation (difference between scenario 1 vs. scenario 2 and 3). However, the different between scenario 2 and scenario 3 (addition of economies of density) is small, shown in panel 2b. Tables

Table I. Definition of units and unit costs per activity – constant and disaggregated (USD 2016).

Table II. Comparison and data requirements for three approaches to modelling costs for economic evaluations using transmission models.