COST-BENEFIT ANALYSIS OF INTERVENTIONS TO REDUCE THE TUBERCULOSIS BURDEN IN GHANA

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Cost-benefit analyses of interventions to reduce the tuberculosis burden in Ghana

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Academic Abstract

TB is responsible for around 5 percent of total deaths in Ghana annually, and the decline in TB burden is markedly slow, with an average 2.5 percent reduction in TB incidence year on year. TB mainly affects the working age population of Ghana (73 percent incident cases aged 15-44 in 2018), and as many as 68 percent of individuals who newly develop TB disease in a given year do not access TB treatment. For those that are enrolled on treatment, around 15 percent show poor treatment adherence and outcomes, or are lost to follow up. Overall, an estimated 15,800 individuals die from TB each year in Ghana.

This paper uses the TIME epidemiological modelling tool to evaluate the costs and benefits of three interventions aimed at reducing the TB burden in Ghana – namely Active Case Finding (ACF) in high risk populations, a sputum transport system to improve accuracy and speed of TB diagnosis, and patient education & counselling to improve TB treatment adherence and outcomes. The analysis indicates that ACF, scaled up over a period of 6 years from the end of 2019 to 2025[1], could have a significant impact on TB burden and mortality reduction, with 5,022 TB cases averted and 2,221 deaths averted during this period, and 33 percent of total estimated prevalent TB cases among high risk populations notified and enrolled on treatment in 2025. With improved diagnosis, the model predicts that scaleup of molecular testing by GeneXpert over a period of 6 years to 2025, would have a marked impact on TB burden and mortality, with 4,832 TB cases averted and 3,087 TB deaths averted during this period

Assessed against the costs and benefits of the interventions, our cost-benefit analyses suggest that sputum transport system and patient education & counselling to improve TB treatment adherence have very high benefit-cost ratios (BCR) of 166 and 190 respectively. These BCRs are the largest in the *Ghana Priorities* series. Active case finding yields a lower, but still large BCR of 38. Sputum transportation system yields the highest net benefits.

Key Words: Cost benefit analysis, Tuberculosis, Active Case Finding, improved accuracy & speed of diagnosis, TB treatment adherence

Policy Abstract

The Problem

TB is responsible for around 5 percent of total deaths in Ghana annually, and the decline in TB burden is markedly slow, with an average 2.5 percent reduction in TB incidence year on year (GTB 2018). TB mainly affects the working age population of Ghana (73 percent* incident cases aged 15-44 in 2018), and as many as 70 percent of individuals with TB disease in a given year don't access TB treatment. For those that are enrolled on treatment, around 15 percent show poor treatment adherence and outcomes, or are lost to follow up. These factors overall resulted in an estimated 15,800 TB-related deaths in 2018.

The program currently estimates that only 32 percent of incident TB cases are notified year on year, and 80 percent of notified cases are enrolled on TB treatment.

To compound this problem, the 2018 WHO Global TB Program report estimated that 16 percent of cases previously treated for TB are resistant to first line anti-TB drugs, and hence are enrolled on a longer treatment course of second-line anti-TB drugs. A number of these drugs are associated with severe side effects, and these regimens have an overall treatment success rate of only 62 percent (GTB 2018).

Intervention 1: Active Case Finding

Overview

Detection of TB cases in Ghana has historically relied on passive case detection, and more recently the National TB Program has piloted an Intensified Case Finding (ICF) clinic-based TB screening tool, which is now implemented at Outpatient Department Clinics (OPDs) at the national level. Around 6,000 additional TB cases are screened, diagnosed and notified annually through this ICF mechanism, but there still exists a significant proportion of TB cases in Ghana that go undetected. Hence, there is a need to expand the reach of current case finding strategies to find missing TB cases at the level of the community, to detect and enroll on to treatment cases that may otherwise not present at the clinic, or at least not be identified by the health system until presenting with more severe TB disease. TB screening in specific high-risk populations, termed Active Case Finding (ACF), has been demonstrated in Ghana and other settings to yield a significant number of additional cases that would otherwise go undetected

(Yuen et al, 2015), refer to technical appendix for estimates of ACF target population size and TB prevalence.

Implementation Considerations

The intervention focuses on active screening for TB with Chest X-ray in high-risk populations including miners, refugees and their host communities, and in vulnerable urban populations, with an assumed average TB prevalence of 1.5 percent - approximately 5x the national estimate from Ghana's 2014 National TB Prevalence Survey – across groups totaling 1.6M population. The intervention aims to screen 600,000 individuals in the period 2020-2025, reaching a maximum number of 220,907 individuals screened in 2025- equivalent to 33 percent of total target population (assuming that the overall size of ACF target population doesn't change over time). This coverage target in terms of absolute numbers screened aligns broadly with Ghana's 2015-2020 National Strategic Plan systematic screening target of screening 60 percent of a target population of 1 million (where the original target year for achieving maximum ACF coverage was 2020).

Costs and Benefits

Costs

The unit cost per person screened was estimated at GH¢ 426 based on the 2015-2020 National Strategic Plan and includes patient time, staff time for outreach and household/work visits etc and overhead organization and management as well as screening tools costs. Total costs are GH¢ 2.6m initially rising to GH¢ 62m by 2040. 85% of costs are screening costs with the remainder for additional treatment that arises from improved identification of TB cases.

Benefits

The modelling results indicate that ACF, scaled up over a period of 6 years from 2019 to 2025, would have a significant impact on TB burden and mortality reduction, with 5,022 TB cases averted and 2,221 deaths averted during this period, and 33 per cent of total prevalent TB cases among high risk groups notified and enrolled on treatment in 2025. Projecting further out, the intervention is estimated to avoid 56,000 TB cases and 26,400 associated deaths from 2019 to 2040.

Intervention 2: Sputum transportation system to improve accuracy and speed of TB diagnosis

Overview

Coverage of molecular testing among all notified cases in 2018 was estimated at 58 percent (GTB report), up 38 percent from 20 percent coverage in 2017. With the lack of a direct estimate of the numbers of presumptive TB cases tested for TB by GeneXpert i.e. at the primary screening stage of the care cascade, it is assumed that this 38 percent increase in the proportion of notified cases diagnosed by GeneXpert, translates to an approximate 10 percent increase in coverage among all presumptive TB cases. This is reflected in the diagnostic algorithm in the baseline year of the model.

The NTP of Ghana is in the preliminary stages of rolling out a novel sputum transportation system, which aims to provide virtual on-site access to GeneXpert testing for >90 percent of OPD attendants, linking 1,000 health facilities to 126 existing GeneXpert testing sites. This system was initially piloted in the Greater Accra and Western Regions, with planning underway to provide coverage across most/all regions and districts. This would effectively enable TB suspects who provide sputum samples at facilities without a GeneXpert machine onsite, to receive molecular testing for TB without needing to travel to provincial or other more centralized facilities.

Implementation Considerations

In this intervention scenario, we modelled an increase in GeneXpert test coverage at the national level to 90 percent by 2025, to reflect the expansion of sputum transportation and utilization of GeneXpert machines at sites distal from the location of sputum sample collection. We estimate that the coverages of screening through passive case detection and ICF in 2018 were 65.5 percent and 34.5 percent of total screening at the national level, respectively, and in the model this ratio remains constant during the implementation period

GeneXpert is also used for molecular Drug Sensitivity Testing (DST) in Ghana, with an estimated 100 percent coverage of DST among previously treated cases and 93 percent among new cases in 2018 (GTB report). Expansion of GeneXpert in the model sees a corresponding increase in coverage of molecular DST among new cases to 99 percent by 2025, resulting in an additional 74 MDR-TB case notifications over the scale-up period.

Costs and Benefits

Costs

The rationale behind this intervention is to transport sputum samples to locations where GeneXpert machines are located. The cost of GeneXpert equals approximately GH¢ 176 per GeneXpert test (50 percent of which is transport cost, while the rest includes the labor cost and cost of cartridges and consumables). The cost of sputum microscopy is estimated at GH¢ 12. The cost of drug susceptible TB treatment is estimated at GH¢ 544 while the cost of MDR treatment is calculated as GH¢ 10,400. The intervention costs GH¢ 1.5m initially, rising to GH¢ 17.0m by 2040. Approximately 60% of the costs are for diagnostics and transport, with the remainder for additional treatment.

Benefits

The model predicts that scaleup of GeneXpert over a period of 6 years from the end of 2019[1], to 2025, would have a marked impact on TB burden and mortality, with 4,832 TB cases averted and 3,087 TB deaths averted during the period 2019-2025. Projecting further out, the intervention is estimated to avoid 65,000 TB cases and 36,600 associated deaths from 2019 to 2040.

Intervention 3: TB patient education and counselling to improve TB treatment adherence

Overview

The second intervention described above- molecular testing to improve TB diagnostic accuracy and speed- is estimated to reduce pre-treatment loss to follow up (LTFU) and increase treatment enrollment. However, this doesn't address the problem of defaulters: those patients already enrolled on treatment who are LTFU; and has a relatively small impact on treatment success. TB continues to persist in the country, largely because of patients' noncompliance with medication (Boateng et al, 2010). Studies in New Juabeng Municipality, Tamale Metropolitan Assembly, and Agogo in Ghana identified patients' noncompliance with medication as a challenge, as it contributes to the overall sustained burden of TB in Ghana. Multiple socioeconomic factors influence attrition at this point along the TB care continuum; most

[1] As noted in comments following the Ghana Priorities presentation in Accra, setting 2019 as the first year of scaleup is not practically feasible, as already in Q4 of 2019. For the purposes of modelling, where only 2018 parameter values available (e.g. burden estimates from GTB), and 2019 values not obtainable at the time of modelling, from modelling perspective, 2019 is the first year of scaleup.

studies focus on the medical aspects of the disease rather than looking at it from a socioeconomic viewpoint (Yahaya and Acquah, 2013).

This intervention model aims to capture the impact of patient education and counselling on adherence to DOTS and treatment LTFU, as well as on treatment success, based on a meta-analysis of RCTs which test strategies to improve TB treatment adherence (Muller et al, 2018). This analysis identified that among the most effective approaches to improving adherence were DOTS and patient education & counselling. Ghana's community-based DOTS strategy is well established, and treatment LTFU estimated to be 2.8 percent of all those enrolled on treatment.

Implementation Considerations

In this scenario, we assume that patient education and counselling requires the formation of groups of 6 patients on average, facilitated by a nurse over the course of one hour. Five meetings are held throughout the DOTS treatment regime.. The meta-analysis estimates that overall, patient education and counselling with coverage for all cases enrolled on treatment leads to a 13 percent decrease in LTFU, and additionally a 16 percent increase in cure rate (Muller, A. M). The setting of these trials varied, and none addressed the implementation of patient education and counselling specifically in Ghana. Its impact is assumed to be generalizable to this setting.

Treatment success (the sum of patients registered as cured, and completing treatment i.e. without bacteriological confirmation of cure) is represented as a single parameter in TIME, and we assume here that proportions cured and LTFU contribute to an overall increase in the value from 85 percent in 2018 to 85.4 percent in 2025.

Costs and Benefits

Costs

The costs of this intervention include the initial cost of course development, nurse training, nurse time and patient costs. The initial cost of course development is estimated at GH¢ 500,000 and is one off. Direct cost of nurse training is assumed to be GH¢ 2500 per 20 nurses. Future costs of training assume a 20 percent turnover of nurses per year. The cost per nurse hour is estimated at GH¢ 16 – based on actual nurse salaries under TB program. The cost per patient hour (assumed to be full productive time) is taken as GH¢ 3.5 – based on Ghana Priorities standard assumptions. Patient travel costs of GH¢ 1 per meeting per patient are also included while each meeting is assumed to require GH¢ 50 in basic consumables such as

stationery or handouts. Total costs of the intervention start at GH¢ 1.6m in the first year rising to GH¢ 4.9m by 2040. Meeting consumables and patient time comprise 39% and 33% of total costs respectively.

Benefits

This intervention has relatively smaller impact on TB burden reduction, compared to the previous scenarios modelled, but is still successful in averting TB cases and deaths. We estimate that the provision of patient education and counselling results in the aversion of 2,654 cases and 999 TB deaths in the period 2019-2025. Projecting further out, the intervention is estimated to avoid 31,000 TB cases and 13,200 associated deaths from 2019 to 2040.

BCR Summary Table

Interventions	Cost (GH¢ millions)	Benefit (GH¢ millions)	BCR	Quality of Evidence
Sputum transportation system	80	13,255	166	Strong
Adherence counselling	26	4,839	190	Medium
Active case finding	256	9,654	38	Strong

Notes: All figures assume an 8 percent discount rate, and a time period spanning 2019 to 2040

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1. Introduction

Approximately one-third of the world's population is infected with the TB bacterium, although the majority are latently infected and without the symptoms that typically accompany active TB disease. About 10.4 million TB cases and 1.7 million TB deaths were recorded globally in 2016 (WHO, 2016). Africa is the second highest TB endemic continent in the world. The continent forms about 11 percent of the world's population, but contributes about one-third of the global burden of TB incidence and 34 percent of TB-related deaths. About three million individuals with TB remain undiagnosed and untreated in Africa.

Ghana is classified as one of the countries with the highest double burden of TB and HIV, with a combined TB/HIV mortality rate of 16 per 100,000 population; the equivalent of 4,800 deaths per annum (Global TB Report, 2018). TB is responsible for around 5 percent of total deaths in Ghana annually, and the decline in TB burden is markedly slow, with an average 2.5 percent reduction in TB incidence year on year.

In Ghana, the second national TB survey conducted revealed a national prevalence (a direct measure of TB prevalence of active pulmonary TB disease among adults 15+, extrapolated to all forms and all ages of TB) of active TB disease of 290 per 100,000 population (Bonsu et al, 2014). TB mainly affects the working age population of Ghana, with 73 percent incident cases aged 15-44 in 2018), and as many as 70 percent of individuals with TB disease in a given year do not access TB treatment[2]. For those that are enrolled on treatment, around 15 percent show poor treatment adherence and outcomes, or are lost to follow up, overall resulting in 15,800 TB deaths in 2018 alone (Global TB Report, 2018).

The Government of Ghana in its aim to reduce the impact of TB on the population over the years has made efforts to expand TB diagnostic services in the country through procurement of GeneXpert MTB/RIF for use in some rural health facilities, and refurbishment of laboratories across the country's hospitals. Despite the continuous efforts made by the government and international organizations, in 2017, out of the 14,550 TB case notifications received in Ghana in this year, only 6 percent of the patients were tested with rapid diagnostics at the time of diagnosis. This has since increased to an estimated 60 percent coverage among

[2] Approx. 32 percent Case Notification Rate (CNR). The average CNR across sub-Saharan Africa is 50percent.

notified cases in 2018 (WHO - GTB report, 2017), owing at least in part to the rapid expansion of the sputum transport system.

The 2018 WHO Global TB Program report estimated that 16 percent of cases previously treated for TB are resistant to first line anti-TB drugs, and hence are enrolled on a longer treatment course of second-line anti-TB drugs; a number of which are associated with severe side effects. Second line treatment in Ghana has an overall treatment success rate of only 62 percent (Treatment success rate of MDR/RR-TB is based on cases started on second-line treatment in 2016. Second-line treatment is up to 2 years long, hence in 2018 GTB profile, refers to 2016 treatment cohort).

Moreover, the program currently estimates that only 32 percent of incident TB cases were notified in 2018 and 80 percent of notified cases enrolled on TB treatment. Early diagnosis and treatment of TB have been shown to reduce TB morbidity and mortality, as well as to reduce the catastrophic cost related to TB treatment (Gupta-Wright et al, 2018).

A shortfall in case detection may be due largely to the low sensitivity of screening and diagnostic tools, poor access to TB services by patients, stigma and low health infrastructure coverage of diagnostic and health care services. To address this, the NTP has evolved new approaches to case finding which are currently implemented successfully in 90 out of a total 244 selected districts across the country with plans for scale up. New diagnostic tools are being continually introduced to improve diagnostic capacity beyond routine use of the standard light microscopes for sputum examination.

However, despite of all the endeavors and effort to eradicate the disease, TB continues to persist in the country largely because of modest case detection and patients' noncompliance with medication (Boateng et al, 2010). Studies in New Juabeng Municipality, Tamale Metropolitan Assembly, and Agogo in Ghana identified patients' noncompliance with medication as a challenge. Patients' noncompliance with TB medication is gradually becoming a health burden in the country, but most studies focus on the medical aspects of the disease rather than looking at it from a social viewpoint (Yahaya and Acquah, 2013).

To reduce the burden of TB morbidity and mortality, more patients with TB need to be screened, diagnosed, and treated or prevented from developing TB illness in the first place. Prevention of TB cases is particularly critical in rural and resource-limited settings, where access to point-of-care (POC) testing and diagnosis of patients with tuberculosis is a

challenge. This paper seeks to provide input to the important question of how best to tackle the tuberculosis burden in the country by conducting a cost-benefit analysis of scaling up three prominent interventions to deal with it, namely:

1. Active case finding (ACF) in high risk populations
2. Improved speed and accuracy of diagnosis via expansion of the nascent sputum transportation system that links health facilities to 126 locations with GeneXpert testing equipment
3. Improved adherence through TB patient education and counselling

The epidemiological modelling conducted indicates that ACF, scaled up over a period of 6 years from 2019 to 2025, would have a significant impact on TB burden and mortality reduction, with 5,022 TB cases averted and 2,221 deaths averted during this period, and 33 percent of total prevalent TB cases[3] among high risk groups notified and enrolled on treatment in 2025. Projecting further out, the intervention is estimated to avoid 56,000 TB cases and 26,400 associated deaths from 2019 to 2040.

The model predicts that scale up of the sputum transportation system (and associated improvements in TB diagnostic accuracy and speed) would have a marked impact on TB burden and mortality, with 4,832 TB cases averted and 3,087 TB deaths averted between 2020 and 2025. The equivalent numbers for projections to 2040 are 65,000 TB cases and 36,600 associated deaths. We estimate that the provision of patient education and counselling results in the aversion of 2,654 cases and 999 TB deaths in the period 2019-2025, and 31,000 TB cases and 13,200 associated deaths in the period 2019-2040.

Assessed against the costs and benefits of the interventions, our cost-benefit analyses suggest that patient education & counselling to improve treatment adherence has the highest benefit-cost ratio (BCR) with a value of 278. Improved TB diagnostic accuracy and speed also has a very high BCR at 214, with Active Case Finding yielding a BCR of 42. While education and counselling has the largest BCR its absolute impact is relatively small, naturally capped by the number of patients identified through existing screening mechanisms. Improved diagnostic accuracy also has a very large BCR and the largest absolute impact in terms of deaths avoided. Additionally, the interventions analysed in this paper have some of the largest BCRs across the

[3] Note that this is based on assumed prevalence of 1.5 percent among target populations percent

entire *Ghana Priorities* project, confirming experience from previous Copenhagen Consensus exercises that addressing TB can be one of the most effective uses of money across all of development (Pathy, 2018a; 2018b, Vassall, 2016; Vassall, 2015). All interventions would be worthy of further investment by the government of Ghana and / or international donors.

The following sections of this paper describe the epidemiological model used to estimate impacts of the interventions (Section 2), the valuation approaches used for avoided morbidity and mortality (Section 3), and the results of the cost-benefit analyses (Sections 4-6).

2. Description of Epidemiological Model

The core of TIME Impact is a dynamic compartmental transmission model[4] which also includes latent Mycobacterium tuberculosis infection and disease following recent (re)infection and reactivation (Fig. 1, top left red box). The TIME Impact model provides the user with the flexibility to calibrate to different country settings, and to capture current and historical trends in TB epidemiology at the national level. Once the model is calibrated to the setting of interest it can be used to provide estimates of future trends in TB burden under current operating conditions, and under alternative intervention scenarios, to address critical policy questions. For this purpose, the model has been stratified by HIV and antiretroviral therapy (ART) status of individuals, their multi-drug resistance status, treatment history, as well as age, the latter aimed at capturing the different epidemiological characteristics of pediatric TB (Fig. 1, lower right red box). Point value and ranges for natural history parameters are based on a review of the literature.

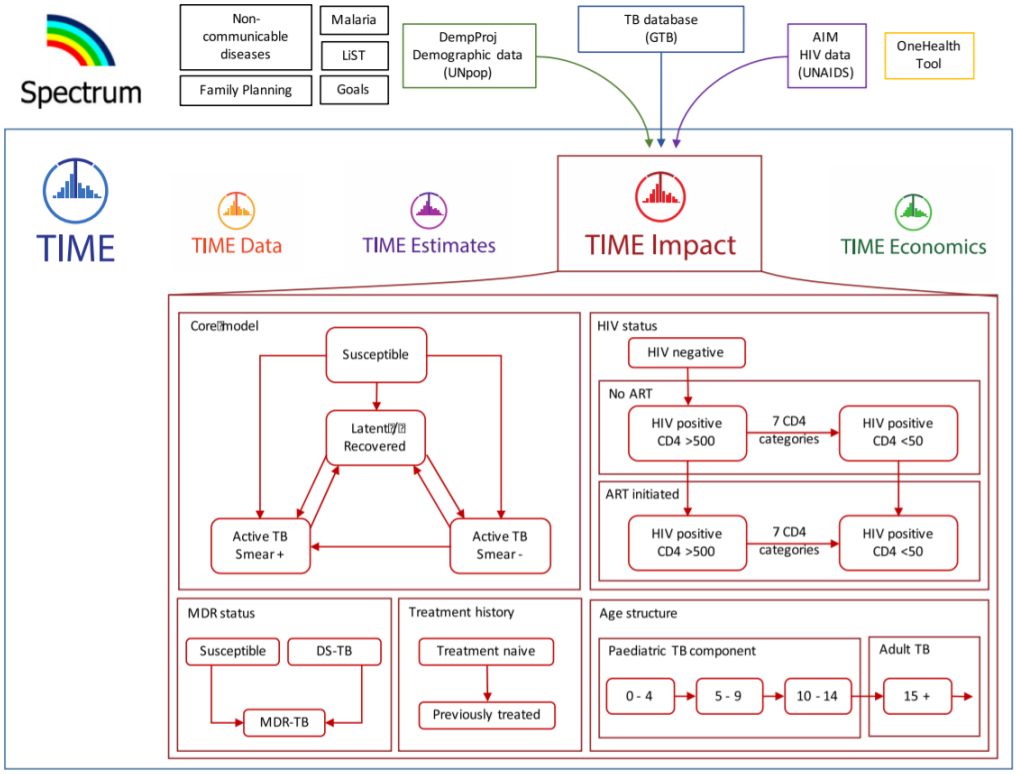
Critical for costing and understanding the value of diagnostic tools, TIME Impact also takes into consideration the population that is screened for TB. The user-implemented screening algorithm thus results in true and false positive diagnoses, which after linking to care, gives rise to true and false positive notifications.

TIME Impact's menu-driven interface improves the accessibility of the model and provides the opportunity to build technical capacity within NTPs, increasing the likelihood of local ownership of modelling results. Through the interface, users can explore the current epidemic

[4] Houben, R. M. G. J., Lalli, M., Sumner, T., Hamilton, M., Pedrazzoli, D., Bonsu, F., ... & Pretorius, C. (2016). TIME Impact–a new user-friendly tuberculosis (TB) model to inform TB policy decisions. *BMC medicine*, *14*(1), 56.

as well as the epidemiological impact of NTP activities either by scaling-up specific TB care and prevention packages or exploring custom activities.

Figure 1: TIME Model



The results window allows users to look at a variety charts and tables that contain model outputs over time, from changes in disease burden (e.g. prevalence, incidence, mortality), to specific TB epidemic dynamics (e.g. proportion latently infected, proportion due to recent transmission, annual risk of infection) and programmatic outputs (e.g. notifications, number screened, positive predictive value of the diagnostic algorithm). Through these outputs, users can see how the modelled epidemic changes over time, and whether current and historical trends are captured with sufficient accuracy to increase confidence of the model's projection of impact of future activities.

2.1 Methods of Epidemiological Modelling

Activities to improve TB care and prevention can be modelled in two ways in TIME Impact, either by making use of the intervention window to incorporate potential NTP activities or by manipulating the care and control parameters to reflect the expected effect and scale-up of existing or alternative NTP activities.

Examples of pre-specified activities include periodic TB screening of people living with HIV (ART naive, or on ART) followed by preventive therapy, or providing HIV testing and ART initiation for diagnosed TB cases; household contact screening, with the provision of isoniazid preventive therapy to under 5-year-olds in contact with an index case.

Alternatively, users can capture the epidemiological impact of interventions by manipulating the care and control parameters in TIME Impact. Such activities include, but are not limited to, different clinic-based screening activities (i.e. expanding the population eligible for TB screening) and the roll-out of new diagnostic algorithms (which would be applied to those being screened).

It is important to emphasize that, for such custom interventions, a comprehensive dialogue between the modelling team and country stakeholders is critical to establish a shared understanding of the proposed activities, their expected effect and the data and assumptions that have been used to calculate this effect.

Modelling of a disease process and a cost-benefit analysis of future interventions incur a lot of uncertainty, in data, natural history and intervention impact. The results presented in this analysis represent indicative central estimates of costs and benefits.

3. Common parameters, methods and assumptions across all cost-benefit analyses

In this section we describe the parameters, methods and assumptions that are the common across all cost benefit analyses conducted in this paper.

3.1 General parameters

All analyses assume a time horizon from 2019 to 2040, with costs and benefits denoted in GH¢ 2018 unless otherwise indicated. Following Ghana Priorities standardized assumptions, we adopt discount rates of 5%, 8% and 14% (Wong and Dubosse, 2019). Population and economic growth projections are drawn from the IIASA database as discussed in Riahi et al. (2017). We use the SSP2 scenario and median estimate by OECD and IIASA as directed by Copenhagen Consensus guidelines.

The output from the TIME model allows us to separately estimate the averted or additional number of patients tested for TB, put on treatment, incident cases, and deaths from TB. The number of patients tested for TB and patients put on treatment are cost drivers in the analysis, while incident cases avoided and deaths from TB are benefits. The next sections describe how monetary values are attached to these parameters.

3.2 Marginal cost of TB diagnosis and treatment

Two of the interventions analyzed in this paper, active case finding and improved diagnosis, increase the number of TB-positive individuals who are identified and receive treatment within the health system. We therefore require an estimate of the marginal health system and patient costs of diagnosing and treating them, relative to the counterfactual of no treatment.

Health system costs of TB diagnosis and treatment are based on a high-level activity flow provided by the National Tuberculosis Control Program (NTCP) in Ghana. It accounts for the major steps in the diagnosis and treatment of patients, including the time taken for each step, the number and level of health workers required and any other necessary inputs such as medicines, consumables and transport. The costs of GeneXpert testing reflect the estimated costs of the nascent sputum transportation system described in Section 5. Salaries for each staff level were also provided by the NTCP to calculate the value of health worker time applied to each step. After initial calculation of health system costs an additional 10% is added to account for overhead / above service-level costs.

Patient costs include the time required to access services as well as direct costs such as out-of-pocket expenses, travel and food. The activity flow provided by NTCP allows for an estimate of patient time for diagnosis (10 min), and is valued at GH¢ 1. For DS-TB treatment we assume a time requirement of 90 hours following Foster et al. (2015). For MDR-TB treatment we assume a time requirement of 165 hours based on the same proportional relationship between months of treatment and patient time required as for DS-TB.[5] These equate to GH¢ 570 and GH¢ 1044 respectively.

For direct costs we draw from a recently conducted, nationally representative TB costing survey by Pedrazzoli et al. (2018). Their analysis reported that the median expenditure for DS-TB patients in Ghana was 2016 US$ 429.6 (154.0–981.2) and for MDR-TB patients was US$

[5] MDR-TB treatment regime in Ghana is around 11 months.

659.0 (93.2–1680.3), despite the fact that TB care is 'free' in Ghana. These values embed a number of costs before and after diagnosis, as well as lost income due to illness.

Given that much of these costs would be incurred regardless of whether the individual is treated for TB – certainly all costs incurred pre-diagnosis as well as income lost – we include only marginal costs that can be reasonably associated with TB treatment: travel to clinics for treatment and, food / supplements outside of the normal diet recommended to support TB treatment.[6] Food and travel comprise 27% of costs for DS-TB patients and 40% of MDR-TB patient costs are incurred after diagnosis as reported in Pedrazzoli et al. (2018). Based on these percentages the direct patient costs for TB treatment are GH¢ 579 and GH¢ 1,260 for DS-TB and MDR-TB respectively.

The cost figures used in the first year of the analysis are summarized below in Table 1. In future years we assume costs rise with projected real GDP per capita growth. Health system costs are larger than patient costs for all categories except DS-TB treatment. The estimated health system costs compare reasonably well to other settings within Africa. We estimate Xpert testing to cost the health system GH¢ 176 or USD 38.59 (in 2018 figures). This compares to an estimated range of USD 17.91 – USD 35.70 (2014 figures) reported in a study examining TB programs in Tanzania, Zambia, Zimbabwe and South Africa (Pooran et al. 2019). Our figure is slightly beyond the upper end of this range. For smear microscopy we estimate a health system cost of GH¢ 12 or USD 2.6 (2018 figures). Pooran et al (2019) note a range of USD 1.90 to USD 2.96 (2014 figures) for the same service.

Table 1 – Marginal health system and patient costs associated with formal TB diagnosis and treatment in the first year

Service	Marginal Health System Costs (GH¢)	Marginal Patient Costs (GH¢)	Total Marginal Costs (GH¢)
Screening and diagnosis (Xpert)	176	1	177
Screening and diagnosis (Smear microscopy)	12	1	13
Treatment (DS-TB)	292	1,148	1,440
Treatment (MDR-TB)	6,211	2,340	8,552

Source: Estimates by the authors'

[6] We do not include after-diagnosis medical costs from Pedrazzoli et al. (2018) since it is likely that TB-positive patients who have yet to be properly diagnosed incur significant medical costs to identify and address their symptoms. The systematic review by Tanimura et al. (2014) notes that in LMICs, 50% of patient costs are incurred before treatment.

3.2 Valuing incident cases avoided

The cost-benefit calculations in this study require valuation of incident cases avoided. Following *Ghana Priorities* standardized assumptions, these are valued using a cost-of-illness approach incorporating the societal costs including health system, direct and indirect household costs. The benefit of an avoided case is simply the cost-of-illness avoided.

For this parameter we use the previously mentioned TB patient cost survey by Pedrazzoli et al (2018). The figures used are 2015 USD 430 for DS-TB which translates to 2018 GH¢ 2143 and 2015 USD 650 for MDR-TB which translates to 2018 GH¢ 3239. These figures account for patient level costs only.

We do not account directly for health system cost savings associated with avoided incident cases. Instead, avoided treatment costs due to lower incidence are factored into the tim series of treatment costs, essentially netted against any increases in treatment costs associated with improved case finding or diagnosis.

3.2 Valuing mortality avoided

Mortality avoided follows *Ghana Priorities* standardized assumptions and is based on guidance provided by Robinson et al. (2019). Each life year lost is valued at 1.2x GDP per capita in the initial year rising to 1.6x GDP per capita in 2030. For child deaths avoided we assume years of life lost avoided of 65.2 and for adults 36.1 as per Ghanaian life tables (WHO, 2019).

4. Active Case Finding

4.1 Description of Intervention

The intervention focuses on active screening for TB with Chest X-ray and testing by GeneXpert in high-risk populations including miners, refugees and their host communities, and in vulnerable urban populations, with an average 1.5% prevalence across target populations totaling 1.5M. Individuals covered by these screening interventions receive a Chest X-ray examination, and those with X-ray results suggestive of TB-related abnormalities are tested for TB disease with highly sensitive and specific GeneXpert testing. Test-positive individuals are

registered as a TB case and linked to a health facility to start TB treatment.[7] In the modelled scenario, the same treatment success rate is applied to all individuals started on TB treatment, whether screened and diagnosed through passive case detection, ICF, or Active Case Finding. The two exceptions are for MDR-TB and HIV-TB cases, where separate treatment success rate values are applied. These model parameters are described in more detail in the technical appendix.

The intervention aims to screen 150,000 individuals in the period 2020-2025, reaching a maximum number of individuals screened among high risk groups of 44,000 in 2025- equivalent to 2.8 percent of total target population (see tables A11, A14 and A15 of the appendix section for detailed account of source data and numbers used to model this intervention).

As ACF is scaled up to 2025, we assume a *proportional* decrease in the coverage of screening via passive detection and ICF mechanisms, such that in 2025, 35 percent of all screening is conducted through the ACF mechanism and 65 percent through passive detection and ICF. However, the absolute numbers of individuals screened by passive detection and ICF increase over the implementation period in the model, to reflect an overall expansion of TB screening. In the baseline model, 708,800 individuals are screened through passive detection and OPD-based ICF in the period 2019-2025. In the ACF scenario model this increases to 860,800 over the same period (see table A18 of the appendix section).

4.2 Epidemiological Impact of Intervention

In the current year we estimate that prevalent TB cases among high risk groups, including PLHIV, accounts for 29 per cent of total TB prevalence in Ghana (see table A14 and corresponding calculation in table A15 of the appendix section) This value is based on the estimated sizes of high-risk groups, an average prevalence of 1.5 per cent among these populations, and the 2014 National Prevalence Survey estimate of 290 TB cases per 100,000 population: the latter equating to around 79,800 prevalent cases nationally. This survey provides the most recent national prevalence estimate available; although in the baseline model,

[7] In the model the same treatment coverage among notified value of 82 percent is applied across passive, intensified and active case finding interventions, in the baseline and subsequent years of this intervention, as it is not possible within TIME's parameter space to differentiate diagnosed TB cases by case finding type/mechanism of identification.

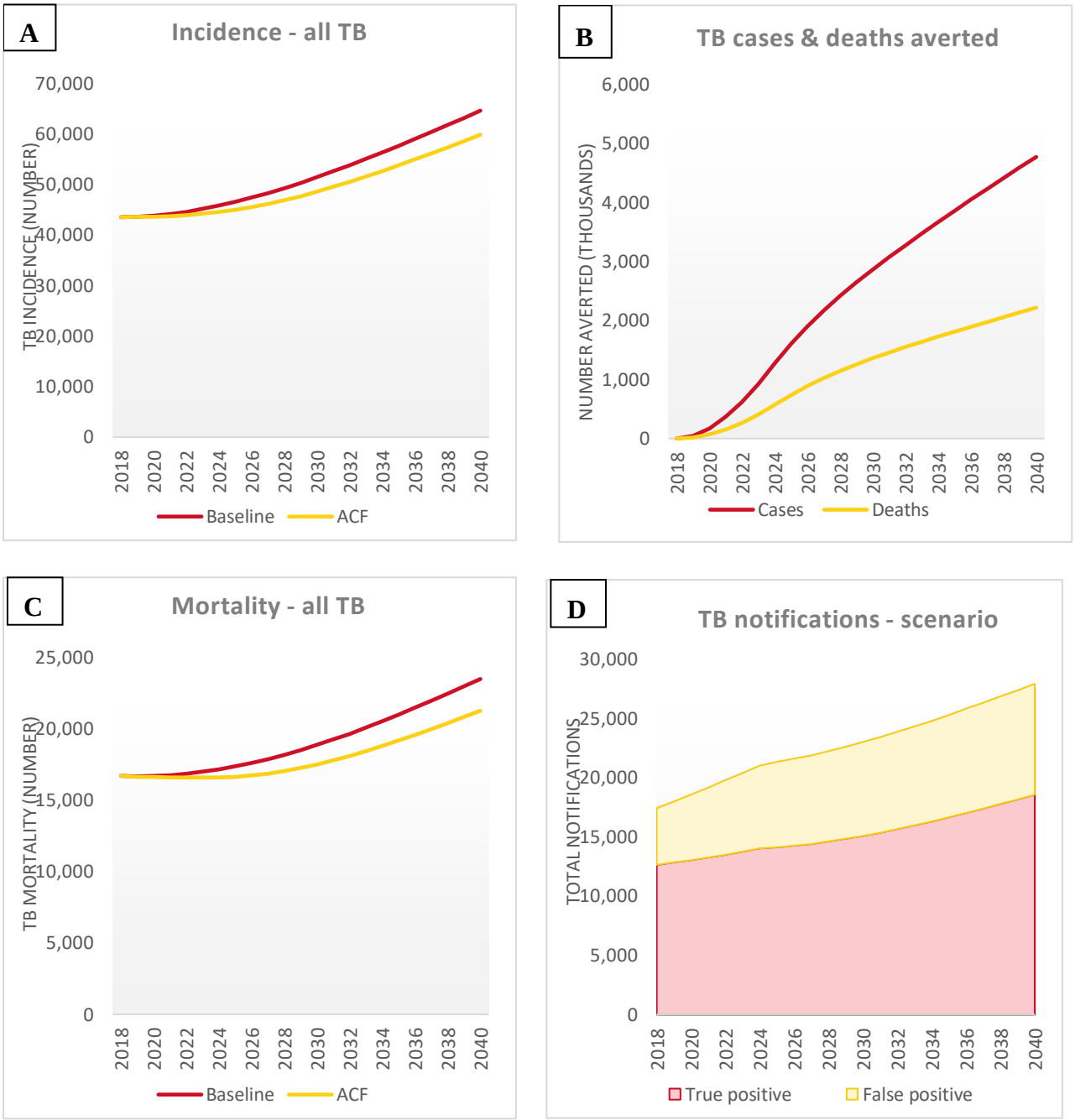
prevalence in 2018 is slightly lower- at 283 cases per 100,00 population. A full account of baseline estimates and adjustments is provided in the appendix section.

This scenario also assumes that screening by ACF takes place continuously during each year of implementation, where screening is scaled up from essentially zero coverage among high risk groups in 2018, to screening 2.8 percent of high-risk populations between 2020 and 2025 (as a proportion of initial starting population).

The modelled scenario does not explicitly capture the overlap of high-risk groups (for example the proportion of refugees and/or miners living in vulnerable urban populations) with one another and with the wider population, and it is assumed here that the bulk of high-risk populations are not accessing TB services passively and through the ICF mechanism at the health centre and OPD. Therefore, the model does not capture the proportion of individuals within these groups who do receive TB screening, diagnosis and TB care through routine mechanisms, and it is possible that the yield of this intervention in terms of additional cases notified, is overestimated.

Figure 2 illustrates the model-estimated epidemiological impact of TB Active Case Finding in terms of TB incidence reduction and TB mortality reduction compared to baseline (panel A), total true and false positive notifications (panel B), and total TB cases and TB deaths averted (panel C). TB cases are averted through a reduction in active disease transmission. By screening, diagnosing and linking more TB cases to treatment, new incident infections and therefore incident TB disease are prevented.

Figure 2: Model estimated Epidemiological Impact of ACF



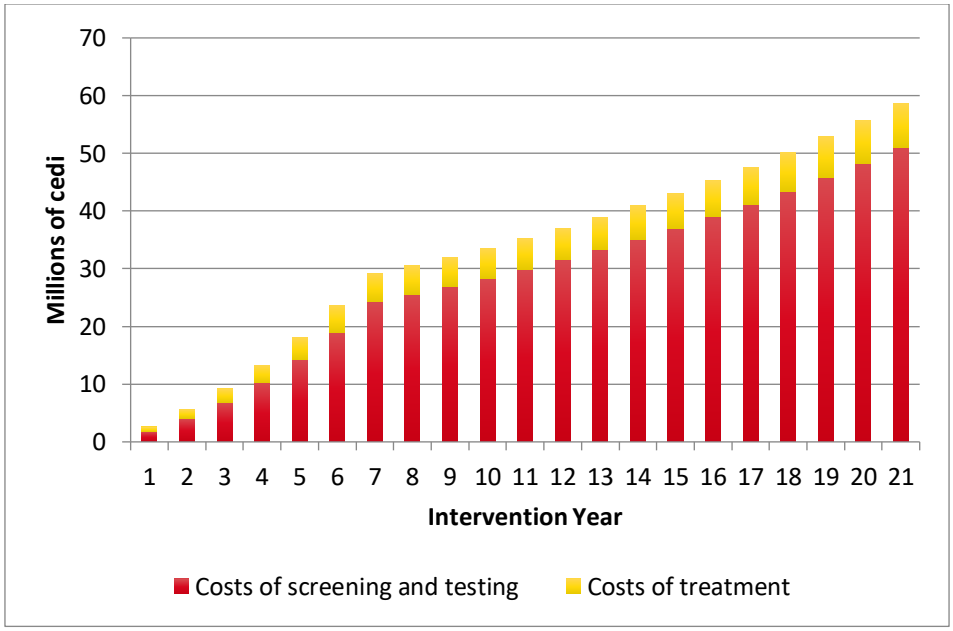
4.3 Calculation of Costs and Benefits

4.3.1 Estimation of Costs

The 2015-2020 National TB Strategic Plan describes an active case finding exercise conducted in 2013, which targeted 317,495 individuals from high-risk groups (miners, refugees, slum dwellers) in the (then) Western Region of the country (Bonsu et al. 2014). This involved a similar approach to what is envisaged in the intervention analyzed in this study – namely door-to-door visits in target communities, followed by testing via GeneXpert for individuals with suspected TB. Budget documents appended to the 2015-2020 National TB Strategic Plan indicate an estimated 2015 USD 80 unit cost per person screened for active case finding for the period of the plan, 2015-2020 (Bonsu et al. 2014). This implies a unit cost value of GH¢ 426 per person screened in 2018 GH¢ after making the necessary inflation and exchange rate adjustments, and adding a small amount of patient opportunity cost, assumed to be 15min per person screened.[8]

The profile of costs over the time horizon over the 21 years of the intervention is presented in the Figure 3. These are based on the epidemiological impacts described in Section 4.2, and the cost assumptions described in Section 3.2. Screening and testing comprise 85% of the intervention costs. The costs of the intervention are GH¢ 256m, discounted at 8%.

Figure 3: Time series of costs for active case finding



Source: Estimates by the authors.

[8] The value of time per patient is only GH¢ 1.

4.3.2 Estimation of Benefits

The modelling results indicate that ACF, scaled up over a period of 6 years from 2020 to 2025, would have a significant impact on TB burden and reduction in TB mortality, with 5,020 TB cases averted and 2,220 deaths averted during this period, and 17.4 per cent of total prevalent TB cases[9] among high risk groups notified and enrolled on treatment in 2025, and a total of 11,670 notifications during the 6 year period of ACF scale-up. Projections out to 2040 indicate that the intervention would avoid 56,000 TB cases and 26,400 associated deaths from 2019 to the end of the time period. Using the valuation approaches documented in Section 3 yields a stream of benefits starting at GH¢ 9m initially, rising quickly to GH¢ 590m by 2025, and then GH¢ 4143m by 2040. Total benefits are equal to GH¢ 9,654 million over the time period, using an 8% discount rate. Mortality avoided comprises 99% of the total benefit.

4.3.3 Summary of Costs and Benefits

The analysis indicates that active case finding yields a central BCR of 38. Costs, benefits and BCRs at all discount rates are reported in Table 2.

Table 2: Summary of costs and benefits from Active Case Finding

Intervention	Discount	Cost (GH¢ millions)	Benefit (GH¢ millions)	BCR
Active Case Finding	5%	375	15,163	40
	8%	256	9,654	38
	14%	132	4,300	33

5. Sputum transportation system to improve accuracy and speed of diagnosis

5.1 Description of Intervention

The NTP of Ghana is in the preliminary stages of rolling out a novel sputum transportation system, which aims to provide virtual on-site access to GeneXpert testing for >90 percent of OPD attendants, linking 1,000 health facilities to 126 existing GeneXpert testing sites. This system was initially piloted in the Greater Accra and Western Regions, with planning underway

[9] Note that this is based on assumed prevalence of 1.5 percent among target populations, increased from original suggestion of 0.8 percent/2.5x national estimate , and also assuming no depletion of prevalent cases in target populations, during ACF campaign.

to provide coverage across most/all regions and districts. This would effectively enable TB suspects who provide sputum samples at facilities without a GeneXpert machine onsite, to receive molecular testing for TB without needing to travel to provincial or other more centralized facilities.

The rationale behind this intervention is improving accuracy and speed- or turnaround time- of TB diagnosis, transitioning from sputum smear microscopy to GeneXpert, as a primary diagnostic test. In this intervention scenario, we modelled an increase in GeneXpert test coverage at the national level to 90 percent by 2025, to reflect the expansion of sputum transportation and utilization of GeneXpert machines at sites distal from the location of sputum sample collection. This target is in line with the upcoming Global Fund Funding Request (GFFR) reprogramming plan as per correspondence with the National Tuberculosis Control Program.

An RCT which assessed the accuracy and clinical outcomes of point of care GeneXpert for TB testing (Theron et al, 2014) estimated that relative to diagnosis by smear microscopy, individuals diagnosed by GeneXpert had an overall 8 percent lower rate of pre-treatment LTFU than individuals receiving a smear microscopic test for TB. This is due at least in part to faster turnaround time from conducting the test to receiving results, and because a higher proportion of sputum smear negative, but Bac/culture positive cases are detected with GeneXpert.This is captured in the model as a 3.5 percent increase in treatment enrollment rate, to reflect an overall 70 percent increase in the coverage of diagnostic pathways using GeneXpert as a primary diagnostic test, in 2025 compared to 2017[10].\

5.2 Epidemiological Impact of Intervention

We estimate that the coverage of screening through passive case detection and ICF in 2018 were 65 percent and 34 percent of total screening at the national level, respectively. In this year, according to NTP-reported data on systematic screening at clinic outpatient departments (OPDs), 7,793 of the estimated 14,289 TB notifications (55 percent) were screened and diagnosed through the ICF mechanism. The coverage of clinical diagnosis among test-negative TB suspects is estimated to be generally higher for passive case detection than for TB suspects

[10] Coverage of GeneXpert in 2017 = 20 percent; target coverage in 2025 = 90 percent, i.e. 70 percent increase. Therefore (5 percent / 100) x 70 = 3.5 percent. Note the start year of intervention is 2017, as data only available up to this year for coverage of molecular testing in Ghana (from GTB report) at time of modelling.

screened through ICF (Ohene, 2018) – see table A16 in the appendix section which summarises coverages of diagnostic pathways for presumptive TB cases in 2018

We assume here that access to GeneXpert testing is scaled up in equal proportions among TB suspects identified through passive case detection, and through ICF. In the model in 2025, the program achieves 90 percent coverage of GeneXpert among OPD attendees that are systematically screened for TB *and* identified as having TB symptoms, and for 90 percent of individuals who self-present at the health centre with symptoms suggestive of TB; with 50 percent coverage of Chest X-ray among suspects with a negative GeneXpert test result. The remaining 10 percent of screen-positive TB suspects receive a smear microscopy test. Rollout of molecular testing sees a corresponding increase in diagnostic sensitivity from 18 percent in 2018 to 35 percent in 2025, based on the model's diagnostic algorithm calculator. This intervention has only a marginal impact on diagnostic specificity (see table A2 of the appendix section)

Finally, we assume that the increase in GeneXpert coverage results in a corresponding increase in rifampicin testing coverage (termed molecular DST), as GeneXpert has the dual functionality of detecting MTB, and rifampicin resistance mutations. As such, DST coverage among new TB cases is increased from the 2018 GTB estimated value of 93 percent, to 99 percent in 2025, to reflect near-universal coverage of DST among new and retreatment cases.

The plots in Figure 4 illustrate the total number of incident cases and TB deaths year on year in the baseline (solid red line) and intervention scenario (solid yellow line). Note that when expressed as rates per 100,000 (not illustrated here), over the timespan of the model projection, incidence and mortality both level off 2019 onwards in the baseline and decrease in the intervention scenario.

Figure 4: Epidemiological Impact of improved accuracy & speedy diagnosis

The reductions in TB incidence and mortality in this scenario (compared to baseline) are in part due to a reduction in the proportion of total notifications arising from false-positive TB diagnosis i.e. individuals diagnosed with TB despite being TB disease free. Figure 5 below illustrates an increase in total notifications year on year in the GeneXpert scaleup intervention compared to baseline (left hand plot – a total of 10,220 additional notifications estimated from 2019-2025), and the contribution of *true* positive notifications to total notifications, expressed as a percentage of total- termed the true positive rate (right hand plot). The true positive rate in the intervention is higher than baseline in all years of scaleup, increasing linearly to a maximum of 73 percent in 2025, corresponding with maximum coverage of GeneXpert. Beyond this year,

the number of notifications continues to increase in accordance with projected population grown (i.e. with a relatively constant notification *rate* year on year from 2025 onwards). Figure 6 illustrates the additional decrease in prevalence (in absolute numbers) resulting from the expansion of GeneXpert testing

Figure 5: programmatic impact of improved accuracy & speed of diagnosis

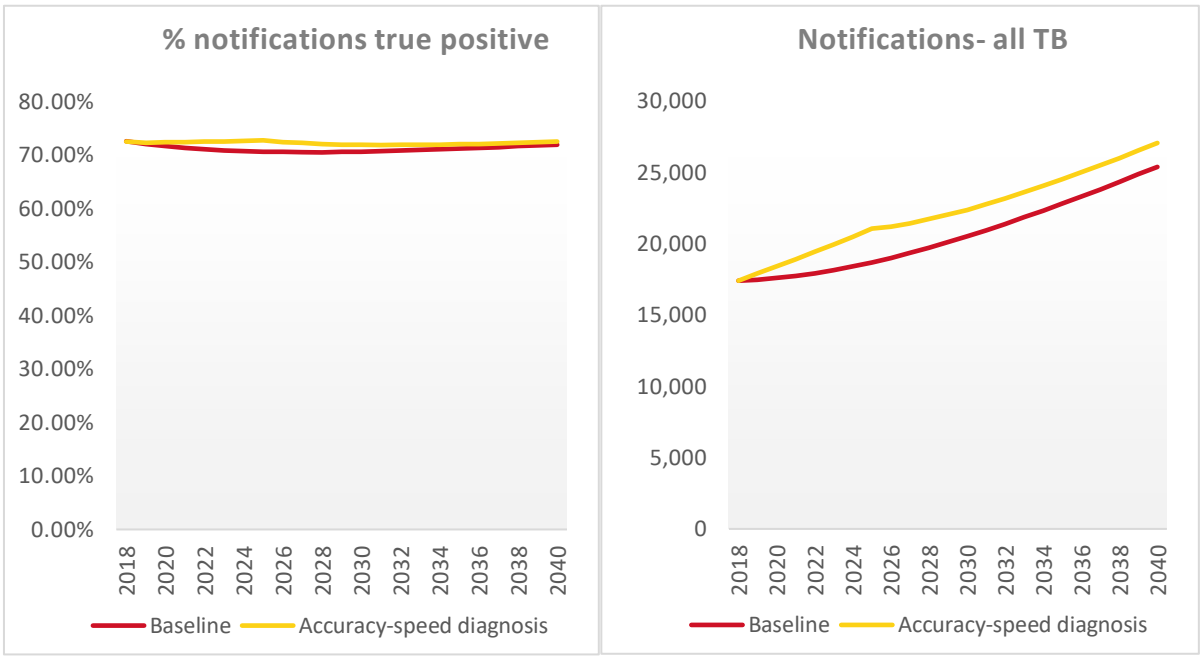
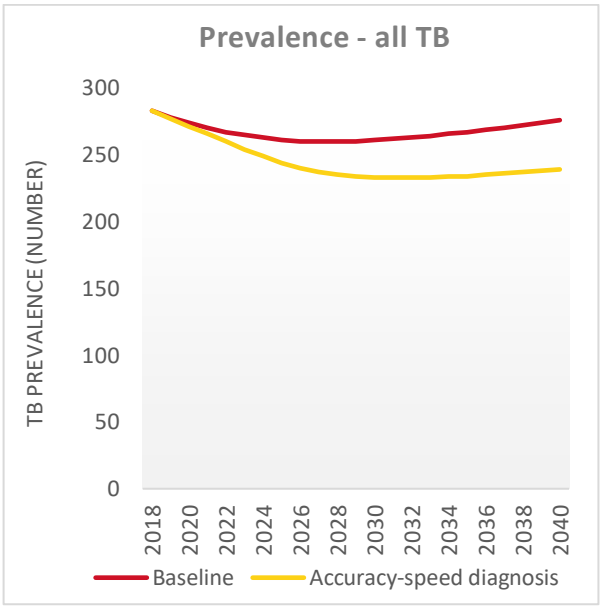


Figure 6: impact of TB prevalence on true positive notification rate



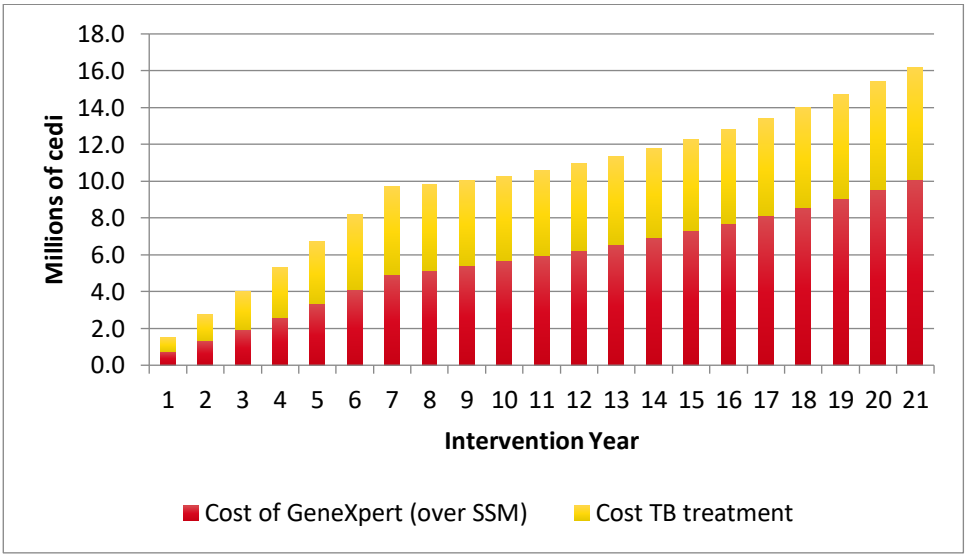
*Prevalence also weighs in on the true positive rate: as prevalence decreases, the positive predictive value of diagnosis decreases.

5.3 Calculation of Costs and Benefits

5.3.1 Estimation of Costs

As discussed in Section 5.1, the intervention increases the use of GeneXpert for testing gradually replacing smear microscopy as the major diagnostic tool. Initially, this implies 4,200 extra GeneXpert tests performed in the first year, rising to a steady state of around 23,000 in year 7 that increases with population growth. The cost profile over 21 years of the intervention is presented in the Figure 7. These are based on the description of the intervention and epidemiological impacts described in Section 5.1 and 5.2 respectively, and the cost assumptions described in Section 3.2. The costs of the intervention are GH¢ 80m, discounted at 8%. Additional costs associated with diagnosis represent 57% of the cost. Note that costs of diagnosis represent the marginal costs of replacing GeneXpert with smear microscopy.

Figure 7: Time series of costs for improved diagnosis



5.3.2 Estimation of Benefits

The model predicts that scale-up of GeneXpert over a period of 6 years from 2019 to 2025, would have a marked impact on TB burden and mortality, with 4,832 TB cases averted and 3,087 TB deaths averted during the period 2019-2025. Projecting further out, the intervention is estimated to avoid 65,000 TB cases and 36,600 associated deaths from 2019 to 2040. Using the valuation approaches documented in Section 3 yields a stream of benefits starting at GH¢ 13m initially, rising quickly to GH¢ 797m by 2025, and then GH¢ 5612m by 2040. Total

benefits are equal to GH¢ 13,225 million over the time period, using an 8% discount rate. Mortality avoided comprises almost all of the total benefit.

5.3.3 Summary of Costs and Benefits

The analysis indicates that sputum transportation system yields a central BCR of 166. Costs, benefits and BCRs at all discount rates are reported in Table 3.

Table 3: Summary of costs and benefits from Sputum transportation system

Interventions	Discount	Cost (GH¢ millions)	Benefit (GH¢ millions)	BCR
Sputum transportation system to improve accuracy and speed of diagnosis	5 %	115	20,805	181
	8 %	80	13,255	166
	14 %	43	5,909	138

6. Patient education and counselling to improve TB treatment adherence

6.1 Description of Intervention

Molecular testing to improve TB diagnostic accuracy and turnaround is estimated to reduce pre-treatment loss to follow up (LTFU) and increase treatment enrollment. However, this doesn't address fully the problem of defaulters: those patients successfully enrolled on treatment who are LTFU. This intervention model aims to capture the impact of patient education and counselling on adherence to DOTS and treatment LTFU, as well as on treatment success, based on a meta-analysis of RCTs which test strategies to improve TB treatment adherence. The analysis referred to studies comparing patient education/counselling with no education/ counselling which showed that patient education/counselling led to better cure rates (RR 1.16, 95% CI 1.05–1.29, P = 0.004) (Muller et al, 2018).

This analysis identified that among the most effective approaches to improving adherence were DOTS and patient education and counselling. Ghana's community-based DOTS strategy is well established, and treatment LTFU estimated to be 2.8 percent of all those enrolled on treatment (GTB 2018).

In this scenario, we assume that patient education and counselling consists of 6 patients per group on average, 5 meetings during DOTS treatment, each meeting conducted for 1 hour with 1 nurse facilitating each meeting based on a study by Alvarez et al, 2003. The beneficiary population are individuals on TB treatment: 17,409 in 2018, increasing to 24,255 in 2040. The meta-analysis estimates that overall, patient education and counselling with coverage for all cased enrolled on treatment leads to a 13 percent decrease in LTFU, and additionally a 16 percent increase in cure rate. The setting of these trials varied, and none addressed the implementation of patient education and counselling specifically in Ghana, however the reported impact is assumed to be generalizable to this setting.

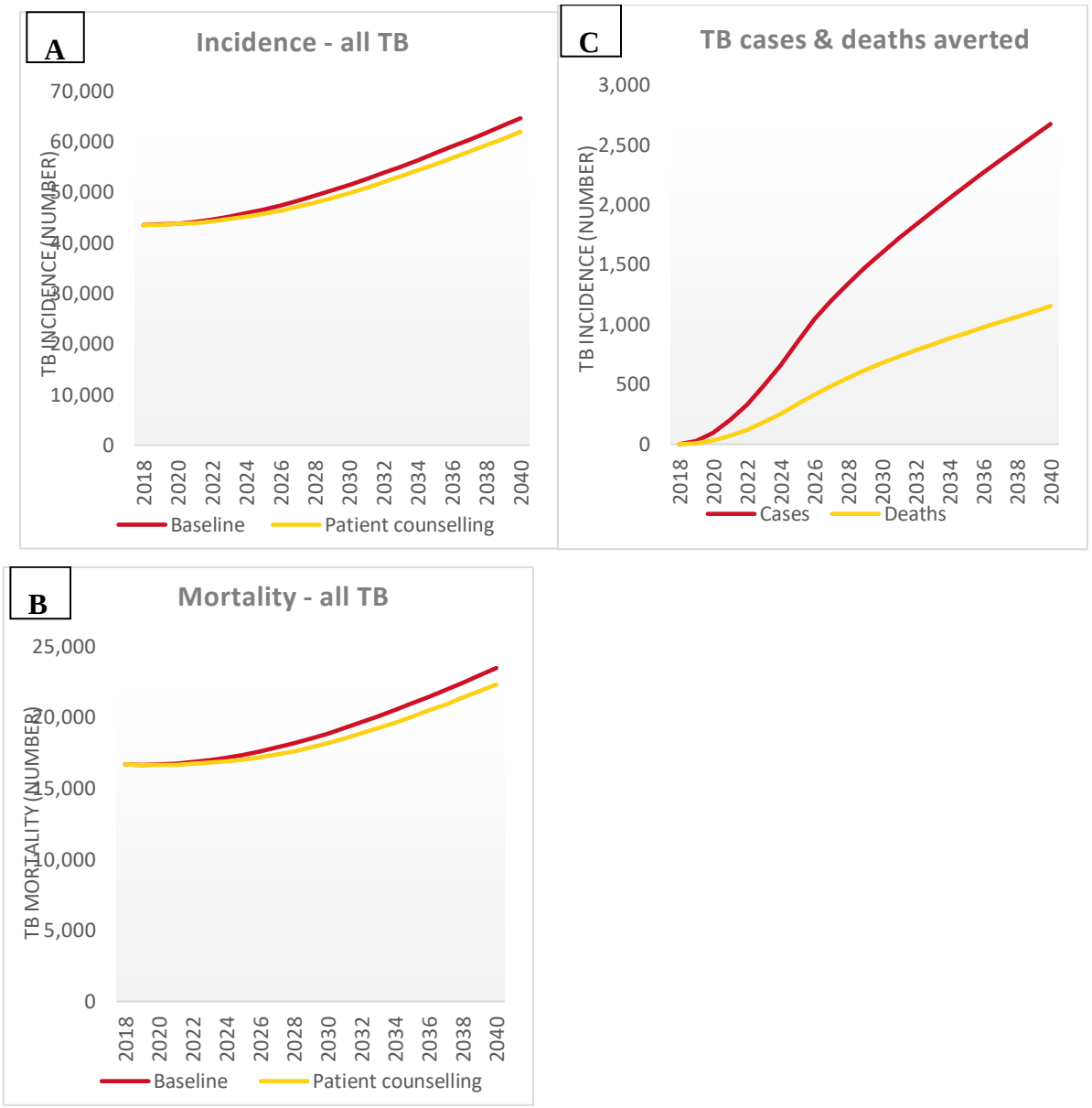
Through patient education and counselling, an increase in the proportion of TB cases cured/successfully treated leads to a reduction in TB transmission, because cases are infectious for less time than if they were to default treatment (assuming before smear conversion), and/or to relapse.

6.2 Epidemiological impact of the intervention

Treatment success (a sum of patients with reported cure, and those completing treatment without bacteriological confirmation of cure) is represented as a single parameter in TIME, and we assume here that the proportions cured and LTFU contribute to an overall increase in the value from 85 percent in 2018, to 85.4 percent in 2025 (refer to first 2 rows in table A13 of the appendix section for model values of treatment success in each year to 2025).

This intervention has a relatively smaller impact on TB burden reduction, compared to the previous scenarios modelled, but is still successful in averting TB cases and deaths, as illustrated in the right-hand plot in the Figure 8. We estimate that the provision of patient education and counselling results in the aversion of 2,654 cases and 999 TB deaths in period 2019-2025 (see table A13 for a breakdown of benefits by year in the intervention model). There is a reduction in the number of individuals initiating TB treatment year on year in this scenario compared to baseline, with the indirect effect of transmission prevention amplified over time i.e. widening the gap in number of treatment initiations, in the modelled scenario vs baseline. The fewer individuals initiating treatment year on year in intervention compared to baseline, could be attributed due to reduction in TB burden, hence fewer cases screened, detected and started on treatment. This links back to the principle of averting infections through reducing the time TB cases are infectious and able to transmit. This indirect effect of preventing transmission is amplified over time, explaining why the gap is widening.

Figure 8: Epidemiological Impact of Adherence Counselling



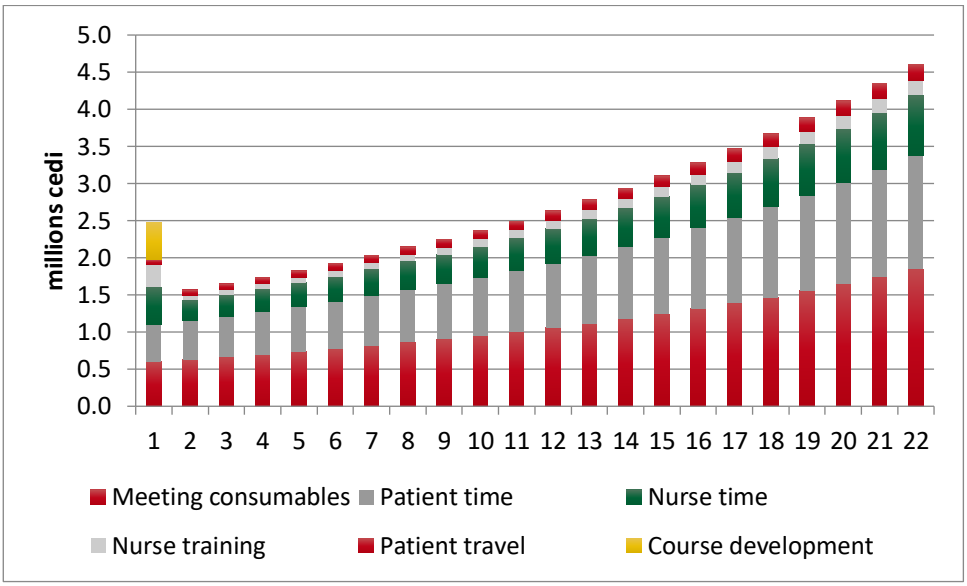
6.3 Calculation of Costs and Benefits

6.2.1 Costs

Based on the description of the intervention in Section 6.1, the intervention requires the formation of 2,937 patient groups, rising to 3,551 by the end of the time period. Initially 31,160 nurse hours are required but around half of this is for initial training (assumed to be 8 hours per nurse). After the first year, the intervention requires 16,180 hours of nurse time rising to 23,900 hours by the end of the period. Patient time required is 143,800 in the first year rising to 213,000 by 2040.

The costs of this intervention include the initial cost of course development, nurse training, nurse time and patient costs. The initial cost of course development is estimated at GH¢ 500,000 and is one off. Direct cost of nurse training is assumed to be GH¢ 2500 per 20 nurses. Future costs of training assume a 20 percent turnover of nurses per year. The cost per nurse hour is estimated at GH¢ 16 – based on actual nurse salaries under TB program. The cost per patient hour (assumed to be full productive time) is taken as GH¢ 3.5 – based on Ghana Priorities standard assumptions. Patient travel costs of GH¢ 1 per meeting are also included based on information provided in Pedrazzoli et al (2018). Each meeting is assumed to require GH¢ 50 in basic consumables such as stationery or handouts. The profile of costs over the time period is presented in Figure 9. Total costs of the intervention are GH¢ 26 million over the period, using an 8% discount rate. Meeting consumables and patient time comprise 39% and 33% of total costs respectively.

Figure 9: Time series of costs of patient counselling



6.3.2 Benefits

Applying the valuation approaches documented in Section 3 to the epidemiological impacts from Section 6.2 a yields a stream of benefits starting at GH¢ 5m initially, rising to GH¢ 267m by 2025, and then GH¢ 2159m by 2040. Total benefits are equal to GH¢ 4,839 million over the time period, using an 8% discount rate. Mortality avoided comprises almost all of the total benefit.

6.3.3 Summary of Costs and Benefit

Table 3 summarizes the costs and benefits of the intervention. The analysis indicates large benefit-cost ratios under all discount rate scenarios, with a central estimate of 190.

Table 3: Summary of costs, benefits and BCRs from adherence counselling

Interventions	Discount	Cost (GH¢ millions)	Benefit (GH¢ millions)	BCR
Adherence counselling	5 %	35	7641	218
	8 %	26	4839	190
	14 %	15	2130	139

7. Conclusion

It is apparent from the benefit-cost ratios obtained from our analysis that the most cost-effective intervention for reducing the burden of tuberculosis in Ghana is improving adherence through patient education and counselling (BCR=190) followed by improving the accuracy and speed of TB diagnosis via the implementation of a sputum transportation system (BCR=166). Active case finding was found to be least cost effective in comparison with the above interventions. However, the central BCR estimate of 38 is still very high relative to other interventions in the *Ghana Priorities* series (the median BCR across all analysed interventions is 3). Implementation of the sputum transportation system to improve accuracy and speed of diagnoses has by far the largest net benefits, followed by active case finding. There is a strong case for scale up of all interventions documented in this paper.

The large BCR of the sputum transportation system is partially attributable to the fact that Ghana already has enough operational GeneXpert machines and does not need to spend on additional procurement. The intervention focuses on shifting diagnosis from an inefficient sputum microscopy mechanism to a far more efficient GeneXpert based diagnosis. The economic logic of this intervention is that GeneXpert molecular testing is a rapid diagnostic tool which is able to detect smear negative, culture (Bac) positive TB cases with a high degree of accuracy; that is cases that would not be detected my smear microscopy. GeneXpert testing can be implemented cheaply because it is applied to TB suspects already engaging with the health system (there are no other costs to society besides switching from smear microscopy to GeneXpert tests, and any additional treatment costs arising from an increase in case detection rate overall). This therefore leads to a high BCR value. It also reduces time from infection to

diagnosis, when incorporated in to a functioning sputum referral system, and therefore lowers the risk of dying from untreated TB, assuming reasonable linkages between diagnosis and successful treatment.

Improving adherence through patient education and counselling also has a very high BCR though the absolute benefits are capped as the intervention cannot be expanded beyond all patients on TB treatment. Policy makers would do well therefore to look at the potential impact of combined interventions/intervention packages e.g. scale-up systematic screening and linking presumptive TB cases to improved diagnosis and adherence support once enrolled on treatment.

Though the benefits accrued from Active Case Finding are large overall the intervention requires a comparatively larger contribution of the health system- both in terms of the expansion of existing health infrastructure, and recruitment and training of health personnel, needed to achieve the scale of screening required to identify missing TB cases. In the other two modelled scenarios, the intervention is applied to patients who are already engaging with the health system which provides them with a natural cost advantage. Further to this, Ghana has a relatively low prevalence of TB, and so Active Case Finding necessarily also has a lower initial yield and therefore lower direct benefits as well as lower transmission effects.

There are some important limitations to our analysis, which should be noted when interpreting the results of this paper. For active case finding there is limited empirical data on the size and TB prevalence of target populations, and so strong reliance on in-country expert opinion to provide these estimates: these estimates are outlined in the technical appendix, tables A14 and A15. The overall size of ACF target populations is assumed not to change over time, and as overall national-level TB prevalence decreases i.e. as case finding is implemented, TB prevalence in target populations is assumed to decrease proportionally in this analysis. As outlined in the main text of this report and detailed in the technical appendix, table A15, it is assumed that in 2018, 29% of total prevalent cases are among target populations with this proportion unchanging; that is, with no differential decrease in TB burden in target populations vs. the general population during implementation of ACF. The impact of notifying more cases among high risk target populations in terms of TB prevalence reduction is not well documented in the context of TB screening in Ghana.

Additional uncertainties arise with respect to effects of interventions, costs of drugs and benefit transfer approach used to monetize health impacts. Intervention effect sizes were drawn from

meta-analyses and randomized control trials. Nevertheless they may not fully account for real world, government-led implementation challenges, especially when the studies relied upon are small-scale academic-led exercises (Muralidharan and Neihaus, 2017). Substantial implementation failures will reduce the reported BCRs. Additionally, changes in drug costs over time are difficult to forecast, as they are a function of wider market dynamics, and in some settings may even decrease. The assumption here is that drug unit costs will increase with real GDP per capita growth rate. Lastly, the benefit transfer approach adopted to monetize mortality avoided benefits uses average GDP per capita levels in Ghana to estimate the value applied to mortality risk reductions. This may substantially overestimate benefits since TB is a disease which predominantly affects the poor. However, as is customary with cost-benefit analyses, mortality risk reductions are assumed to be equal within a given a population (in this case all of Ghana) and independent of income to ensure adherence to the 'all lives are equal' maxim.

BCR Summary Table

Interventions	Discount	Cost (GH¢ millions)	Benefit (GH¢ millions)	BCR	Quality of Evidence
Sputum transportation system to improve accuracy and speed of diagnosis	5 %	115	20,805	181	Strong
	8 %	80	13,255	166	
	14 %	43	5,909	138	
Active case finding	5%	375	15,163	40	Strong
	8%	256	9,654	38	
	14%	132	4,300	33	
Adherence counselling	5 %	35	7641	218	Medium
	8 %	26	4839	190	
	14 %	15	2130	139	

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Technical Appendix – TIME modelling specifications

Overview

This appendix provides a breakdown of methods used to i) develop the baseline calibration for TB burden estimation; and ii) intervention scenarios for the Ghana Priorities Benefit Cost Analysis. Whilst the authors have tried to include as much detail possible on the modelling process, reference should be made to the TIME technical appendix[1] wherever any concepts require further explanation. The TIME technical appendix describes the structure of the dynamic TB transmission model which all projections of TB burden in this report are based on and includes definitions for the parameters described in Tables A2 and A4, as well as a schematic showing where these parameters are positioned in the transmission model.

Key definitions

TIME baseline model

- Model input: user-specified parameter values in the TIME model which define how the program functions along the TB care cascade. Parameters include linkage to care for DS-TB and DR-TB, treatment success for HIV- and HIV+, DST coverage for new and retreatment cases, etc.
- Calibration target: the value of an indicator e.g. no. of notifications each year of the program, which the model projection is aiming to 'hit' during the calibration process.
- Model output: the model-projected value of an indicator for a given year. This is the result of fitting to calibration targets and is often adjusted multiple times before the model value falls within the uncertainty bounds of the target.

Ghana Priorities intervention scenarios

- Model target: the value of an indicator which the program is aiming to reach, e.g. 85% treatment coverage in 2024.
- Model output: program intervention coverages, e.g. coverage of rapid diagnostic testing by GeneXpert; the % DR-TB cases starting a second-line treatment regimen, etc.
- Model outcome: Performance indicators e.g. treatment success for DS-TB and DR-TB patients.

TIME modelling timeline

1) **August - October 2019**: calibrating the baseline model to Ghana's epidemiological and program indicators (incidence, prevalence, notifications and mortality; treatment

success DS-TB and DR-TB etc) to produce a model which describes recent (up to Q4 of 2018) and historic trends in TB epidemiology, and provides projections of these indicators under business as usual (BAU) conditions i.e. assuming the program continues to operates as it does currently;

2) **October 2019 – January 2020**: using the baseline model to carry out modelling of 3 main intervention areas used to inform the Ghana Priorities Benefit-Cost Analysis (see below for a summary of the intervention areas)

Parameterising the baseline TIME model

Table A1 below summarises the parameters in TIME baseline model (0) and in the intervention scenarios (1-3) which define the program's efficiency along the TB care cascade, from screening and diagnosis to notification and linkage to care (enrolment on DOTS) as well as treatment success for DS-TB and DR-TB. The values of these parameters are scaled up according to the specifications of each of the intervention scenarios. Diagnostic coverages directly impact on model-projected notification trends, as well as indirectly on other indicators including incidence.

Table A1: description of baseline and intervention scenario models developed in TIME

Model identifier	Description
Baseline (0)	Baseline calibration finalised in October 2019, fitted to TB burden estimates and program performance indicators (e.g. treatment success value) up until 2018 (where data available) – see model inputs on pages 8 & 9.
Active Case Finding (1)	ACF and systematic screening scaleup model, screening an additional 639,820 TB suspects in the period 2019-2025
Molecular testing to improve accuracy and speed of TB diagnosis (2)	Transitioning from smear microscopy to GeneXpert as a primary diagnostic test, achieving coverage of GeneXpert of 90% of total presumptive, TB screen-positive individuals accessing TB diagnostic facilities, by 2025.
TB patient education and counselling to improve TB treatment adherence (3)	Modelling increase in treatment success resulting from a reduction in on-treatment loss to follow up (LTFU) and an increase in treatment completion/success

*Program indicators scaled up according to intervention specifications (see **Table A8**)

Table 2. TIME model care cascade parameters and the values inputted in the baseline model (0) and intervention scenario models (1-3)

TIME model parameter	Baseline (0)	ACF (1)		Accuracy/speed diagnosis (2)		Patient education/counselling (3)	
	2018	2025	2030	2025	2030	2025	2030
Input (user-defined) unless otherwise stated							
Screening parameters (used to model past and future case finding)							
New, smear positive screening rate (HIV-)*	108.0	**118.0**	**118.0**	108.0	108.0	108.0	108.0
New, smear positive screening rate (HIV+)*	270.0	**280.0**	**280.0**	270.0	270.0	270.0	270.0
Relative screening rate* smear negative	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Relative screening rate* previously treated	1	**1**	**1**	1	1	1	1
Relative screening rate* disease-free population	0.003	**0.005**	**0.005**	0.003	0.003	0.003	0.003
Proportion notifications false positive (output)+	0.27	0.34	0.34	0.27	0.26	0.27	
Drug sensitive linkage to care	0.82	0.82	0.82	**0.86**	**0.86**	0.82	0.82
Drug sensitive treatment success (HIV-)	0.85	0.85	0.85	0.85	0.85	**0.90**	**0.90**
Drug sensitive treatment success (HIV+)	0.77	0.77	0.77	0.77	0.77	**0.82**	**0.82**
MDR case detection: new cases (output)+	0.35	0.35	0.35	0.35	0.35	0.35	0.35
MDR case detection: previously treated cases (output)+	0.99	0.99	0.99	0.99	0.99	0.99	0.99
MDR linkage to care	0.40	0.40	0.40	0.40	0.40	0.40	0.40
MDR treatment success (HIV-)	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Diagnostic** and preventative interventions							
Coverage of PCF1: prolonged cough -> smear microscopy -> CD with CXR	0.09	0.07	0.07	0.07	0.07	0.09	0.09
Coverage of PCF2: prolonged cough -> smear microscopy -> CD (no CXR)	0.37	0.29	0.29	**0.00**	**0.00**	0.37	0.37
Coverage of PCF3: prolonged cough -> GeneXpert -> CD with CXR	0.02	0.02	0.02	**0.29**	**0.29**	0.02	0.02
Coverage of PCF4: prolonged cough -> GeneXpert -> CD (no CXR)	0.18	0.14	0.14	**0.29**	**0.29**	0.18	0.18
Coverage of ICF1: any TB symptom -> smear microscopy -> CD with CXR	0.12	0.10	0.10	**0.03**	**0.03**	0.12	0.12
Coverage of ICF2: any TB symptom -> smear microscopy -> CD (no CXR)	0.12	0.10	0.10	**0.00**	**0.00**	0.12	0.12
Coverage of ICF3: any TB symptom -> GeneXpert -> CD with CXR	0.05	0.04	0.04	**0.31**	**0.31**	0.05	0.05
Coverage of ICF4: any TB symptom -> GeneXpert -> CD (no CXR)	0.05	0.04	0.04	**0.00**	**0.00**	0.05	0.05
Coverage of ACF1: any TB symptom -> CXR -> GeneXpert -> diagnose	0	0.20	0.20	**0**	**0**	0	0
Smear positive net sensitivity (output: dependent on diagnostic coverages)	0.60	0.59	0.59	**0.60**	**0.60**	0.60	0.60
Smear negative net sensitivity (output: dependent on diagnostic coverages)	0.18	0.24	0.24	**0.35**	**0.35**	0.18	0.18
Net specificity (output: dependent on diagnostic coverages)	0.94	0.95	0.95	**0.96**	**0.96**	0.94	0.94

* The screening rate parameter in the TIME model reflects how quickly or often an individual with active TB disease will present for TB screening. As it increases, screening and therefore diagnosis of TB will be more rapid, leading to an increase in case finding. The screening rate can be different for those with less serious TB disease (smear negative), and previously treated individuals. The screening rate of disease- free individuals is necessary to estimate how many people without TB present for TB screening, so that the diagnostic algorithm can be applied to estimate, for example, the proportion true and false positive TB diagnoses. All screening rates are relative to the rate for individuals with new, smear positive disease.

** Diagnostic pathways and coverages are specified by the user in TIME Impact's Diagnostic Algorithm Tool

+ All outputs are non-user defined values except for diagnostic sensitivity and specificity values for individual tests, which can be adjusted within literature-informed ranges.

Table A3: linking TIME model parameter changes to programmatic activities.

Program performance indicator (model parameter[2])	Detail	Example of programmatic strategies to improve indicator*
New, smear positive screening rate	Rate of screening for active TB	Increase lab capacity e.g. build more labs, expand existing lab facilities to accommodate more samples, improving specimen transport, faster test turn-around etc.
Relative screening rate smear negative	Rate, relative to new smear positive	Conduct community-based case finding to preferentially screen more smear negative cases (more likely to encounter smear negative in the community, and similarly encounter more smear positive active TB at the clinic, because individuals are generally sicker)
Relative screening rate previously treated	Rate, relative to previously treated	Closer monitoring of retreatment cases following end of treatment or after loss to follow up/relapse
Relative screening rate, disease-free population	Percentage of smear positive screening rate [generally a constant over time]	Screening in more targeted ways, as outlined in the example below for decreasing the proportion of false positive notifications.
Smear positive net sensitivity	Number	Investing in and rolling out more sensitive and specific diagnostic tools, e.g. phasing out smear microscopy and clinical diagnosis, and expanding GeneXpert coverage, as a strategy for increasing the Positive Predictive Value (PPV)** of diagnosis and improving overall diagnostic efficiency.
Smear negative net sensitivity	Number	
Net specificity	Net value	
Proportion false positive	Proportion of total notifications which are false positive	Increasing the prevalence in the screening population and hence the PPV of diagnosis, by screening in more targeted ways e.g. transitioning from passive case finding at the clinic, to Active Case Finding (ACF) in specific groups known to have a higher prevalence of TB.
Drug sensitive linkage to care	Proportion diagnosed DS-TB that are enrolled on treatment	Improving service delivery for DR case detection and management.
Drug sensitive treatment success	Proportion linked to care that complete treatment	Improve adherence to DOTS and ensure availability of first-line drugs to treat DS-TB. Reduce time from diagnosis to enrollment on treatment.
MDR case detection: new cases	Proportion of total MDR	Increase lab capacity for molecular testing (DST), including expansion of GeneXpert.
MDR case detection: previously treated cases	Proportion of total MDR [Increase]	Increase lab capacity for molecular testing (DST), including expansion of GeneXpert.
MDR linkage to care	Proportion of diagnosed MDR cases that are enrolled on treatment [Increase]	Improving quality of care at MDR-TB facilities: improved service delivery, improved coordination between lab and clinic etc.
MDR treatment success	Proportion of MDR cases on treatment that complete treatment and/or are cured*	Increase availability of second-line drugs and improve adherence to treatment.

*all examples are for illustrative purposes only, and do not reflect the full package of activities needed to achieve the 2030 TB elimination target.
**PPV = the probability that subjects with a positive screening test truly have the disease.

Table A4. Model natural history parameters in TIME baseline model (refer to TIME Impact paper and technical appendices[2]);

Effective contact rate	13.0
Proportion of cases developing smear positive TB, HIV-	40
Proportion of cases developing smear positive TB, HIV+	36
Relative infectiousness smear negative TB, HIV-	25
Relative infectiousness smear negative TB, HIV+	25
Smear conversion rate, HIV-	1.0
Smear conversion rate, HIV+	2.25
Self-cure rate, HIV-	20
Self-cure rate, HIV+	10
Relative fitness of MDR strains, HIV-	58
Relative fitness of MDR strains, HIV+	58
Rate of acquiring MDR, HIV-	1.7
Rate of acquiring MDR, HIV+	1.7
Relative treatment success of first-line anti-TB treatment for MDR treatment naïve, HIV-	70
Relative treatment success of first-line anti-TB treatment for MDR treatment naïve, HIV+	70
Relative treatment success of first-line anti-TB treatment for MDR previously treated, HIV-	35
Relative treatment success of first-line anti-TB treatment for MDR previously treated, HIV+	35
Proportion of infections developing primary TB, HIV-	11.5
Proportion of infections developing primary TB, HIV+	29.9
Reactivation rate, HIV-	0.12
Reactivation rate, HIV+	0.38
Protection provided by prior infection, HIV-	65
Protection provided by prior infection, HIV+	32.5
Smear positive TB mortality rate, HIV-	20
Smear positive TB mortality rate, HIV+	82
Smear negative TB mortality rate, HIV-	18
Smear negative TB mortality rate, HIV+	50

Infectiousness of smear negative TB is relative to smear positive TB within the same HIV stratum. Fitness of MDR strains is relative to drug sensitive strains within the same HIV stratum. Relative treatment success of first-line anti-TB treatment for MDR is relative to treatment success of first-line anti-TB treatment for drug sensitive TB within the same HIV and treatment history stratum (i.e. new vs retreatment).

The final calibrated model should be able to replicate historical and current epidemiological trends as accurately as possible. The modellers aimed to hit values for estimated incidence, notifications, prevalence and mortality at baseline (2017/18), as detailed in **Tables A5-A7:**

Table A5: Coverages of TB bacteriological testing among TB screen-positive suspects in the baseline model (0)

Diagnostic pathway coverages in 2018	
HIV-	
GeneXpert Smear microscopy Clinical diagnosis (only)*	30.0% 70.0% -
HIV+ (assumed same coverages of main diagnostic tools as above, among HIV+ presumptive)	
GeneXpert Smear microscopy Clinical diagnosis (only)	30.0% 70.0% -

Values of sensitivity and specificity are informed by the literature[3,4] but are not shown here.
GeneXpert has been scaled up in the model from 15% coverage in 2017, to the baseline value (2018) shown in the table.
*Proportion total presumptive diagnosed clinically not know/available at time of analysis.

Table A6: Coverages of diagnostic pathways for presumptive TB cases in the baseline model (0)

Passive detection			Baseline coverages (% all screened)
	1) Cough -> 2 weeks -> SSM (+ clinical diagnosis with CXR for negative smear)		9.2
	2) Cough -> 2 weeks -> SSM (+ clinical diagnosis without CXR)		36.8
	3) Cough -> 2 weeks -> Xpert -> (+ clinical diagnosis with CXR for negative Xpert)		1.9
	4) Cough -> 2 weeks -> Xpert -> (+ clinical diagnosis without CXR)		17.7
ICF			Baseline coverages (% all screened)
	5) Cough -> 2 weeks OR cough any duration + TB symptom -> SSM (+ CXR)		12
	6) Cough -> 2 weeks OR cough any duration + TB symptom -> SSM		12
	7) Cough -> 2 weeks OR cough any duration + TB symptom -> Xpert (+ CXR)		5.2
	8) Cough -> 2 weeks OR cough any duration + TB symptom -> Xpert		5.2

SSM = Sputum Smear Microscopy; Xpert = GeneXpert; CXR = Chest X-ray. In 2018, 7,793 of estimated 14,883 TB notifications (53%) were through ICF mechanism. Coverage of screening through passive case detection and ICF in 2018, estimated at 65.5% and 34.5%, respectively. Coverage of testing with sputum smear microscopy and GeneXpert in 2018, estimated at 70% and 30% respectively.

Table A7:

Indicator	Year	Target value	Source	Model value
Total incidence (per 100,000)	2014	165 (80-281)	GTB	167
Total incidence (per 100,000)	2018	148 (72-251)	GTB	154
HIV+ incidence (number)	2018	8,600 (4,100–15,000)	GTB	5,210
Total notifications (number)	2018	14,289*	NTP	17,808
MDR notifications (number)	2018	148**	NTP	158
Proportion of prevalence that is MDR (new)	2018	1.3% (1–1.6)	DRS	5.4
Proportion of prevalence that is MDR (retreatment)	2018	16% (14–19)	DRS	16.9
Mortality (per 100,00)	2018	52 (confirm)	GTB	61

*No under or over-reporting assumption applied to this estimate.
**Number of MDR-TB cases on treatment (GTB); actual no. lab confirmed RR/MDR = 231

Table A8: Target indicators for fitting to all forms and age 15+ smear positive TB prevalence, as illustrated in Figure A3 right hand graph:

Indicator (per 100,000)	Year	Target value	Source	Model value
15+ smear positive prevalence	2014	111 (76 – 145)	Prevalence survey	95
15+ all forms prevalence	2014	419 (339 – 500)		393

TIME baseline model inputs - programmatic data used during model fitting:

Inputs in the care & control window of TIME Impact for 2018:

Drug sensitive TB: linkage to care = 82%

- MacPherson et al. and is within the range for the average value for Africa,

Drug sensitive TB treatment success: 85%

- Direct communication with NTP, may be subject to revision

MDR-TB linkage to care = 40.0%

- NTP data for 2016; matches GTP data for same year

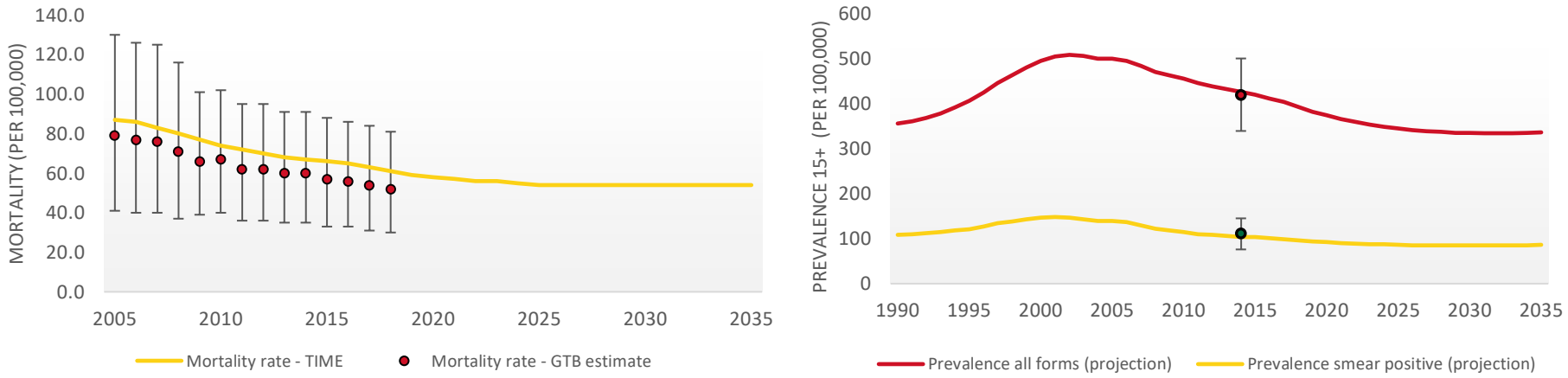
MDR-TB treatment success = 62.0%

- NTP data for 2014 & 2015. Previous years GTB database.

DST coverage: new = 35%; retreatment = 99%

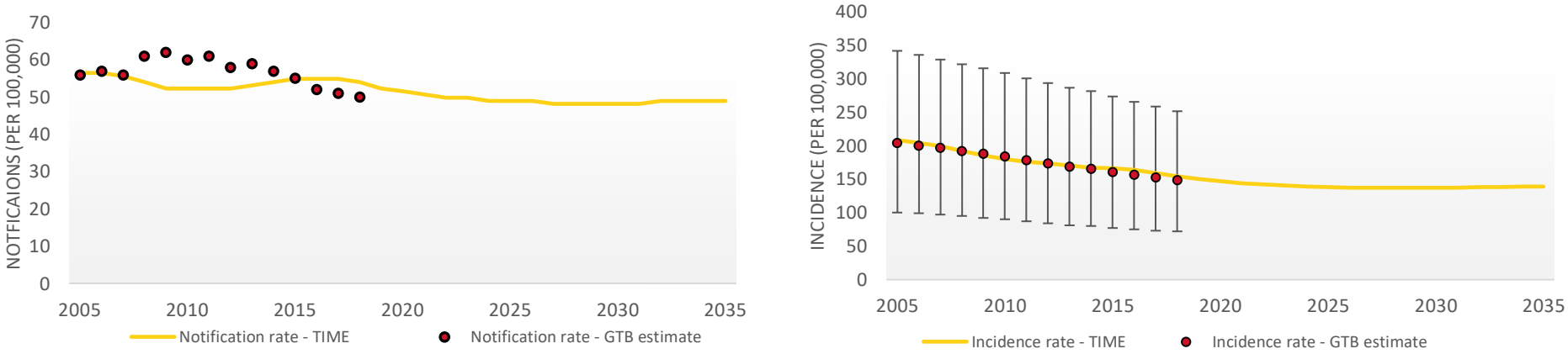
- NTP data 2018 Q1 & Q2 for retreatment cases: assumed linear increase to these values

Figure A3: Projections of TB burden at baseline. Left = mortality (numbers); right = prevalence (per 100,000)



Dots and crosses are NTP point estimates with upper and lower bounds for prevalence and mortality; for prevalence these are 2013/14 prevalence survey point estimates for 15+ all forms TB (blue) and 15+ smear+ prevalence (orange).

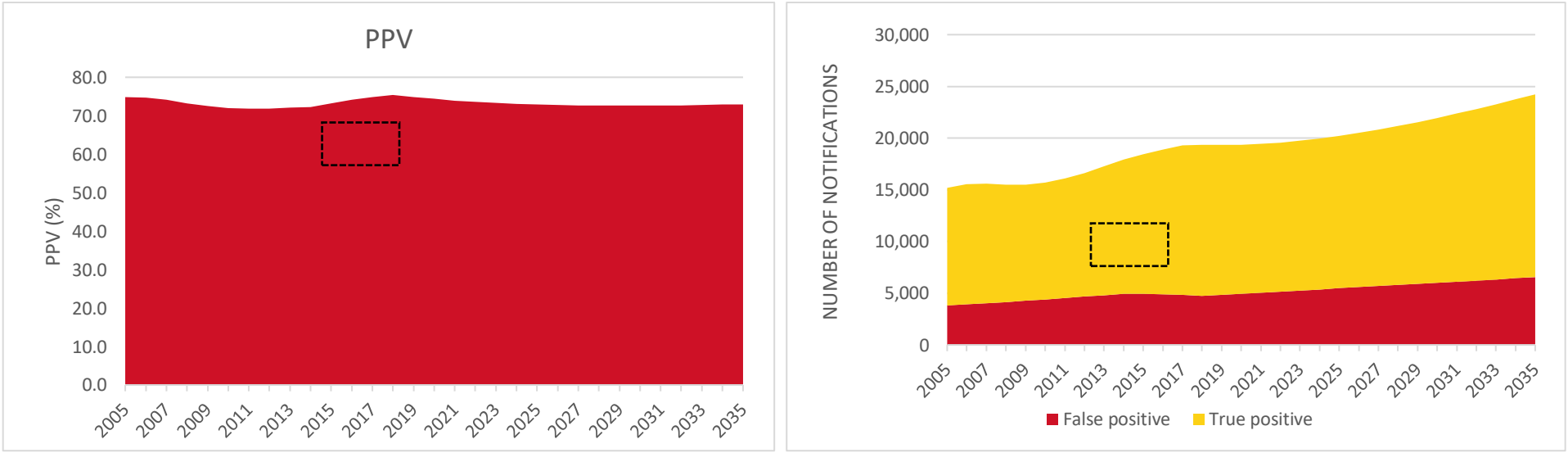
Figure A4: Projections of TB burden at baseline. Left = notifications (numbers); right = incidence (per 100,000)



Positive Predictive Value and True and False Positive Diagnoses

Figure A6 The Positive Predictive Value (PPV) is a measure of the proportion of individuals identified as TB positive upon diagnosis which truly have TB. This is calculated based on the sensitivity and specificity of the TB diagnostic algorithm, and the prevalence of TB in the screening population. PPV is displayed for Ghana's baseline model in Figure 3 below. There is a noticeable increase in PPV from 2014 – 2018, which coincides with the expansion of the ICF screening tool at OPDs in Ghana. The proportion of true positive and false positive notifications among total notifications is illustrated in Figure 3, right hand graph. The proportion true positive notifications predicted to increase gradually over time

Figure A5: model projections of PPV and True and False Positive Diagnoses:



* left: TIME model projection of Positive Predictive Value of notifications, right: TIME model projection of true positive and false positive notifications. Black squares highlight increase in PPV and the number of true positive notifications, owing to expansion of molecular testing for TB with Xpert.

Fitting to MDR-TB burden

MDR-TB cases make up a small fraction of total TB burden in Ghana, with an estimated 1.3% prevalence of MDR-TB among new cases and 16% among retreatment cases in 2018, with a GTB estimate of 870 incident MDR-TB cases in the same year. The model fits reasonably well to MDR-TB prevalence among retreatment cases, and reproduces the total number of MDR-TB notifications reported in GTB for 2018 (158 in model vs 147 reported):

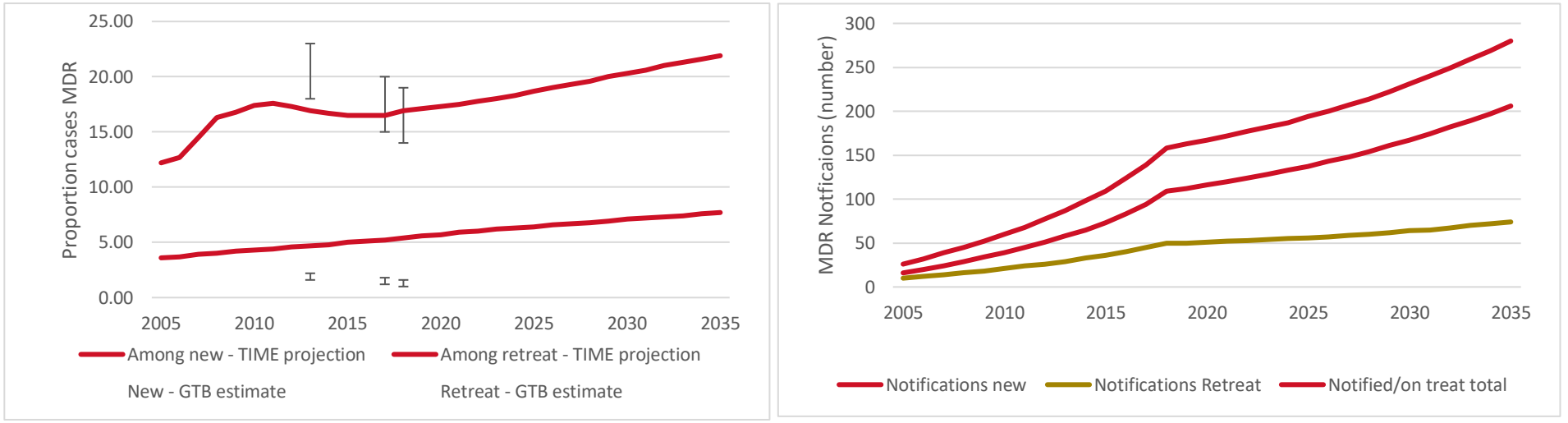


Figure **A6**: left: TIME model projection of MDR-TB prevalence among new (dark blue line) and retreatment (light blue line) cases, with GTB estimates and ranges for years 2013, 2017 and 2018 represented by orange-black dots and error bars; right: TIME model projection of MDR-TB notifications, disaggregated by treatment history.

TIME model outputs – baseline and intervention scenarios

Table A9 summarises the source Spectrum TIME Impact files for each graph in **Figure A4**, and the incidence projection generated from each of these models. Annual incidence numbers can be populated in these Spectrum files from **Results -> TB Epidemiology -> TB Incidence -> Total** and selecting 'Number of cases' under the Population index heading

Table A9: incidence projections from corresponding Spectrum Impact files used to model the baseline (0) and Ghana Priorities intervention scenarios (1) to (3):

Graph	Spectrum file		2017	**2018**	2019	2020	2021	2022	2023	2024	**2025**	2026	2027	2028	2029	**2030**
4a base	Baseline (0)	Incidence absolute numbers	43,741	**43,544**	43,636	43,836	44,133	44,597	45,167	45,825	**46,571**	47,403	48,313	49,295	50,342	**51,447**
4a ACF	Active Case Finding (1)		43,741	**43,544**	43,592	43,663	43,763	43,975	44,241	44,551	**44,958**	45,498	46,143	46,879	47,696	**48,582**
4a accuracy/speed	Molecular testing to improve accuracy and speed of TB diagnosis (2)		43,741	**43,544**	43,600	43,687	43,802	44,022	44,289	44,594	**44,939**	45,364	45,907	46,554	47,294	**48,113**
4a patient education	TB patient education and counselling to improve TB treatment adherence (3)		43,741	**43,544**	43,610	43,739	43,932	44,266	44,682	45,165	**45,717**	46,360	47,111	47,951	48,866	**49,848**

Graph	Spectrum file		2031	2032	2033	2034	2035	2036	2037	2038	2039	**2040**
4a base	Baseline (0)	Incidence absolute numbers	52,605	53,811	55,061	56,349	**57,670**	59,020	60,394	61,790	63,205	**64,638**
4a ACF	Active Case Finding (1)		49,530	50,534	51,586	52,681	**53,812**	54,975	56,165	57,378	58,613	**59,867**
4a accuracy/speed	Molecular testing to improve accuracy and speed of TB diagnosis (2)		49,001	49,952	50,956	52,006	**53,096**	54,219	55,372	56,549	57,749	**58,969**
4a patient education	TB patient education and counselling to improve TB treatment adherence (3)		50,887	51,979	53,117	54,295	**55,509**	56,754	58,024	59,317	60,631	**61,964**

Table A10: notification projections from corresponding Spectrum Impact files used to model the baseline (0) and Ghana Priorities intervention scenarios (1) to (3):

Total annual notifications can be populated in these Spectrum files from **Results -> TB Epidemiology -> TB Notification -> Total** and selecting 'Number of cases' under the Population index heading.

Graph	Spectrum file		2017	**2018**	2019	2020	2021	2022	2023	2024	**2025**	2026	2027	2028	2029	**2030**
4a base	Baseline (0)	Notifications absolute numbers	16,906	**17,409**	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**	19,015	19,356	19,723	20,112	**20,522**
4a ACF	Active Case Finding (1)		16,906	**17,409**	17,981	18,575	19,163	19,762	20,375	20,997	**21,336**	21,588	21,884	22,218	22,585	**22,980**
4a accuracy/ speed	Molecular testing to improve accuracy and speed of TB diagnosis (2)		16,906	**17,409**	17,937	18,431	18,923	19,431	19,956	20,495	**21,049**	20,393	20,680	21,001	21,354	**21,736**
4a patient education	TB patient education and counselling to improve TB treatment adherence (3)		16,906	**17,409**	17,452	17,532	17,623	17,742	17,890	18,062	**18,256**	18,488	18,767	19,080	19,421	**19,786**

Graph	Spectrum file		2031	2032	2033	2034	2035	2036	2037	2038	2039	**2040**
4a base	Baseline (0)	Notifications absolute numbers	16,906	17,409	17,469	17,593	**17,742**	17,930	18,156	18,413	18,700	**19,015**
4a ACF	Active Case Finding (1)		23,401	23,843	24,305	24,784	**25,279**	25,787	26,305	26,833	27,370	**27,915**
4a accuracy/ speed	Molecular testing to improve accuracy and speed of TB diagnosis (2)		16,906	17,409	17,937	18,431	**18,923**	19,431	19,956	20,495	21,049	**20,393**
4a patient education	TB patient education and counselling to improve TB treatment adherence (3)		20,172	20,576	20,997	21,431	**21,879**	22,338	22,805	23,281	23,765	**24,255**

Table **A11**: TIME model outputs from Active Case Finding scenario (1): summary of cost drivers and benefits from 2019-2040. Baseline year (2018) included for reference.

	Years 2018 - 2025	2018	2019	2020	2021	2022	2023	2024	2025
baseline	Total number screened	133,703	135,665	137,755	139,904	142,158	144,523	146,990	**149,552**
	Number needed to test to find 1 case	7.7	7.8	7.8	7.9	7.9	8	8	**8**
Intervention	Total number screened	133,703	144,746	156,395	168,625	181,511	195,093	209,382	**220,907**
	Number needed to test to find 1 case	7.7	8	8.4	8.8	9.2	9.6	10	**10.4**
Intervention	No. screened/tested through ACF	133,703	135,665	137,755	139,904	142,158	144,523	146,990	**149,552**
								Actual no. screened through ACF pathway 2020-2025	**152,080**
Cost drivers	**Additional no. screened/tested**	0	9,081	18,641	28,722	39,353	50,570	62,392	71,356
baseline	Total TB notifications	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
Intervention	Total TB notifications	17,409	17,981	18,575	19,163	19,762	20,375	20,997	**21,336**
	Additional no. notifications	0	512	982	1,421	1,832	2,219	2,584	2,636
								Additional notifications 2020-2025	**11,674**
baseline	Total true positive notifications	12,629	12,587	12,609	12,656	12,741	12,863	13,017	**13,199**
	Proportion true positive	72.54%	72.05%	71.67%	71.33%	71.06%	70.85%	70.69%	70.58%
Intervention	Total true positive notifications	12,629	12,820	13,035	13,249	13,480	13,733	14,005	**14,124**
	Proportion true positive	72.54%	71.30%	70.17%	69.14%	68.21%	67.40%	66.70%	66.20%
baseline	Total false positive notifications	4,780	4,882	4,984	5,086	5,189	5,292	5,396	**5,501**
	Proportion false positive	27.46%	27.95%	28.33%	28.67%	28.94%	29.15%	29.31%	**29.42%**
Intervention	Total false positive notifications	4,780	5,161	5,539	5,914	6,282	6,642	6,993	**7,211**
	Proportion false positive	27.46%	28.70%	29.82%	30.86%	31.79%	32.60%	33.30%	33.80%
	Additional false positive notifications	0	279	555	828	1,093	1,350	1,597	**1,710**
	Increase in proportion of notifications false positive	0.00%	0.76%	1.49%	2.20%	2.85%	3.45%	4.00%	4.38%
Baseline	No. clinical diagnosis + CXR as follow up to diagnostic test	5,838	5,918	5,997	6,077	6,161	6,249	6,343	**6,442**
Intervention	No. CXR as screening step in ACF	0	1,321	2,785	4,402	6,185	8,149	10,308	**12,493**
	No. clinical diagnosis + CXR as follow up to diagnostic test	5,838	6,104	6,362	6,613	6,857	7,097	7,329	**7,436**
Cost driver	**Additional no. CXR for ACF intervention**	**0**	**1,507**	**3,150**	**4,938**	**6,882**	**8,997**	**11,294**	**13,487**
Baseline	Number of sputum smear tests performed	21174	21,290	21,459	21,650	21,878	22,147	22,451	**22,787**
Intervention	Number of sputum smear tests performed	21174	21,455	21,735	21,992	22,243	22,491	22,729	**22,630**
	Additional no. sputum smear tests	**1**	**165**	**276**	**342**	**365**	**344**	**278**	**-157**
Baseline	Number of Xpert tests performed	9072	9,122	9,194	9,276	9,374	9,489	9,619	**9,763**
Intervention	Number of Xpert tests performed	9072	9,879	10,714	11,564	12,444	13,356	14,303	**15,078**
Cost driver	**Additional no. Xpert tests**	**0**	**758**	**1,519**	**2,289**	**3,070**	**3,867**	**4,684**	**5,315**
Baseline	Total cases to treat	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
	MDR cases to treat	170	177	181	185	188	191	195	**199**
Intervention	Total cases to treat	17,409	17,981	18,575	19,163	19,762	20,375	20,997	21,336
	MDR cases to treat	171	181	189	197	204	211	219	223
Cost driver	**Total additional numbers on treatment**	**0**	**512**	**982**	**1,421**	**1,832**	**2,219**	**2,584**	**2,636**
	Incidence number	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
	Incidence rate	170	177	181	185	188	191	195	**199**
	Incidence number	17,409	17,981	18,575	19,163	19,762	20,375	20,997	**21,336**
	Incidence rate	171	181	189	197	204	211	219	**223**
Benefits	**Cases averted**	**0**	**44**	**173**	**370**	**622**	**926**	**1,274**	**1,613**
								Cases averted 2019 - 2025	5,022
Baseline	Mortality	16,678	16,648	16,675	16,734	16,842	16,985	17,159	**17,364**
Intervention	Mortality	16,678	16,633	16,607	16,581	16,574	16,577	16,588	**16,626**
Benefits	**Deaths averted**	**0**	**15**	**68**	**153**	**268**	**408**	**571**	**738**
								Deaths averted 2019 - 2025	2,221

	Years 2026 - 2033	2026	2027	2028	2029	2030	2031	2032	2033
baseline	Total number screened	152,207	154,953	157,784	160,696	**163,683**	166,740	169,861	173,041
	Number needed to test to find 1 case	8	8	8	8	**8**	8	7.9	7.9
Intervention	Total number screened	224,612	228,461	232,438	236,529	**240,725**	245,014	249,390	253,843
	Number needed to test to find 1 case	10.4	10.4	10.5	10.5	**10.5**	10.5	10.5	10.4
Intervention	No. screened/tested through ACF	44,922	45,692	46,488	47,306	**48,145**	49,003	49,878	50,769
Cost drivers	**Additional no. screened/tested**	**72,404**	**73,508**	**74,653**	**75,833**	**77,041**	**78,274**	**79,529**	**80,801**
baseline	Total TB notifications	9,921	10,092	10,275	10,470	**10,675**	10,889	11,112	11,343
Intervention	Total TB notifications								
	Additional no. notifications	**2,573**	**2,528**	**2,495**	**2,473**	**2,458**	**2,450**	**2,446**	**2,446**
baseline	Total true positive notifications	13,409	13,645	13,906	14,189	**14,492**	14,813	15,151	15,503
	Proportion true positive	70.52%	70.49%	70.51%	70.55%	70.62%	70.70%	70.81%	70.92%
Intervention	Total true positive notifications	14,239	14,397	14,592	14,818	**15,073**	15,352	15,652	15,970
	Proportion true positive	65.96%	65.79%	65.68%	65.61%	65.59%	65.60%	65.65%	65.71%
baseline	Total false positive notifications	5,605	5,711	5,817	5,923	**6,030**	6,138	6,247	6,356
	Proportion false positive	29.48%	29.51%	29.49%	29.45%	**29.38%**	29.30%	29.20%	29.08%
Intervention	Total false positive notifications	7,349	7,487	7,626	7,766	**7,907**	8,049	8,191	8,335
	Proportion false positive	34.04%	34.21%	34.32%	34.39%	34.41%	34.40%	34.35%	34.29%
	Additional false positive notifications	1,744	1,776	1,809	1,843	**1,877**	1,911	1,944	1,979
	Increase in proportion of notifications false positive	4.57%	4.71%	4.83%	4.94%	**5.03%**	5.10%	5.16%	5.22%
Baseline	No. clinical diagnosis + CXR as follow up to diagnostic test	6,545	6,654	6,767	6,885	**7,006**	7,132	7,261	7,393
Intervention	No. CXR as screening step in ACF	12,664	12,853	13,057	13,274	**13,503**	13,742	13,990	14,246
	No. clinical diagnosis + CXR as follow up to diagnostic test	7,547	7,665	7,788	7,917	**8,050**	8,187	8,328	8,473
Cost driver	**Additional no. CXR for ACF intervention**	**13,666**	**13,864**	**14,078**	**14,306**	**14,546**	**14,797**	**15,057**	**15,325**
Baseline	Number of sputum smear tests performed	23,156	23,555	23,983	24,437	**24,915**	25,415	25,935	26,474
Intervention	Number of sputum smear tests performed	22,916	23,240	23,597	23,984	**24,397**	24,832	25,288	25,761
	Additional no. sputum smear tests	-240	-315	-385	-453	**-518**	-583	-648	-713
Baseline	Number of Xpert tests performed	9,921	10,092	10,275	10,470	**10,675**	10,889	11,112	11,343
Intervention	Number of Xpert tests performed	15,245	15,443	15,667	15,915	**16,184**	16,471	16,773	17,090
Cost driver	**Additional no. Xpert tests**	**5,324**	**5,351**	**5,392**	**5,445**	**5,509**	**5,581**	**5,661**	**5,747**
Baseline	Total cases to treat	19,015	19,356	19,723	20,112	20,522	20,951	21,397	21,859
	MDR cases to treat	203	207	212	216	222	227	233	239
Intervention	Total cases to treat	21,588	21,884	22,218	22,585	22,980	23,401	23,843	24,305
	MDR cases to treat	228	232	238	243	249	255	261	268
Cost driver	**Total additional numbers on treatment**	**2,573**	**2,528**	**2,495**	**2,473**	**2,458**	**2,450**	**2,446**	**2,446**
Baseline	Incidence number	47,403	48,313	49,295	50,342	**51,447**	52,605	53,811	55,061
	Incidence rate	135	136	136	136	**137**	138	138	139
Intervention	Incidence number	45,498	46,143	46,879	47,696	**48,582**	49,530	50,534	51,586
	Incidence rate	130	129	129	129	**129**	129	130	130
Benefits	**Cases averted**	**1,905**	**2,170**	**2,416**	**2,646**	**2,865**	**3,075**	**3,277**	**3,475**
Baseline	Mortality	17,602	17,872	18,171	18,500	**18,856**	19,237	19,642	20,067
Intervention	Mortality	16,712	16,847	17,025	17,243	**17,495**	17,779	18,091	18,427
Benefits	**Deaths averted**	**890**	**1,025**	**1,146**	**1,257**	**1,361**	**1,458**	**1,551**	**1,640**

	Years 2034 - 2040	2034	2035	2036	2037	2038	2039	2040	Totals
baseline	Total number screened	176,276	179,564	182,901	186,275	189,682	193,117	**196,579**	**3,733,607**
	Number needed to test to find 1 case	7.9	7.9	7.8	7.8	7.8	7.8	**7.7**	
Intervention	Total number screened	258,365	262,960	267,619	272,328	277,077	281,863	**286,682**	**5,228,267**
	Number needed to test to find 1 case	10.4	10.4	10.4	10.4	10.3	10.3	**10.3**	
Intervention	No. screened/tested through ACF	51,673	52,592	53,524	54,466	55,415	56,373	**57,336**	919,797
Cost drivers	**Additional no. screened/tested**	82,090	83,396	84,719	86,053	87,395	88,746	90,103	**1,494,660**
baseline	Total TB notifications	22,334	22,821	23,319	23,826	24,340	24,862	**25,391**	473,240
Intervention	Total TB notifications	24,784	25,279	25,787	26,305	26,833	27,370	**27,915**	522,675
	Additional no. notifications	2,450	2,458	2,468	2,479	2,493	2,508	2,524	**49,435**
baseline	Total true positive notifications	15,868	16,245	16,632	17,027	17,429	17,838	**18,254**	
	Proportion true positive	71.05%	71.18%	71.32%	71.46%	71.61%	71.75%	71.89%	
Intervention	Total true positive notifications	16,306	16,655	17,016	17,387	17,768	18,157	**18,553**	
	Proportion true positive	65.79%	65.88%	65.99%	66.10%	66.22%	66.34%	66.46%	
baseline	Total false positive notifications	6,465	6,576	6,687	6,799	6,911	7,024	**7,137**	
	Proportion false positive	28.95%	28.82%	28.68%	28.54%	28.39%	28.25%	**28.11%**	
Intervention	Total false positive notifications	8,479	8,624	8,771	8,918	9,065	9,213	**9,362**	
	Proportion false positive	34.21%	34.12%	34.01%	33.90%	33.78%	33.66%	**33.54%**	
	Additional false positive notifications	2,014	2,048	2,084	2,119	2,154	2,189	**2,225**	**37,128**
	Increase in proportion of notifications false positive	5.26%	5.30%	5.34%	5.37%	5.39%	5.41%	5.43%	
Baseline	No. clinical diagnosis + CXR as follow up to diagnostic test	7,529	7,667	7,808	7,952	8,097	8,243	**8,392**	
Intervention	No. CXR as screening step in ACF	14,510	14,780	15,056	15,337	15,623	15,912	**16,204**	
	No. clinical diagnosis + CXR as follow up to diagnostic test	8,620	8,771	8,924	9,080	9,237	9,396	**9,557**	
Cost driver	**Additional no. CXR for ACF intervention**	**15,601**	**15,884**	**16,172**	**16,466**	**16,763**	**17,065**	**17,369**	**281,213**
Baseline	Number of sputum smear tests performed	27,029	27,599	28,181	28,775	29,378	29,989	**30,609**	
Intervention	Number of sputum smear tests performed	26,250	26,754	27,270	27,797	28,332	28,876	**29,427**	
	Additional no. sputum smear tests	-778	-844	-911	-978	-1,045	-1,113	**-1,182**	
Baseline	Number of Xpert tests performed	11,580	11,825	12,074	12,328	12,587	12,849	**13,114**	
Intervention	Number of Xpert tests performed	17,419	17,760	18,110	18,468	18,833	19,205	**19,582**	
Cost driver	**Additional no. Xpert tests**	**5,839**	**5,935**	**6,036**	**6,140**	**6,247**	**6,356**	**6,468**	**108,533**
Baseline	Total cases to treat	22,334	22,821	23,319	23,826	24,340	24,862	**25,391**	
	MDR cases to treat	245	251	258	265	272	279	**286**	
Intervention	Total cases to treat	24,784	25,279	25,787	26,305	26,833	27,370	27,915	
	MDR cases to treat	275	282	289	297	305	313	321	
Cost driver	**Total additional numbers on treatment**	**2,450**	**2,458**	**2,468**	**2,479**	**2,493**	**2,508**	**2,524**	**49,435**
Baseline	Incidence number	56,349	57,670	59,020	60,394	61,790	63,205	**64,638**	
	Incidence rate	140	141	142	143	144	145	**146**	
Intervention	Incidence number	52,681	53,812	54,975	56,165	57,378	58,613	**59,867**	
	Incidence rate	131	131	132	133	133	134	**135**	
Benefits	**Cases averted**	**3,668**	**3,858**	**4,045**	**4,229**	**4,412**	**4,592**	**4,771**	**56,426**
Baseline	Mortality	20,512	20,973	21,450	21,939	22,440	22,951	**23,470**	
Intervention	Mortality	18,784	19,161	19,554	19,962	20,381	20,812	**21,251**	
Benefits	**Deaths averted**	**1,728**	**1,812**	**1,896**	**1,977**	**2,059**	**2,139**	**2,219**	**26,379**

Table **A12**: TIME model outputs from Molecular testing to improve accuracy and speed of TB diagnosis scenario (2): summary of cost drivers and benefits from 2019-2025. Baseline year (2018) included for reference.

		2018	2019	2020	2021	2022	2023	2024	2025
Baseline	Number of sputum smear tests performed	21,174	21,290	21,459	21,650	21,878	22,147	22,451	**22,787**
	Number of Xpert tests performed	9,072	9,122	9,194	9,276	9,374	9,489	9,619	**9,763**
Intervention	Number of sputum smear tests performed	21,174	21,198	18,372	15,498	12,591	9,647	6,659	**3,622**
	Number of Xpert tests performed	9,072	13,319	16,401	19,519	22,690	25,924	29,224	**32,596**
Baseline	Total number tested	133,701	135,665	137,755	139,904	142,158	144,523	146,990	**149,55**
	Number needed to test to find 1 case	7.7	7.8	7.8	7.9	7.9	8.0	8.0	**8.0**
Intervention	Total number tested	133,701	135,610	137,543	139,453	141,400	143,400	145,448	**147,54**
	Number needed to test to find 1 case	7.6	7.6	7.5	7.4	7.3	7.2	7.1	**7.0**
	Reduction in no. tested	0	55	212	451	758	1,123	1,542	2,006
	Reduction in NNT	0.1	0.2	0.3	0.5	0.6	0.8	0.9	1.0
Cost driver	**Additional no. Xpert tests performed**	0	4,197	7,207	10,244	13,316	16,435	19,605	22,833
Baseline	Total true positive notifications	12,629	12,587	12,609	12,656	12,741	12,863	13,017	**13,199**
	Proportion true positive	72.54%	72.05%	71.67%	71.33%	71.06%	70.85%	70.69%	70.58%
Intervention	Total true positive notifications	12,629	12,963	13,332	13,698	14,077	14,473	14,882	**15,305**
	Proportion true positive	72.54%	72.27%	72.33%	72.39%	72.45%	72.52%	72.61%	72.71%
Baseline	Total false positive notifications	4,780	4,882	4,984	5,086	5,189	5,292	5,396	**5,501**
	Proportion false positive	27.46%	27.95%	28.33%	28.67%	28.94%	29.15%	29.31%	29.42%
Intervention	Total false positive notifications	4,780	4,974	5,099	5,226	5,353	5,482	5,613	**5,744**
	Proportion false positive	27.46%	27.73%	27.67%	27.62%	27.55%	27.47%	27.39%	27.29%
	Reduction in proportion notifications false positive	0.00%	0.22%	0.66%	1.05%	1.39%	1.68%	1.92%	2.13%
Baseline	Total TB notifications	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
								Total notifications 2019-2025	**143,412**
Intervention	Total TB notifications	17,409	17,937	18,431	18,923	19,431	19,956	20,495	**21,049**
								Total notifications 2019-2025	**153,631**
	Additional no. notifications	**0**	**468**	**838**	**1,181**	**1,501**	**1,800**	**2,082**	**2,349**
								Additional notifications 2019-2025	**10,219**
Baseline	Total cases to treat	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
	MDR cases to treat	170	177	181	185	188	191	195	**199**
Intervention	Total cases to treat	17,479	17,937	18,431	18,923	19,431	19,956	20,495	**21,049**
	MDR cases to treat	170	181	191	199	208	217	226	**237**
Cost driver	Additional total number of cases on treatment	70	468	838	1,181	1,501	1,800	2,082	2,349
Baseline	Incidence number	43,544	43,636	43,836	44,133	44,597	45,167	45,825	**46,571**
Intervention	Incidence number	43,544	43,600	43,687	43,802	44,022	44,289	44,594	**44,939**
Benefits	**Total cases averted**	0	36	149	331	575	878	1,231	1,632
Baseline	Mortality	16,677	16,648	16,675	16,734	16,842	16,985	17,159	**17,364**
Intervention	Mortality	16,677	16,621	16,571	16,511	16,463	16,420	16,382	**16,352**
	Total deaths averted	0	27	104	223	379	565	777	1,012

Table **A13**: TIME model outputs from patient education and counselling scenario (3): summary of cost drivers and benefits from 2019-2025. Baseline year (2018) included for reference.

		2018	2019	2020	2021	2022	2023	2024	2025
	Treatment success (HIV- TB)	85.00	85.71	86.43	87.14	87.86	88.57	89.29	**90.00**
	Treatment success (HIV+ TB)	77.00	77.71	78.43	79.14	79.86	80.57	81.29	**82.00**
Baseline	Total cases to be treated	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
Intervention	Total cases to be treated	17,409	17,452	17,532	17,623	17,742	17,890	18,062	**18,256**
	Reduction in no. cases to be treated	0	17	61	119	188	266	351	444
Baseline	MDR incidence number	450	456	463	470	479	489	498	**509**
Intervention	MDR incidence number	450	455	461	466	474	481	489	**496**
	MDR-TB cases averted	0	1	2	4	5	8	9	13
Baseline	MDR mortality	504	514	524	533	542	551	561	570
Intervention	MDR mortality	504	514	524	532	541	549	558	**566**
	MDR-TB deaths averted	0	0	0	1	1	2	3	4
Baseline	Total incidence number	43,544	43,636	43,836	44,133	44,597	45,167	45,825	**46,571**
Intervention	Total Incidence number	43,544	43,610	43,739	43,932	44,266	44,682	45,165	**45,717**
	Total cases averted	0	26	97	201	331	485	660	854
Baseline	Mortality (baseline model)	16,677	16,648	16,675	16,734	16,842	16,985	17,159	**17,364**
Intervention	Mortality (adherence intervention)	16,677	16,640	16,643	16,664	16,722	16,803	16,905	**17,031**
	Total deaths averted	0	8	32	70	120	182	254	333

Table **A14**: estimates of TB prevalence and (where data available) yields of screening for TB in high risk target populations

Target population	Pop size	Estimated TB Prevalence	Source of prevalence estimate	No. prevalent cases	Year	Note/assumptions	No. screened/ tested for TB in year of study	No. cases reported (during study/pilot)	Note/assumptions
Prisoners	14,000	0.2%	2015-2020 NSP	28	2013	Prevalence estimate of 0.2% is proxy, based on no. cases detected by routine screening of TB in prisons	not stated	171	Yield of screening in prisons in 2013
PLHIV	330,000	1.2%	Ghana UNADIS profile	3,960	2018	Estimated prevalence in adults 15-49 years	not stated	2759	GTB Ghana profile. No. TB cases among individuals with known HIV status of which HIV+
Miners	1,000,000	2.9%	Stop TB key populations brief, 10x TB prevalence in miners vs popn	29,000	2012	Estimated population affected by precious mineral mining = 1M across 21 districts	2,564,913	1,927	Total number tested by routine case finding across 21 districts in 2012
HHCs of notified index cases	46,818	0.7%	Yield of TB among HHC in Accra - Bonsu, F. 2018	304		Population size = total TB notifications x 3 (HH size of 4 - index case)	96% of HHCs in study	n/a	Assume same national coverage as Accra study
Refugees & host communities	36,695	1.0%	2015-2020 NSP	367		Target populations of Active TB Screening (High Branch Interventions) in high incidence Western Region	not stated	n/a	No data available on yields of screening in target population
								n/a	
Vulnerable urban populations	137,556	1.0%	2015-2020 NSP	1,376			not stated		No data available on yields of screening in target population
Overall target pop size		Mean TB prevalence in target popn (%)		Total no. prevalent cases (based on 1.5% prevalence)					
	1,565,069	1.50%		**23,476**					

Table **A15**: summary of TB prevalence estimates based on 2013 National TB Prevalence Survey, and estimated proportion of total prevalent TB cases in target populations (latter based on total number of TB cases calculated in table A14.

Total population of Ghana in 2013 (DemProj)				National prevalence p100K (2013 prevalence Survey)	As % of total population
27,518,248				**290**	**0.29%**
ACF target populations as % of total population				Total number of prevalent cases in 2013	
5.7				**79,803**	
Total no. prevalence cases in ACF target populations				Proportion total prevalent TB among ACF target populations	
23,476				**29.4%**	

Table **A16**: TIME model estimates of yield of ACF intervention (1)
in terms of additional no. TB notifications. PNR = Prevalence Notification Ratio.

		2018	2019	2020	2021	2022	2023	2024	2025	TOTALS 2019-2040
Baseline	Total screened	133,701	135,665	137,755	139,904	142,158	144,523	146,990	**149,552**	
Intervention	No. screened/tested ACF	0	4,136	8,937	14,454	20,744	27,870	35,894	**44,181**	
	Total screened	133,703	144,746	156,395	168,625	181,511	195,093	209,382	**220,907**	
								No. screened ACF 2020-2025	**152,080**	
Cost drivers	**Additional no. screened/tested**	1	9,081	18,641	28,722	39,353	50,570	62,392	**71,356**	**1,494,662**
Baseline	Total TB notifications	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**	
	Notification rate	58	57	56	56	55	55	55	**54**	
Intervention	Total TB notifications	17,409	17,981	18,575	19,163	19,762	20,375	20,997	**21,336**	
	Notification rate	58	59	60	60	61	62	62	**62**	
	Additional no. notifications	0	512	982	1,421	1,832	2,219	2,584	2,636	**49,435**
								Additional not. 2020-2025	**11,674**	
Baseline	Prevalence (no.)	84,670	85,065	85,521	86,061	86,749	87,597	88,610	89,790	
	Prevalence per 100K	283	278	274	270	267	265	263	261	
								PNR in 2025	**20.7%**	
Intervention	Prevalence (no.)	84,682	84,889	84,981	85,000	85,029	85,095	85,215	85,561	
	Prevalence per 100K	283	278	272	267	262	257	253	249	
								PNR in 2025	**24.9%**	

Table **A17**: Coverages of diagnostic pathways for presumptive TB cases in the ACF scenario model (1). Note: pathway 9) is the principle ACF screening and diagnosis algorithm.

Passive detection		Baseline coverages (% all screened)	2025 coverages (% all screened)
	1) Cough -> 2 weeks -> SSM (+ clinical diagnosis with CXR for negative smear)	9.2	7.4
	2) Cough -> 2 weeks -> SSM (+ clinical diagnosis without CXR)	36.8	29.4
	3) Cough -> 2 weeks -> Xpert -> (+ clinical diagnosis with CXR for negative Xpert)	1.9	1.5
	4) Cough -> 2 weeks -> Xpert -> (+ clinical diagnosis without CXR)	17.7	14.2
ICF		Baseline coverages (% all screened)	2025 coverages (% all screened)
	5) Cough -> 2 weeks OR cough any duration + TB symptom -> SSM (+ CXR)	12	9.6
	6) Cough -> 2 weeks OR cough any duration + TB symptom -> SSM	12	9.6
	7) Cough -> 2 weeks OR cough any duration + TB symptom -> Xpert (+ CXR)	5.2	4.2
	8) Cough -> 2 weeks OR cough any duration + TB symptom -> Xpert	5.2	4.2
	9) Any TB symptom -> CXR (screen) -> GXP (diagnosis without clinical workup)	0	20

Table **A18**: summary of numbers of individuals screened for TB in the baseline (0) and ACF scenario model (1):

Baseline (0)		ACF scenario (1)
No. Screened 2019-2025		
All passive/ICF		All passive/ICF
996,545		1,120,443
ACF		ACF
0		156,216

References

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4) Van't Hoog, et. al A systematic review of the sensitivity and specificity of symptom- and chest-radiography screening for active pulmonary tuberculosis in HIV-negative persons and persons with unknown HIV status. *Cochrane Database of Systematic Reviews (2014), Issue 1.*
5) Vassall 2011, et. al. Rapid Diagnosis of Tuberculosis with the Xpert MTB/RIF Assay in High Burden Countries: A Cost-Effectiveness Analysis. *PLOS Medicine (2011)*
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ACF Output Tables

		2018	2019	2020	2021	2022	2023	2024	2025
baseline									**149,55**
	Total number screened	133,703	135,665	137,755	139,904	142,158	144,523	146,990	**2**
	Number needed to test to find 1 case	7.7	7.8	7.8	7.9	7.9	8	8	**8**
Intervention									**220,90**
	Total number screened	133,703	144,746	156,395	168,625	181,511	195,093	209,382	**7**
	Number needed to test to find 1 case	7.7	8	8.4	8.8	9.2	9.6	10	**10.4**
Intervention									**149,55**
	No. screened/tested through ACF	133,703	135,665	137,755	139,904	142,158	144,523	146,990	**2**
								Actual no. screened through ACF pathway 2019-2025	**156,21 6**
Cost drivers	**Additional no. screened/tested**	0	9,081	18,641	28,722	39,353	50,570	62,392	71,356
baseline	Total TB notifications								
Intervention	Total TB notifications	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
	Additional no. notifications								
								Additional notifications 2019-2025	**39,737**
baseline	Total true positive notifications	12,629	12,587	12,609	12,656	12,741	12,863	13,017	**13,199**
	Proportion true positive	72.54%	72.05%	71.67%	71.33%	71.06%	70.85%	70.69%	70.58 %
Intervention	Total true positive notifications	12,629	12,820	13,035	13,249	13,480	13,733	14,005	**14,124**
	Proportion true positive	72.54%	71.30%	70.17%	69.14%	68.21%	67.40%	66.70%	66.20 %
baseline	Total false positive notifications	4,780	4,882	4,984	5,086	5,189	5,292	5,396	**5,501**
	Proportion false positive	27.46%	27.95%	28.33%	28.67%	28.94%	29.15%	29.31%	**29.42 %**
Intervention	Total false positive notifications	4,780	5,161	5,539	5,914	6,282	6,642	6,993	**7,211**
	Proportion false positive	27.46%	28.70%	29.82%	30.86%	31.79%	32.60%	33.30%	33.80 %
	Additional false positive notifications	0	279	555	828	1,093	1,350	1,597	**1,710**
	Increase in proportion of notifications false positive	0.00%	0.76%	1.49%	2.20%	2.85%	3.45%	4.00%	4.38%
Baseline	No. clinical diagnosis + CXR as follow up to diagnostic test	5,838	5,918	5,997	6,077	6,161	6,249	6,343	**6,442**
Intervention									
	No. CXR as screening step in ACF	0	1,321	2,785	4,402	6,185	8,149	10,308	**12,493**
	No. clinical diagnosis + CXR as follow up to diagnostic test	5,838	6,104	6,362	6,613	6,857	7,097	7,329	**7,436**
Cost driver	**Additional no. CXR for ACF intervention**	**0**	**1,507**	**3,150**	**4,938**	**6,882**	**8,997**	**11,294**	**13,487**
Baseline	Number of sputum smear tests performed	21174	21,290	21,459	21,650	21,878	22,147	22,451	**22,787**
Intervention	Number of sputum smear tests performed	21174	21,455	21,735	21,992	22,243	22,491	22,729	**22,630**
	Additional no. sputum smear tests	**1**	**165**	**276**	**342**	**365**	**344**	**278**	**-157**
Baseline	Number of Xpert tests performed	9072	9,122	9,194	9,276	9,374	9,489	9,619	**9,763**
Intervention	Number of Xpert tests performed	9072	9,879	10,714	11,564	12,444	13,356	14,303	**15,078**
Cost driver	**Additional no. Xpert tests**	**0**	**758**	**1,519**	**2,289**	**3,070**	**3,867**	**4,684**	**5,315**
Baseline	Total cases to treat	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
	MDR cases to treat	170	177	181	185	188	191	195	**199**
Intervention	Total cases to treat	17,409	17,981	18,575	19,163	19,762	20,375	20,997	21,336
	MDR cases to treat	171	181	189	197	204	211	219	223
Cost driver	**Total additional numbers on treatment**	**0**	**512**	**982**	**1,421**	**1,832**	**2,219**	**2,584**	**2,636**
	Incidence number	17,409	17,469	17,593	17,742	17,930	18,156	18,413	**18,700**
	Incidence rate	170	177	181	185	188	191	195	**199**
	Incidence number	17,409	17,981	18,575	19,163	19,762	20,375	20,997	**21,336**
	Incidence rate	171	181	189	197	204	211	219	**223**
Benefits	**Cases averted**	**0**	**44**	**173**	**370**	**622**	**926**	**1,274**	**1,613**
								Cases averted 2019 - 2025	5,022
Baseline	Mortality	16,678	16,648	16,675	16,734	16,842	16,985	17,159	**17,364**
Intervention	Mortality	16,678	16,633	16,607	16,581	16,574	16,577	16,588	**16,626**
Benefits	**Deaths averted**	**0**	**15**	**68**	**153**	**268**	**408**	**571**	**738**
								Deaths averted 2019 - 2025	2,221

		2026	2027	2028	2029	2030	2031	2032	2033
baseline	Total number screened	152,207	154,953	157,784	160,696	**163,683**	166,740	169,861	173,041
	Number needed to test to find 1 case	8	8	8	8	**8**	8	7.9	7.9
Intervention	Total number screened	224,612	228,461	232,438	236,529	**240,725**	245,014	249,390	253,843
	Number needed to test to find 1 case	10.4	10.4	10.5	10.5	**10.5**	10.5	10.5	10.4
Intervention	No. screened/tested through ACF	44,922	45,692	46,488	47,306	**48,145**	49,003	49,878	50,769
Cost drivers	**Additional no. screened/tested**	**72,404**	**73,508**	**74,653**	**75,833**	**77,041**	**78,274**	**79,529**	**80,801**
baseline	Total TB notifications	9,921	10,092	10,275	10,470	**10,675**	10,889	11,112	11,343
Intervention	Total TB notifications								
	Additional no. notifications	**2,573**	**2,528**	**2,495**	**2,473**	**2,458**	**2,450**	**2,446**	**2,446**
baseline	Total true positive notifications	13,409	13,645	13,906	14,189	**14,492**	14,813	15,151	15,503
	Proportion true positive	70.52%	70.49%	70.51%	70.55%	70.62%	70.70%	70.81%	70.92%
Intervention	Total true positive notifications	14,239	14,397	14,592	14,818	**15,073**	15,352	15,652	15,970
	Proportion true positive	65.96%	65.79%	65.68%	65.61%	65.59%	65.60%	65.65%	65.71%
baseline	Total false positive notifications	5,605	5,711	5,817	5,923	**6,030**	6,138	6,247	6,356
	Proportion false positive	29.48%	29.51%	29.49%	29.45%	**29.38%**	29.30%	29.20%	29.08%
Intervention	Total false positive notifications	7,349	7,487	7,626	7,766	**7,907**	8,049	8,191	8,335
	Proportion false positive	34.04%	34.21%	34.32%	34.39%	34.41%	34.40%	34.35%	34.29%
	Additional false positive notifications	1,744	1,776	1,809	1,843	**1,877**	1,911	1,944	1,979
	Increase in proportion of notifications false positive	4.57%	4.71%	4.83%	4.94%	**5.03%**	5.10%	5.16%	5.22%
Baseline	No. clinical diagnosis + CXR as follow up to diagnostic test	6,545	6,654	6,767	6,885	**7,006**	7,132	7,261	7,393
Intervention	No. CXR as screening step in ACF	12,664	12,853	13,057	13,274	**13,503**	13,742	13,990	14,246
	No. clinical diagnosis + CXR as follow up to diagnostic test	7,547	7,665	7,788	7,917	**8,050**	8,187	8,328	8,473
Cost driver	**Additional no. CXR for ACF intervention**	**13,666**	**13,864**	**14,078**	**14,306**	**14,546**	**14,797**	**15,057**	**15,325**
Baseline	Number of sputum smear tests performed	23,156	23,555	23,983	24,437	**24,915**	25,415	25,935	26,474
Intervention	Number of sputum smear tests performed	22,916	23,240	23,597	23,984	**24,397**	24,832	25,288	25,761
	Additional no. sputum smear tests	-240	-315	-385	-453	**-518**	-583	-648	-713
Baseline	Number of Xpert tests performed	9,921	10,092	10,275	10,470	**10,675**	10,889	11,112	11,343
Intervention	Number of Xpert tests performed	15,245	15,443	15,667	15,915	**16,184**	16,471	16,773	17,090
Cost driver	**Additional no. Xpert tests**	**5,324**	**5,351**	**5,392**	**5,445**	**5,509**	**5,581**	**5,661**	**5,747**
Baseline	Total cases to treat	19,015	19,356	19,723	20,112	20,522	20,951	21,397	21,859
	MDR cases to treat	203	207	212	216	222	227	233	239
Intervention	Total cases to treat	21,588	21,884	22,218	22,585	22,980	23,401	23,843	24,305
	MDR cases to treat	228	232	238	243	249	255	261	268
Cost driver	**Total additional numbers on treatment**	**2,573**	**2,528**	**2,495**	**2,473**	**2,458**	**2,450**	**2,446**	**2,446**
	Incidence number	47,403	48,313	49,295	50,342	**51,447**	52,605	53,811	55,061
	Incidence rate	135	136	136	136	**137**	138	138	139
	Incidence number	45,498	46,143	46,879	47,696	**48,582**	49,530	50,534	51,586
	Incidence rate	130	129	129	129	**129**	129	130	130
Benefits	**Cases averted**	**1,905**	**2,170**	**2,416**	**2,646**	**2,865**	**3,075**	**3,277**	**3,475**
Baseline	Mortality	17,602	17,872	18,171	18,500	**18,856**	19,237	19,642	20,067
Intervention	Mortality	16,712	16,847	17,025	17,243	**17,495**	17,779	18,091	18,427
Benefits	**Deaths averted**	**890**	**1,025**	**1,146**	**1,257**	**1,361**	**1,458**	**1,551**	**1,640**

		2034	2035	2036	2037	2038	2039	2040	Totals
baseline	Total number screened	176,276	179,564	182,901	186,275	189,682	193,117	**196,579**	**3,733,607**
	Number needed to test to find 1 case	7.9	7.9	7.8	7.8	7.8	7.8	**7.7**	
Intervention	Total number screened	258,365	262,960	267,619	272,328	277,077	281,863	**286,682**	**5,228,267**
	Number needed to test to find 1 case	10.4	10.4	10.4	10.4	10.3	10.3	**10.3**	
Intervention	No. screened/tested through ACF	51,673	52,592	53,524	54,466	55,415	56,373	**57,336**	919,797
Cost drivers	**Additional no. screened/tested**	82,090	83,396	84,719	86,053	87,395	88,746	90,103	**1,494,660**
baseline	Total TB notifications	22,334	22,821	23,319	23,826	24,340	24,862	**25,391**	473,240
Intervention	Total TB notifications	24,784	25,279	25,787	26,305	26,833	27,370	**27,915**	522,675
	Additional no. notifications	2,450	2,458	2,468	2,479	2,493	2,508	2,524	**49,435**
baseline	Total true positive notifications	15,868	16,245	16,632	17,027	17,429	17,838	**18,254**	
	Proportion true positive	71.05%	71.18%	71.32%	71.46%	71.61%	71.75%	71.89%	
Intervention	Total true positive notifications	16,306	16,655	17,016	17,387	17,768	18,157	**18,553**	
	Proportion true positive	65.79%	65.88%	65.99%	66.10%	66.22%	66.34%	66.46%	
baseline	Total false positive notifications	6,465	6,576	6,687	6,799	6,911	7,024	**7,137**	
	Proportion false positive	28.95%	28.82%	28.68%	28.54%	28.39%	28.25%	**28.11%**	
Intervention	Total false positive notifications	8,479	8,624	8,771	8,918	9,065	9,213	**9,362**	
	Proportion false positive	34.21%	34.12%	34.01%	33.90%	33.78%	33.66%	**33.54%**	
	Additional false positive notifications	2,014	2,048	2,084	2,119	2,154	2,189	**2,225**	**37,128**
	Increase in proportion of notifications false positive	5.26%	5.30%	5.34%	5.37%	5.39%	5.41%	5.43%	
Baseline	No. clinical diagnosis + CXR as follow up to diagnostic test	7,529	7,667	7,808	7,952	8,097	8,243	**8,392**	
Intervention	No. CXR as screening step in ACF	14,510	14,780	15,056	15,337	15,623	15,912	**16,204**	
	No. clinical diagnosis + CXR as follow up to diagnostic test	8,620	8,771	8,924	9,080	9,237	9,396	**9,557**	
Cost driver	**Additional no. CXR for ACF intervention**	**15,601**	**15,884**	**16,172**	**16,466**	**16,763**	**17,065**	**17,369**	**281,213**
Baseline	Number of sputum smear tests performed	27,029	27,599	28,181	28,775	29,378	29,989	**30,609**	
Intervention	Number of sputum smear tests performed	26,250	26,754	27,270	27,797	28,332	28,876	**29,427**	
	Additional no. sputum smear tests	-778	-844	-911	-978	-1,045	-1,113	**-1,182**	
Baseline	Number of Xpert tests performed	11,580	11,825	12,074	12,328	12,587	12,849	**13,114**	
Intervention	Number of Xpert tests performed	17,419	17,760	18,110	18,468	18,833	19,205	**19,582**	
Cost driver	**Additional no. Xpert tests**	**5,839**	**5,935**	**6,036**	**6,140**	**6,247**	**6,356**	**6,468**	**108,533**
Baseline	Total cases to treat	22,334	22,821	23,319	23,826	24,340	24,862	**25,391**	
	MDR cases to treat	245	251	258	265	272	279	**286**	
Intervention	Total cases to treat	24,784	25,279	25,787	26,305	26,833	27,370	27,915	
	MDR cases to treat	275	282	289	297	305	313	321	
Cost driver	**Total additional numbers on treatment**	**2,450**	**2,458**	**2,468**	**2,479**	**2,493**	**2,508**	**2,524**	**49,435**
	Incidence number	56,349	57,670	59,020	60,394	61,790	63,205	**64,638**	
	Incidence rate	140	141	142	143	144	145	**146**	
	Incidence number	52,681	53,812	54,975	56,165	57,378	58,613	**59,867**	
	Incidence rate	131	131	132	133	133	134	**135**	
Benefits	**Cases averted**	**3,668**	**3,858**	**4,045**	**4,229**	**4,412**	**4,592**	**4,771**	**56,426**
Baseline	Mortality	20,512	20,973	21,450	21,939	22,440	22,951	**23,470**	
Intervention	Mortality	18,784	19,161	19,554	19,962	20,381	20,812	**21,251**	
Benefits	**Deaths averted**	**1,728**	**1,812**	**1,896**	**1,977**	**2,059**	**2,139**	**2,219**	**26,379**

GHANA PRIORITIES

The Ghanaian economy has been growing swiftly, with remarkable GDP growth higher than five per cent for two years running. This robust growth means added pressure from special interest groups who demand more public spending on certain projects. But like every country, Ghana lacks the money to do everything that citizens would like. It has to prioritise between many worthy opportunities. What if economic science and data could cut through the noise from interest groups, and help the allocation of additional money, to improve the budgeting process and ensure that each cedi can do even more for Ghana? With limited resources and time, it is crucial that focus is informed by what will do the most good for each cedi spent. The Ghana Priorities project will work with stakeholders across the country to find, analyze, rank and disseminate the best solutions for the country.

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