Standardized framework for evaluating the cost-effectiveness of tuberculosis (TB) case-finding and treatment initiation projects in TB REACH Wave 5

Draft Report to the Stop TB Partnership

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Executive Summary

Interventions that can help streamline and reduce gaps in the tuberculosis (TB) care cascade can play crucial roles in TB control efforts. Such interventions are often operationally complex and resource intensive, given the heterogenous nature of the needs and settings where the care cascade gaps exist. Therefore, there is a need to better understand their comparative values to support decisions for future funding, strategic adoption, and project scale-up.

In this study, we comprehensively reviewed TB REACH Wave 5 program reports and financial statements to collect and analyze relative cost-effectiveness of ACF interventions funded through the wave 5 grant. Two independent reviewers abstracted cost (in 2017 US dollars) and key programmatic data, including project type ("Case-Finding Only", "Case-Finding and Treatment', or 'Other (Non-Case-Finding)'), operational settings (urban vs. rural), and project outputs (numbers of people with TB diagnosed by the project, started on treatment, and successfully completing treatment). Cost-effectiveness for each program output was calculated as the ratio of apportioned programmatic expenditures (costs) and respective service output estimates (effectiveness assessed as TB cases detected, TB patients initiating on treatment, and TB patients completing treatment).

Of 29 eligible projects, 11 were exclusively case-finding, 18 further included treatment support in addition to case-finding, and 2 focused on technology. Most projects were implemented in the African or South-East Asian regions, and 19 focused on serving urban areas. Among all eligible projects, 9 explicitly mentioned the provision of preventive therapy. Average program cost per case diagnosed across all projects was $184 (Range: $30-$10,497), which was higher for projects with objectives beyond case-finding and increased with per-capita GDP. For projects conducting activities beyond case-finding, the average cost per treatment initiation was $332 (Range: $123-$10,608) and per treatment completion was $40 (Range: $8-$160).

Our work demonstrates that costs and cost-effectiveness of TB case-finding are highly heterogenous, reflecting each project's context-specific and dependent on programmatic objectives. Costs were generally higher in areas with greater economic development. As our analytic framework can be extended to collect and analyze cost-effectiveness of similar interventions funded through earlier (or later) TB REACH initiative (and may be able to extend to other funding initiatives that support ACF interventions) more research effort in systematically collecting and analyzing cost-effectiveness data on ACF interventions can help improve comparability, monitoring, and evaluation of programs designed to improve the TB care cascade.

Introduction

Tuberculosis (TB) is the leading infectious cause of morbidity and mortality worldwide with 10 million new TB cases and 1.5 million deaths reported in 2018 alone[1]. In 2014, the World Health Organization's End TB Strategy called for a reduction in TB incidence and mortality rates by 90 and 95% of 2015 estimates by 2035[2]. Similarly, the Stop TB Partnership's Global Plan to End TB, launched in 2019, calls for UN member states to successfully treat 40 million people with TB and provide TB preventive therapy to at least 30 million people by 2022[3]. But despite such efforts, the reduction in TB incidence and mortality rates remains at roughly 2 and 3% per year—far below the reduction needed (10% or more) to achieve End TB's targets[1].

Currently, it is estimated that more than 30% of people who develop active TB every year will not be notified to public health authorities – largely reflecting underdiagnosis and undertreatment.[4] As people with TB who are missed can perpetuate transmission and suffer the adverse consequences of untreated disease (including death), it is imperative to identify these individuals and ensure the rapid uptake of TB treatment, particularly among at-risk populations. Public health interventions such as active case finding (ACF) and other approaches to reduce barriers to care-seeking, improve patient management, and address gaps in the TB care cascade are therefore critical components of a comprehensive strategy to reduce the burden of TB worldwide[5,6].

Since 2010, the TB REACH initiative of the Stop TB partnership (UNOPS), supported by Global Affairs Canada, USAID, and the Bill and Melinda Gates Foundation, has funded 313 projects in 54 countries that focus on different aspects of improving TB case detection and treatment. These projects have made important contributions in innovating and promoting TB case finding activities in many high-burden TB countries. However, TB case finding and treatment projects are resource intensive, and the cost-effectiveness of these projects – both from a high-level perspective and in comparing different types of projects – remains uncertain[7,8].

Given the substantial investment made in these projects (over 155 million USD since the inception of the initiative), it is critical to understand the value generated in a comparative manner. Cost-effectiveness – assessed as a ratio of cost inputs and a project's programmatic yield (e.g. number of people with TB identified and notified) – is one widely-recognized metric used to assess value for money. In this study, we used the project database of the TB REACH wave 5 funded projects to develop a comprehensive and systematic assessment of costs and cost-effectiveness across the wide range of case finding and treatment support projects supported by this initiative.

Methods

An Overview of the TB REACH Wave 5: During the wave 5 funding cycle, TB REACH funded 32 projects across 20 different countries with total support of 16 million USD. The scope

of these projects was broad; some examples of these innovations included novel approaches to case finding (e.g. use of community health workers and strengthening public-private partnerships), scaling up previously proven concepts, improving treatment referral and adherence following case finding, and increasing awareness regarding TB infection in the community (e.g. involvement of mass media, implementation of educational programs, and community engagement).

Screening and Data Extraction: The authors were given access to a complete set of documentation and data – including program applications, reviews of program activity and financial reports – for each project funded during the TB REACH wave 5 cycle. We then created a standardized extraction spreadsheet, the composition of which was informed by data available in program reviews and financial reports.

Two authors independently performed the data extraction by reviewing all relevant documentation and data for each project. All disagreements between the two authors were resolved by discussion. If a consensus could not be reached, the two senior investigators were consulted during weekly meetings. During these meetings, the four authors re-evaluated the financial report in question and/or sought intervention by TB REACH technical officers, who were able to provide further detail and clarification regarding any successes and/or challenges programs may have experienced during the wave 5 funding cycle.

For each program, we assigned a letter-number code and a five-letter code (See Table 1); and extracted data from the finalized financial statement from each project. Variables directly collected from financial statements included the characteristics of each program, the country in which the program was executed, a brief description of the program's primary activities (i.e. community-based screening, scale-up of previous concept studies, testing of new sample transport or drug delivery systems, etc.), detail regarding the program's target population (i.e. general population, gender-based or geographical subpopulations, etc.), as well as reported measures of costs incurred. For each project, all financial items reported, including total budget, income received, and cumulative expenditure, were extracted separately and reported in US dollars (not shown).

We also included subgroupings within each activity category to allow for further costing sub-analyses. These subgroupings include: 1. Technology Innovation, 2. Public-Private Partnerships (or Private Sector Involvement), 3. Hard-to-reach Populations (e.g. villages, camps, geographically isolated regions), 4. Pregnant Women or Pediatric Cases, and 5. Door-to-Door Screening. We also noted the projects that supplied or linked patients to preventive therapy (See Table 2).

Additionally, we extracted data on program service outputs, including number of people diagnosed with any type of TB, number of people started on TB treatment (notifications), and number of TB patients successfully treated (See Tables 3, S1 and S2).

Data Analysis: In order to develop a standardized and comparative analytic framework that could be used in the retrospective evaluation of various multi-dimensional TB control programs, we categorized programs based on their respective WHO regions, national GDP per capita (reported in 2017 US dollars), and program setting (urban versus rural/remote). Based on a review of all TB REACH wave 5 projects, we defined three types of programmatic activities— 1. Case Finding, 2. Treatment, and 3. Other (Non-Case Finding) (See Box 1) —and assigned each program to one or more activity categories[2].

Within screening and treatment categories, we allowed for different permutations of screening, diagnosis and treatment services; available technology (e.g. mobile-health tools for screening, mobile chest X-rays, Xpert MTB/RIF assay); and location of program operations (facility-based, door-to-door screening by community health workers, etc.).

Box 1: Principles and Definitions of activity-based costing categories

Case Finding: Program activities aim to register the target population and screen people with presumptive TB. Activities include population enrollment and systematic symptom screening. Screening may be conducted in community settings through door-to-door visits of households or risk groups (active case finding) or in facility settings through passive surveillance. Screening tools may use a mobile phone or tablet-based platform. Some projects also used mobile diagnostic technologies such as mobile X-ray with computer aided diagnosis (CXR-CAD) and GeneXpert machines installed in mobile vans/trucks. A select few projects also explored use of novel sample transport technologies such as drones to improve case finding. "Case finding only" projects may also provide at-risk patients with preventive therapy; however, they are not directly involved in treatment support or adherence (i.e. intensive patient follow-up).

Treatment: Program activities aim to improve patients' linkage to care post diagnosis (refer patients for treatment initiation) and management of patients' TB treatment. Activities include open access tents which serves as the first stop point in the clinics for patients referred from different part of the clinic or community screening, outpatient care or hospitalization based on the severity of TB conditions, and use of drug adherence and patient management technologies.

The main outcome of our analysis was the cost-effectiveness ratio, calculated as the **total estimated cost**, assessed based on the cumulative expenditure, as reported by each project's Project Annual Review or Grantee Annual Narrative Report, divided by the number of relevant service outputs (**beneficiaries served**). Assuming that the service output in the population of interest would otherwise be zero, this cost-effectiveness ratio can be conceptualized as the incremental cost-effectiveness ratio (ICER) relative to a "no-activity" standard of care. In summarizing cost-effectiveness ratios across multiple programs, we calculated an average cost-effectiveness ratio across all contributing programs (i.e., total cost of all programs divided by total beneficiaries served). This is

equivalent to a weighted average of each program's cost-effectiveness ratio, weighted by the number of beneficiaries.

Box 2: Example project - CIDRZ

Brief project descriptions: Aims to perform community mobilization via educational campaigns and TB messaging; and compare community-based versus facility-based TB screening.

Types of programs: Mobile truck installed with Chest X-ray with the Computer Aided Diagnosis (CAD) software (CAD-CXR), community-based events and door-to-door patient screening, clinic-based Open Access tent (to facilitate patient referral process for TB services for those identified within the clinic and from the communities), and laboratory-based Xpert MTB/RIF testing

Key project yield estimates:

1. Total number of presumptive TB patients identified: 6,707
2. Total number of TB patients diagnosed by the project: 1,030
3. Total number of TB patients initiated on treatment: 1,027

Key cost estimates:

#	Cost parameter	Costs	Notes
1	Total reported project expenditure	$722,266	Includes operational research costs
2	Cost of operational research	$223,334	Subtracted
3	Total project minus operational costs	$498,932	Main estimate used to calculate the cost-effectiveness ratio
4	Total cost for case-finding efforts	$432,511	Apportioned cost of #3 by 6,707 / (6,707 + 1,030)

Calculation of cost-effectiveness ratio:

1. Case finding (cost per TB patient diagnosed by project): $420
2. Treatment linkage (cost per diagnosed TB patient initiated on treatment): $486
3. Treatment management (cost per TB patient completing treatment): Not Applicable

For our primary analysis, cumulative expenditure was defined as the total cost of human resources, program activities, procurement of medical items, procurement of non-medical items, and direct program support, minus the cost of operational research (as specified in each project's financial statement). In cases where data on cumulative expenditure was limited, we used income reported by each program. We assessed the cost-effectiveness ratios for the following three key programmatic outputs: number of TB cases diagnosed, TB cases initiated on TB treatment and TB patients successfully completing treatment. Cost-effectiveness ratios were calculated for projects individually, and (as described above) as weighted averages across projects conducting similar activities (e.g. projects solely focusing on case finding).

For certain outcomes, costs were apportioned to relevant activity categories based on ratios of programmatic outputs. Programs with multiple objectives (i.e. treatment initiation and adherence) as opposed to case finding only were weighed more heavily in terms of resource distribution. Costs to these additional objectives were based on the number of patients started on treatment (patient volumes). In this way, under the general categories of activity grouping (see Box 1), the various resource cost components were allocated to the relevant implementation stages and operational activities, allowing for better visibility in the identification of cost drivers from the perspective of program management[2].

Wave 5 projects that did not report relevant cost or patient yield data to TB REACH were excluded from the study. After consultation with TB REACH technical officers, three additional projects were excluded from the analysis. The first project (NTRL, EPHI) was a lab-based assessment of a novel transport and decontaminating reagent for TB testing, called OMNIgene® SPUTUM. The second project (Ifakara Health Institute) intended to assess the use of Xpert Omni /Xpert MTB Ultra cartridges. However, these cartridges were unavailable during the wave 5 funding cycle; therefore, the project was not able to begin activities. The third project (AIGHD) aimed to establish TB screening in HIV community testing program and was also postponed.

Sensitivity analyses were performed by varying the total costs, as well as each of the different service outputs, by +/-25% independently for each program to evaluate the potential sensitivity of the results to those outcomes. This was done for programs conducting case finding only activities, as well as programs conducting case finding and treatment-related activities.

Results

Of the 29 remaining projects that were supported by the TB REACH wave 5 funding cycle, 11 were case finding only projects and 18 focused on both case finding and treatment. Two also focused on technology. Among the projects with multiple objectives, 9 included

treatment follow-up beyond initiation. Most projects were implemented in the African region or South-East Asia region, accounting for 12 (41%) and 9 (31%) of the total respectively. Considering the project setting, 10 were implemented in rural areas, and the other 19 focused on urban settings. In addition, 11 projects specifically targeted highly vulnerable populations (e.g. IDPs, children, miners, female sex workers, PLWH, pregnant women, etc.) (See Table 1).

The mean cost-effectiveness ratio for case finding was $184 per TB case identified across all projects. For projects that included activities beyond case finding, the average cost-effectiveness ratio per treatment initiation was $332. Projects that extended programmatic efforts toward treatment adherence were estimated to cost $40 per TB patient completing the treatment. Six projects were identified as programs with cost-effectiveness ratios falling above a $1,000-per-case-detected threshold. Two of these projects – NAANK and ASOCI – were implemented in upper-middle income countries. Only four projects (CHEAS, IRDSA, FUNDA, and GLOHI) had an estimated cost per case diagnosed higher than the corresponding country's per-capita GDP (See Table 3).

The cost-effectiveness ratio per TB case detected ranged from $30 (TBALI) to 10,497 (IRDSA). The results also varied with different characteristics of the project operations and settings. Projects that included both case finding and treatment support had higher costs per case detected, on average, than projects focused only on case finding. Among the projects with multiple objectives, five managed to initiate treatment for all cases diagnosed. Projects in urban settings similarly tended to have higher cost-effectiveness ratios than those in rural contexts. Moreover, the cost-effectiveness ratios of projects in the African region were generally higher than of projects performed in Southeast Asia. (See Fig. 1).

We also evaluated cost-effectiveness ratios of projects categorized into five subgroups defined on the basis of readily identifiable characteristics based on the project reports (see Table S4). The average cost-effectiveness ratio per TB case diagnosed was $169 for projects involved in technology innovation, $68 for projects involving the private sector, $187 for projects serving hard-to-reach populations, $192 for projects targeting pregnant women and pediatric cases, and $361 for projects conducting door-door screening.

Among all eligible projects, nine explicitly mentioned the provision of preventive therapy (see Table 2). The cost of preventive therapy operations was not explicitly reported; thus, a cost-effectiveness ratio for provision of preventive therapy could not be calculated.

Sensitivity analysis

Variation in effectiveness estimates tended to have greater influence on estimated cost-effectiveness ratios than variation in costs. Varying both costs and outcomes by +/- 25% did not affect on the characterization of projects as cost-effective (based on a cost per

case diagnosed below a threshold of GDP per capita), with the sole exception of the ACREO project, which fell above this threshold when total costs increased or case detection decreased by 25%. (See Tables S1 and S2.)

Discussion

In this study, we developed a standardized framework for evaluating the cost-effectiveness of case-finding and treatment support programs funded through the TB REACH wave 5 funding cycle. Based on our results, we found a wide diversity of cost-effectiveness ratios across projects. These findings suggest that TB case finding has the potential to be highly cost-effective in a variety of settings. However, there were no clearly demarcating characteristics suggesting that specific subtypes of projects were more cost-effective than others. Thus, for TB case finding projects to be cost-effective, appropriate adaptation to the local context is critical.

Of 29 eligible TB REACH funded projects, 86.2% (25 projects) were able to diagnose people with TB within a cost-effectiveness threshold of GDP per capita for each setting, though determinants of cost-effectiveness were context-specific. For example, cost-effectiveness ratios were high for projects implemented in urban settings compared to those implemented in the rural areas. As expected, projects with multiple objectives and projects carried out in higher-income countries had a higher cost per detection compared to those projects with a single case-finding objective and those performed in lower-income settings. Furthermore, the cost of treatment support was generally lower than the cost to diagnose a TB case.

In this study, we used the budgets and outcomes directly drawn from the Stop TB Partnership databases from which the data extracted using standard systematic review process. Likewise, our method facilitates comparison across projects can also be applied for other grant wave cycles for comparisons of cost-effectiveness and trends across different funding cycles. To assess the validity of our analysis, we compared our estimates with the results from a recent study by Jo et al[9] which evaluated the costs and cost-effectiveness of the comprehensive ACF program in Zambia conducted by CIDRZ, one of the wave 5 grantees. In that study, Jo and colleagues used a much more detailed approach in evaluating costs of each programmatic component using a standardized data collection and analysis tool and reported a cost of $435 per patient initiating on treatment who diagnosed by all types of method, including Xpert[7]. For patients who were diagnosed exclusively on Xpert testing algorithm, the study reported $755 per patient diagnosed and initiated on treatment[9]. Our simplified budget/finance statement-based calculation of the cost-effectiveness ratio for this project was $420 per TB case diagnosed and $486 per patient initiating on treatment; thus, showed a good agreement.

Four projects were identified as having higher than average cost-effectiveness ratios: CHEAS, IRDSA, FUNDA, and GLOHI. These projects each confronted major operational difficulties during implementation, which could explain the projects' diminished cost-

effectiveness compared to other projects. CHEAS stated significant implementation delay owing to human resource crises and political unrest in the evaluation report. IRDSA reported challenges in making household visits (threatened by unexpected security problems) and a lower-than-expected number of patients with undiagnosed TB seeking services in the clinics. By contrast, GLOHI noted that TB incidence in their region may have been overestimated and underlying population sizes underestimated. Another issue related to small numbers of TB cases is that GLOHI, as a project using drones for observed therapy, came across multiple technical failures in drone usage, which hindered efficiency and implementation. The FUNDA project was reported as heavily delayed due to the need to receive ethical approval. It is assumed that missing cases manifested as fewer case notifications reported compared with the estimated incidence of TB for Mozambique. Such logistical challenges speak to the performance of a variety of projects undertaken in real-world settings and the resulting variation in cost-effectiveness that will likely be observed in actual implementation of TB case-finding activities. However, these project-specific findings should not be interpreted as favoring one intervention over another – as such barriers to implementation are generally unexpected and often not related to the actual type of intervention performed.

There are several limitations to this analysis. First, we used simplified apportionment criteria to allocate total costs for major programmatic activities only: case finding, treatment initiation (linkage to care), and treatment management. This was largely due to the type of data that was available and the overall scope of our analysis. Given the growing complexity of ACF interventions and the importance of understand costs of implementation process, individual project level engagement of cost assessment using the standardized costing approach is recommended to evaluate costs and cost drivers of each program[7,10,11]. Second, we did not use estimates of health utility such as QALYs and DALYs, as conversion from cases detected to these measures is inherently context-specific. Therefore, our study findings may not be comparable to programs with other epidemiologic targets. However, our effectiveness measure may be more readily measurable and can be compared to cost-per-DALY estimates using standardized published tools.[3] Third, the main outcome we measured was related to case-finding, which was often considered as an intermediate step in the TB cascade of care. Future research should examine adherence and future health benefits as well. Finally, one important aspect of active case finding that was not deeply explored in this analysis was the provision of preventive therapy. TB preventive therapy has the potential to substantially increase the impact of case finding activities on long-term TB incidence and can be cost-effective; however, it is generally challenging to separate the costs of providing preventive therapy from the costs of case finding, as part of providing PT is ruling out active TB disease[12]. As such, we did not attempt to separate out these costs nor were they reported separately. Future investigations should compare the cost-effectiveness of projects engaged in case finding alone to projects with objectives beyond case finding.

Conclusions

Our study demonstrates that costs of ACF interventions are highly heterogeneous, which reflects the diversity of the programmatic approach and design, target population, types of settings and regions in which the interventions are implemented. We also provide a systematic approach in evaluating relative cost-effectiveness of ACF interventions funded through the TB REACH initiative. As such, our methods can be extended to projects beyond wave 5 funding cycle as well as other institutions that fund similar initiatives and this will help establish larger systematic databases on cost and cost-effectiveness of ACF interventions. As ACF interventions become more innovative and complex to close gaps – both in term of use of technology and process – in the TB care cascade beyond TB case detection, more efforts in establishing higher resolution data that can provide improved understanding of costs and cost-effectiveness of ACF interventions are urgently needed.

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Tables and Figures

Table 1. Project characteristics and description.

#[a]	Project Code	Project Title	Region[b]	Setting (Target Population)[c]	Project Type[d]	Country	GDP per capita (2017)	Total Expenditure	Project Description
A1	**HEAAI**	Health Alliance International	AFRO	Urban	Casefinding and Other (Non-Case Finding)	Mozambique	$461	$527,978	Aims to improve TB linkage-to-care by scaling up diagnostic and lab connectivity technologies and creating a comprehensive national electronic MDR-TB testing database.
A2	**GOMSA**	GomSACA	AFRO	Rural (Internally Displaced Persons)	Casefinding	Nigeria	$1,969	$337,109	Aims to promote TB/HIV awareness and improve case detection and linkage-to-care among Internally Displaced Persons by engaging community volunteers and organizations.
A3	**CIDRZ**	CIDRZ	AFRO	Urban	Casefinding	Zambia	$1,535	$722,266	Aims to perform community mobilization via educational campaigns and TB messaging; and compare community-based versus facility-based TB screening.
A4	**SHDEP**	SHDEPHA +kAHAMA	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	Casefinding and Treatment	Tanzania	$1,005	$295,736	Aims to conduct community outreach TB case finding in the general population, focusing on children, female sex workers, small-scale miners and MSM via door-to-door sputum collection.
A5	**LSTME**	LSTM	AFRO	Rural	Casefinding and Treatment	Ethiopia	$768	$192,504	Aims to expand program that engages government-employed female Health Extension Workers in conducting community TB case finding in rural areas.
A6	**CHEAS**	Center for Health Solutions	AFRO	Urban (Children)	Casefinding	Kenya	$1,568	$873,335	Aims to build healthcare worker capacity in the management of pediatric TB (involves a pilot project of the naso-pharyngeal aspirate procedure).
A7	**GLRAN**	GLRA	AFRO	Urban (Mothers, HIV patients, Outpatients)	Casefinding and Treatment	Nigeria	$1,969	$164,520	Aims to improve case detection and contact tracing in MNCH clinics, PLHIV/ART clinics and outpatient clinics; and improve access to TB diagnostic services and access to DOTS.
A8	**LSTMN**	LSTM	AFRO	Urban	Casefinding	Nigeria	$1,969	$178,605	Aims to engage proprietary patent medicine vendors in enrolling participants and notifying community healthcare workers, who then conduct at-home/on-site testing and treatment initiation.

A9	**FUNDA**	Fundacao Manhica	AFRO	Urban	Casefinding	Mozambique	$461	$315,064	Aims to screen TB/HIV household and social contacts, perform Xpert Ultra across samples, and follow up with chest X-rays and clinical visits for presumptive cases.
A10	**IRDSA**	IRD FZC / IRD South Africa	AFRO	Urban (Children, Pregnancy)	Casefinding	South Africa	$6,133	$325,415	Aims to improve TB case finding, linkage-to-care and treatment uptake among children and pregnancy TB cases.
A11	**NAANK**	N/a'an ku sê Foundation - Lifeline Clinic	AFRO	Rural	Casefinding and Treatment	Namibia	$5,647	$51,576	Aims to improve TB detection and reduce loss to follow up, catastrophic costs and TB mortality in health camps.
A12	**GLOHI**	Global Health Institute	AFRO	Rural	Casefinding and Treatment, and Other (Non-Case Finding)	Madagascar	$515	$282,754	Aims to conduct TB screening and testing in remote areas via community healthcare workers, human porters and drones.
E1	**MERCY**	Mercy Corps	EMRO	Urban	Casefinding	Pakistan	$1,465	$295,048	Aims to engage a provincial female health worker program to set up house-to-house TB screening and to facilitate referrals to health facilities.
E2	**ACREO**	ACREOD	EMRO	Urban (Women)	Casefinding	Afghanistan	$556	$293,980	Aims to improve TB awareness and TB screening programs via gender-sensitive, mobile TB screening services.
E3	**BRICF**	Bridge Consultants Foundation	EMRO	Urban (Transgender People, Male Sex Workers)	Casefinding and Treatment	Pakistan	$1,465	$239,703	Aims to train outreach workers in active case finding and improving linkage-to-care in transgender people and male sex workers.
P1	**ASOCI**	Asociacion Benefica PRISMA	PARO	Urban	Casefinding and Treatment	Peru	$6,711	$353,897	Aims to train "TB finders" in community case finding activities and providing peer support to newly diagnosed TB patients.
S1	**ICCDR**	ICDDR	SEARO	Urban	Casefinding	Bangladesh	$1,564	$783,292	Aims to expand a private-sector TB screening program, which involves conducting chest X-rays and using the revenue to subsidize the operational costs, diagnostic testing and treatment.
S2	**REACH**	REACH	SEARO	Urban	Casefinding	India	$1,981	$934,125	Aims to engage the private sector (practitioners, hospitals and pharmacies) in TB control through incentives; and to encourage the notification of missing TB patients across urban settings.
S3	**TBALI**	TB Alert India	SEARO	Urban	Casefinding	India	$1,981	$170,735	Aims to map private sector resources and establish one-stop diagnostic hubs with Xpert testing to improve case detection.

S4	**ASHAK**	Asha Kalp	SEARO	Rural (Indigenous populations)	Casefinding and Treatment	India	$1,981	$321,924	Aims to strengthen community-based TB screening, sample transportation and follow up care services provided by lay health workers.
S5	**INNOV**	Innovators in Health	SEARO	Rural	Casefinding and Treatment	India	$1,981	$308,777	Aims to conduct door-to-door screening in rural areas and minimize loss to follow up by supporting TB patients throughout the care cascade.
S6	**BNMTN**	BNMT Nepal	SEARO	Rural (High Risk populations)	Casefinding and Treatment	Nepal	$911	$534,740	Aims to increase case notification of remote or high-risk populations via contact tracing in TB health camps and outpatient screening in district hospitals using GeneXpert.
S7	**OPASH**	Operation ASHA	SEARO	Rural	Casefinding and Treatment	India	$1,981	$321,924	Aims to improve TB case detection at non-functional medical centers in a mountainous region via area mapping, sputum collection and transport, and recruitment of samples to labs.
S8	**MAPIN**	MAP International	SEARO	Rural	Casefinding	Indonesia	$3,837	$341,921	Aims to raise TB awareness and facilitate linkage-to-care, TB treatment and follow-up care for patients in remote island communities.
S9	**RUMAH**	Rumah Sakit Islam	SEARO	Urban (Children)	Casefinding and Treatment	Indonesia	$3,837	$188,183	Aims to conduct pediatric TB case finding, which includes screening, contact investigation and reverse contact investigation via mobile X-rays and sputum induction.
W1	**CATAC**	CATA	WPRO	Rural (Elderly population)	Casefinding and Treatment	Cambodia	$1,386	$425,709	Aims to implement a mobile/roving active case finding initiative targeted towards the elderly population and to fund treatment at health facilities.
W2	**KHANA**	KHANA	WPRO	Urban	Casefinding and Treatment	Cambodia	$1,386	$357,965	Aims to implement and evaluate three community-based case finding strategies.
W3	**VNTPV**	VNTP	WPRO	Urban	Casefinding and Treatment	Vietnam	$2,366	$766,510	Aims to conduct household and social contact investigation, door-to-door community screening, facility-based screening at hospitals, and post-exposure therapy.
W4	**FITVT**	FIT	WPRO	Urban	Casefinding and Treatment	Vietnam	$2,366	$137,008	Aims to build the capacity of private sector providers to increase case notification and to integrate private sector TB treatment into national notification data.

a. Numbering code is assigned considering the scale of the project and the region. The letter represents the region where the project was implemented, and the number is aligned with the ordering of number of patients diagnosed, which is taken as the benchmark of project size.
b. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
c. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
d. Projects are considered as treatment related when they include treatment initiation or/and adherence activities.

Table 2. Projects description by subgroups.

#	Project Code	Bullet List
Technology		
A1	**HEAAI**	- linked technology (GeneXpert machines to GxAlert), created a DR-TB result database, piloted video conferencing and telementoring platform
A3	**CIDRZ**	- used CAD CXR, PAD based system, and electronic registry
A7	**GLRAN**	- used SMS for test result transmission
A9	**FUNDA**	- used Xpert Ultra in the ACF package
A10	**IRDSA**	- used mhealth app in case-finding
A12	**GLOHI**	- used drones, evriMED devices (pillbox dispenser) and Open Data Kit (ODK) with tablets
S2	**REACH**	- applied e-health to support case-finding
S3	**TBALI**	- used ehealth to support case-finding
S9	**RUMAH**	- used mobile phone screening software
W1	**CATAC**	- deployed new mobile Xpert Ultra/CXR systems
PPM (private sector involvement)		
A8	**LSTMN**	- engaged patent medicine vendors
S1	**ICDDR**	- organized training and network for private providers, health workers and DOTS facilities
S2	**REACH**	- engaged private sectors in case-finding, notification, and linkage to care
S3	**TBALI**	- targeted private provider attendees for case-finding
W4	**FITVT**	- trained private providers for diagnosis, notification, referral, treatment and follow-up
Hard-to-reach populations (villages, camps, isolated regions)		
A2	**GOMSA**	- conducted screening and contact tracing among internally displaced populations in camps and child contacts
A12	**GLOHI**	- conducted activities at village levels (using drones)
E1	**MERCY**	- served patients in chest camps and community support groups
S4	**ASHAK**	- CHWs conduced oral screening and sputum collection in tribal villages
S9	**RUMAH**	- conducted activities at village level
W1	**CATAC**	- conducted active case finding among elderly (55+) in villages
W2	**KHANA**	- community leaders conducted snowball active case finding in villages
Pregnant women/pediatric TB cases		
A1	**HEAAI**	- served pediatric cases
A2	**GOMSA**	- included pediatric cases (children under 6)
A3	**CIDRZ**	- included children in target population
A4	**SHDEP**	- included children in target populations
A6	**CHEAS**	- served pediatric cases (children aged 0-14)
A10	**IRDSA**	- served both women and pediatric cases
A11	**NAANK**	- attended to pediatric cases (testing via gastric aspirates)
E2	**ACREO**	- included pregnant women in patient population

S1	**ICDDR**	- served pediatric cases
S8	**MAPIN**	- health promoters conducted screening at schools and in households to find pediatric cases
S9	**RUMAH**	- served pediatric cases
W2	**KHANA**	- included pediatric TB cases
W3	**VNTPV**	- served pediatric cases
Door-door screening		
A3	**CIDRZ**	- conducted door-to-door visits
A4	**SHDEP**	- conducted door-to-door screening in rural communities
S5	**INNOV**	- CHWs conducted door-to-door screening and TB diagnosis in rural areas
S8	**MAPIN**	- conducted door-door screening
W3	**VNTPV**	- conducted door-to-door verbally screening strategy
Provision of preventive therapy[a]		
A3	**CIDRZ**	- These projects indicated provision of TB preventive therapy, but did not specify how this was operationalized nor provided number of patients to whom TPT was provided.
A4	**SHDEP**	
A6	**CHEAS**	
A7	**GLRAN**	
A9	**FUNDA**	
A10	**IRDSA**	
S9	**RUMAH**	
P1	**ASOCI**	
W3	**VNTPV**	

Table 3. Case-finding outcome and cost-effectiveness ratio of TB REACH Wave 5 projects by project type.

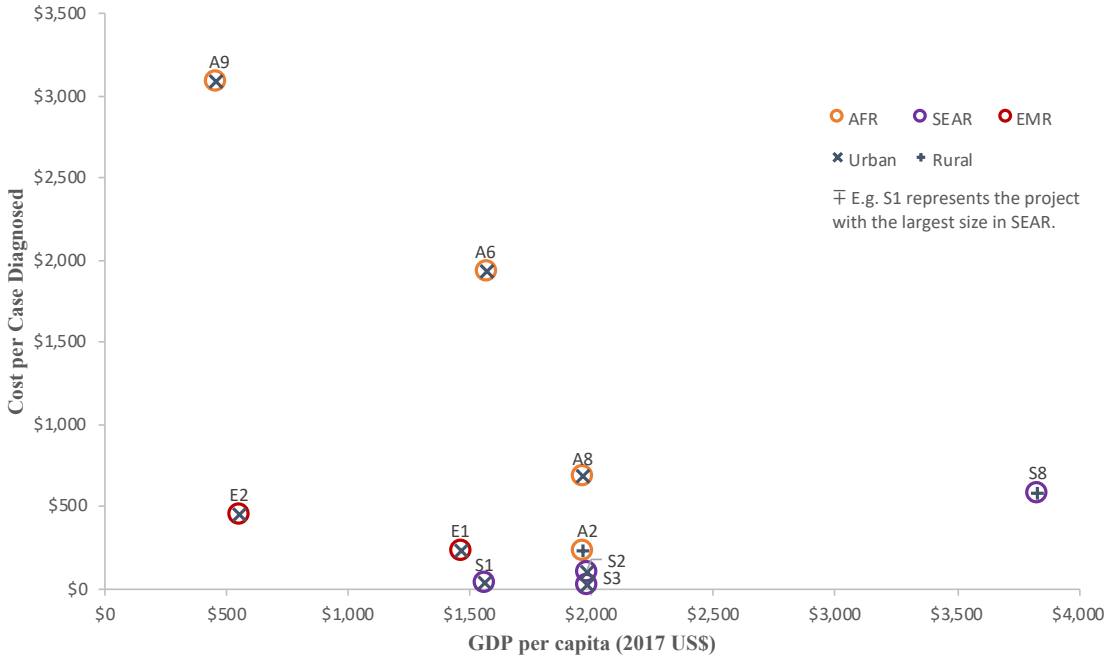
#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Diagnosed	Cost per Case Diagnosed[c]
Case-finding only Project						
S3	**TBALI**	SEAR	Urban	$170,735	5,765	$30
S1	**ICCDR**	SEAR	Urban	$783,292	17,100	$46
S2	**REACH**	SEAR	Urban	$934,125	8,675	$108
E1	**MERCY**	EMR	Urban	$269,388	1,165	$231
A2	**GOMSA**	AFR	Rural (Internally Displaced Persons)	$335,312	1,423	$236
E2	**ACREO**	EMR	Urban (Women)	$287,080	626	$459
S8	**MAPIN**	SEAR	Rural	$341,921	581	$589
A8	**LSTMN**	AFR	Urban	$170,594	247	$691
A6	**CHEAS**	AFR	Urban (Children)	$852,498	440	$1,937
A9	**FUNDA**	AFR	Urban	$306,335	99	$3,094
A10	**IRDSA**	AFR	Urban (Children, Pregnancy)	$325,415	31	$10,497
Average cost ratio						$132
Project with case-finding and treatment initiation						
S4	**ASHAK**	SEAR	Rural (Indigenous populations)	$269,670	2,626	$103
A5	**LSTME**	AFR	Rural	$167,519	599	$280
S9	**RUMAH**	SEAR	Urban (Children)	$165,645	532	$311
S7	**OPASH**	SEAR	Rural	$268,708	648	$415
A3	**CIDRZ**	AFR	Urban	$432,511	1,030	$420
A7	**GLRAN**	AFR	Urban (Mothers, HIV patients, Outpatients)	$146,241	334	$438
W3	**VNTPV**	WPR	Urban	$715,774	1,400	$511
W4	**FITVT**	WPR	Urban	$126,339	171	$739
A12	**GLOHI**	AFR	Rural	$227,997	23	$9,913
Average cost ratio						$342
Project completed treatment						
W1	**CATAC**	WPR	Rural (Elderly population)	$393,924	2,801	$141
W2	**KHANA**	WPR	Urban	$245,619	1,620	$152
S5	**INNOV**	SEAR	Rural	$276,568	1,730	$160
A1	**HEAAI**	AFR	Urban	$412,494	1,516	$272

A4	**SHDEP**	AFR	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$279,082	922	$303
E3	**BRICF**	EMR	Urban (Transgender People, Male Sex Workers)	$222,230	625	$356
S6	**BNMTN**	SEAR	Rural (High Risk populations)	$463,257	1,092	$424
A11	**NAANK**	AFR	Rural	$49,335	24	$2,056
P1	**ASOCI**	PAR	Urban	$303,919	94	$3,233
Average cost ratio						$254
Average cost ratio (All Projects)						$184

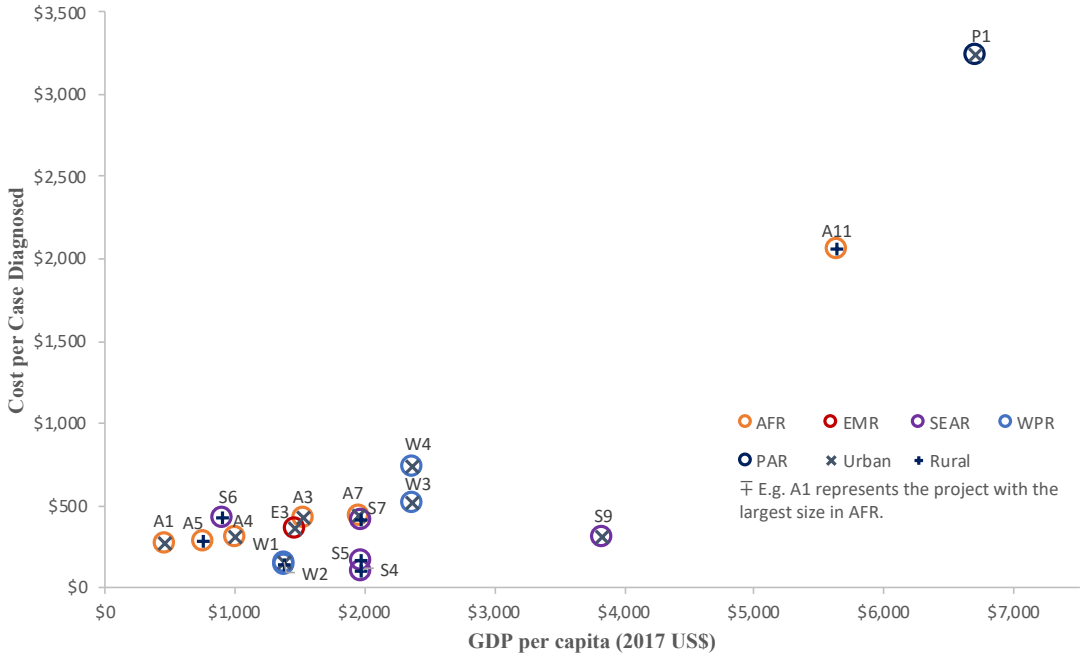
a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
c. Cost per case diagnosed is calculated as respective case-finding costs divided by a number of patients diagnosed.

Figure 1. Cost-effectiveness (cost per case diagnosed) of TB REACH Wave 5 projects focused on a) case-finding only and b) case-finding and treatment support. This plot illustrates the cost-effectiveness ratio (2017 US dollars per case of tuberculosis diagnosed) associated with projects, according to the gross domestic product (GDP) per capita in each corresponding country. Letters represent the geographic region in which the projects were performed, and numbers order projects from largest (1) to smallest within each region. In each panel, there was one project that was not shown because its associated cost-effectiveness ratio was exceptionally high (Panel A, project A10, cost per case diagnosed $10,497, GDP per capita: $6,133; Panel B, project A12, cost per case diagnosed $9,913, GDP per capita: $515).

a)



b)


$3,500
$3,000
$2,500
$2,000
$1,500
$1,000
$500
$0
Cost per Case Diagnosed
$0
$1,000
$2,000
$3,000
$4,000
$5,000
$6,000
$7,000
GDP per capita (2017 US$)
P1
A11
W4
W3
S6
A3
A7
S7
E3
A1
A5
A4
W1
S5
S4
W2
S9
AFR
EMR
SEAR
WPR
PAR
Urban
Rural
∓ E.g. A1 represents the project with the largest size in AFR.

Supplementary Materials

Table S1. Treatment initiation outcome and cost-effectiveness ratio of TB REACH Wave 5 projects by project type.

#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Started on Treatment	Cost per Case Initiated Treatment[c]
Project with case-finding and treatment initiation						
S4	**ASHAK**	SEAR	Rural (Indigenous populations)	$321,924	2,626	$123
A5	**LSTME**	AFR	Rural	$192,259	599	$321
S9	**RUMAH**	SEAR	Urban (Children)	$188,183	520	$362
A3	**CIDRZ**	AFR	Urban	$498,932	1027	$486
A7	**GLRAN**	AFR	Urban (Mothers, HIV patients, Outpatients)	$157,890	319	$495
S7	**OPASH**	SEAR	Rural	$321,924	648	$497
W3	**VNTPV**	WPR	Urban	$726,634	1,139	$638
W4	**FITVT**	WPR	Urban	$130,135	165	$789
A12	**GLOHI**	AFR	Rural	$243,985	23	$10,608
Average cost ratio						$394
Project completed treatment						
W1	**CATAC**	WPR	Rural (Elderly population)	$414,704	2,669	$155
S5	**INNOV**	SEAR	Rural	$308,777	1,641	$188
W2	**KHANA**	WPR	Urban	$316,420	1,614	$196
A1	**HEAAI**	AFR	Urban	$491,441	1,507	$326

A4	**SHDEP**	AFR	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$295,736	863	$343
E3	**BRICF**	EMR	Urban (Transgender People, Male Sex Workers)	$237,799	614	$387
S6	**BNMTN**	SEAR	Rural (High Risk populations)	$481,011	1,061	$453
A11	**NAANK**	AFR	Rural	$51,528	24	$2,147
P1	**ASOCI**	PAR	Urban	$309,155	72	$4,294
Average cost ratio						$289
Average cost ratio (All Projects)						$332

a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
c. Cost per treatment initiation is calculated as total project costs divided by a number of patients initiated on treatment.

Table S2. Treatment completion outcome and cost-effectiveness ratio of TB REACH Wave 5 projects (with treatment support costs).

#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Completed Treatment	Cost per Case Completed Treatment[c]
Project completed treatment						
W1	**CATAC**	WPR	Rural (Elderly population)	$20,780	2,634	$8
S6	**BNMTN**	SEAR	Rural (High Risk populations)	$17,754	631	$28
E3	**BRICF**	EMR	Urban (Transgender People, Male Sex Workers)	$15,569	552	$28
S5	**INNOV**	SEAR	Rural	$32,209	1,099	$29
W2	**KHANA**	WPR	Urban	$70,801	839	$84
P1	**ASOCI**	PAR	Urban	$5,236	57	$92
A4	**SHDEP**	AFR	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$16,654	122	$137
A11	**NAANK**	AFR	Rural	$2,193	15	$146
A1	**HEAAI**	AFR	Urban	$78,947	494	$160
Average cost ratio						$40

a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
c. Cost per treatment completed is calculated as respective treatment support costs divided by a number of patients completed treatment.

Table S3. Treatment completion outcome and cost-effectiveness ratio of TB REACH Wave 5 projects (with total costs).

#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Completed Treatment	Cost per Case Completed Treatment[c]
Project completed treatment						
W1	**CATAC**	WPR	Rural (Elderly population)	$414,704	2,634	$157
S5	**INNOV**	SEAR	Rural	$308,777	1,099	$281
W2	**KHANA**	WPR	Urban	$316,420	839	$377
E3	**BRICF**	EMR	Urban (Transgender People, Male Sex Workers)	$237,799	552	$431
S6	**BNMTN**	SEAR	Rural (High Risk populations)	$481,011	631	$762
A1	**HEAAI**	AFR	Urban	$491,441	494	$995
A4	**SHDEP**	AFR	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$295,736	122	$2,424
A11	**NAANK**	AFR	Rural	$51,528	15	$3,435
P1	**ASOCI**	PAR	Urban	$309,155	57	$5,424
Average cost ratio						$451

a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).

b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.

c. Cost per treatment completed is calculated as total project costs divided by a number of patients completed treatment.

Table S4. Case-finding outcome and cost-effectiveness ratio of TB REACH Wave 5 projects by subgroups.

#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Diagnosed	Cost per Case Diagnosed[c]
Technology						
S3	**TBALI**	SEARO	Urban	$170,735	5,765	$30
S2	**REACH**	SEARO	Urban	$934,125	8,675	$108
W1	**CATAC**	WPRO	Rural (Elderly population)	$393,924	2,801	$141
A1	**HEAAI**	AFRO	Urban	$412,494	1,516	$272
S9	**RUMAH**	SEARO	Urban (Children)	$165,645	532	$311
A3	**CIDRZ**	AFRO	Urban	$432,511	1030	$420
A7	**GLRAN**	AFRO	Urban (Mothers, HIV patients, Outpatients)	$146,241	334	$438
A9	**FUNDA**	AFRO	Urban	$306,335	99	$3,094
A12	**GLOHI**	AFRO	Rural	$227,997	23	$9,913
A10	**IRDSA**	AFRO	Urban (Children, Pregnancy)	$325,415	31	$10,497
Average cost ratio						$169
PPM (private sector involvement)						
S3	**TBALI**	SEARO	Urban	$170,735	5,765	$30
S1	**ICDDR**	SEARO	Urban	$783,292	17,100	$46
S2	**REACH**	SEARO	Urban	$934,125	8,675	$108
A8	**LSTMN**	AFRO	Urban	$170,594	247	$691
W4	**FITVT**	WPRO	Urban	$126,339	171	$739
Average cost ratio						$68
Hard-to-reach populations (villages, camps, isolated regions)						
S4	**ASHAK**	SEARO	Rural (Indigenous populations)	$269,670	2,626	$103
W1	**CATAC**	WPRO	Rural (Elderly population)	$393,924	2,801	$141
W2	**KHANA**	WPRO	Urban	$245,619	1,620	$152

E1	**MERCY**	EMRO	Urban	$269,388	1,165	$231
A2	**GOMSA**	AFRO	Rural (Internally Displaced Persons)	$335,312	1,423	$236
S9	**RUMAH**	SEARO	Urban (Children)	$165,645	532	$311
A12	**GLOHI**	AFRO	Rural	$227,997	23	$9,913
Average cost ratio						$187
Pregnant women/pediatric TB cases						
S1	**ICDDR**	SEARO	Urban	$783,292	17,100	$46
W2	**KHANA**	WPRO	Urban	$245,619	1,620	$152
A2	**GOMSA**	AFRO	Rural (Internally Displaced Persons)	$335,312	1,423	$236
A1	**HEAAI**	AFRO	Urban	$412,494	1,516	$272
A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$279,082	922	$303
S9	**RUMAH**	SEARO	Urban (Children)	$165,645	532	$311
A3	**CIDRZ**	AFRO	Urban	$432,511	1030	$420
E2	**ACREO**	EMRO	Urban (Women)	$287,080	626	$459
W3	**VNTPV**	WPRO	Urban	$715,774	1,400	$511
S8	**MAPIN**	SEARO	Rural	$341,921	581	$589
A6	**CHEAS**	AFRO	Urban (Children)	$852,498	440	$1,937
A11	**NAANK**	AFRO	Rural	$49,335	24	$2,056
A10	**IRDSA**	AFRO	Urban (Children, Pregnancy)	$325,415	31	$10,497
Average cost ratio						$192
Door-door screening						
S5	**INNOV**	SEARO	Rural	$276,568	1,730	$160
A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$279,082	922	$303

A3	**CIDRZ**	AFRO	Urban	$432,511	1030	$420
W3	**VNTPV**	WPRO	Urban	$715,774	1,400	$511
S8	**MAPIN**	SEARO	Rural	$341,921	581	$589
Average cost ratio						$361
Average cost ratio (All Projects)						$184

a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
c. Cost per case diagnosed is calculated as respective case-finding costs divided by a number of patients diagnosed.

Table S5. Treatment initiation outcome and cost-effectiveness ratio of TB REACH Wave 5 projects by subgroups.

#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Started on Treatment	Cost per Case Initiated Treatment[c]
Technology						
W1	**CATAC**	WPRO	Rural (Elderly population)	$414,704	2,669	$155
A1	**HEAAI**	AFRO	Urban	$491,441	1,507	$326
S9	**RUMAH**	SEARO	Urban (Children)	$188,183	520	$362
A3	**CIDRZ**	AFR	Urban	$498,932	1027	$486
A7	**GLRAN**	AFRO	Urban (Mothers, HIV patients, Outpatients)	$157,890	319	$495
A12	**GLOHI**	AFRO	Rural	$243,985	23	$10,608
Average cost ratio						$329
PPM (private sector involvement)						
W4	**FITVT**	WPRO	Urban	$130,135	165	$789
Average cost ratio						$789
Hard-to-reach populations (villages, camps, isolated regions)						
S4	**ASHAK**	SEARO	Rural (Indigenous populations)	$321,924	2,626	$123
W1	**CATAC**	WPRO	Rural (Elderly population)	$414,704	2,669	$155
W2	**KHANA**	WPRO	Urban	$316,420	1,614	$196
S9	**RUMAH**	SEARO	Urban (Children)	$188,183	520	$362
A12	**GLOHI**	AFRO	Rural	$243,985	23	$10,608
Average cost ratio						$199

Pregnant women/pediatric TB cases						
W2	**KHANA**	WPRO	Urban	$316,420	1,614	$196
A1	**HEAAI**	AFRO	Urban	$491,441	1,507	$326
A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$295,736	863	$343
S9	**RUMAH**	SEARO	Urban (Children)	$188,183	520	$362
A3	**CIDRZ**	AFR	Urban	$498,932	1027	$486
W3	**VNTPV**	WPRO	Urban	$726,634	1,139	$638
A11	**NAANK**	AFRO	Rural	$51,528	24	$2,147
Average cost ratio						$384
Door-door screening						
S5	**INNOV**	SEARO	Rural	$308,777	1,641	$188
A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$295,736	863	$343
A3	**CIDRZ**	AFR	Urban	$498,932	1027	$486
W3	**VNTPV**	WPRO	Urban	$726,634	1,139	$638
Average cost ratio						$392
Average cost ratio (All Projects)						$332

a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
c. Cost per treatment initiation is calculated as total project costs divided by a number of patients initiated on treatment.

Table S6. Treatment completion outcome and cost-effectiveness ratio of TB REACH Wave 5 projects by subgroups (regarding treatment support costs).

#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Completed Treatment	Cost per Case Completed Treatment[c]
Technology						
W1	**CATAC**	WPRO	Rural (Elderly population)	$20,780	2,634	$8
A1	**HEAAI**	AFRO	Urban	$78,947	494	$160
Average cost ratio						$32
Hard-to-reach populations (villages, camps, isolated regions)						
W1	**CATAC**	WPRO	Rural (Elderly population)	$20,780	2,634	$8
W2	**KHANA**	WPRO	Urban	$70,801	839	$84
Average cost ratio						$26
Pregnant women/pediatric TB cases						
W2	**KHANA**	WPRO	Urban	$70,801	839	$84
A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$16,654	122	$137
A11	**NAANK**	AFRO	Rural	$2,193	15	$146
A1	**HEAAI**	AFRO	Urban	$78,947	494	$160
Average cost ratio						$115
Door-door screening						
S5	**INNOV**	SEARO	Rural	$32,209	1,099	$29

A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$16,654	122	$137
Average cost ratio						$40
Average cost ratio (All Projects)						$40

a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
c. Cost per treatment completed is calculated as respective treatment support costs divided by a number of patients completed treatment.

Table S7. Treatment completion outcome and cost-effectiveness ratio of TB REACH Wave 5 projects by subgroups (regarding total costs).

#	Project Code	Region[a]	Setting (Target Population)[b]	Apportioned Costs	Number of Patients Completed Treatment	Cost per Case Completed Treatment[c]
Technology						
W1	**CATAC**	WPRO	Rural (Elderly population)	$414,704	2,634	$157
A1	**HEAAI**	AFRO	Urban	$491,441	494	$995
Average cost ratio						$290
Hard-to-reach populations (villages, camps, isolated regions)						
W1	**CATAC**	WPRO	Rural (Elderly population)	$414,704	2,634	$157
W2	**KHANA**	WPRO	Urban	$316,420	839	$377
Average cost ratio						$211
Pregnant women/pediatric TB cases						
W2	**KHANA**	WPRO	Urban	$316,420	839	$377
A1	**HEAAI**	AFRO	Urban	$491,441	494	$995
A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$295,736	122	$2,424
A11	**NAANK**	AFRO	Rural	$51,528	15	$3,435
Average cost ratio						$786
Door-door screening						
S5	**INNOV**	SEARO	Rural	$308,777	1,099	$281

A4	**SHDEP**	AFRO	Urban (General population; Children, Female Sex Workers, Small-Scale Miners, MSM)	$295,736	122	$2,424
Average cost ratio						$495
Average cost ratio (All Projects)						$451

a. Region is grouped by the WHO definition: African Region (AFR), Region of the Americas (PAR), South-East Asia Region (SEAR), European Region (EUR), Eastern Mediterranean Region (EMR), and Western Pacific Region (WPR).
b. Projects are categorized into urban or rural setting based on the primary implementation environments. Targeted population is specified when being emphasized in the TB REACH narrative reports.
c. Cost per treatment completed is calculated as total project costs divided by a number of patients completed treatment.

Table S8. Sensitivity analysis of assessing the effects of total cost and diagnosed case number change on the cost-effectiveness ratio per case diagnosed in case-finding only projects.

Case-finding only Project		Total Cost +/- 25%[a]			Number Diagnosed +/- 25%[b]		
#	Code	Base Value	Low Value	High Value	Base Value	Low Value	High Value
S3	TBALI	$30	$22	$37	$30	$24	$39
S1	ICDDR	$46	$34	$57	$46	$37	$61
S2	REACH	$108	$81	$135	$108	$86	$144
E1	MERCY	$231	$173	$289	$231	$185	$308
A2	GOMSA	$236	$177	$295	$236	$189	$314
E2	ACREO	$459	$344	$573	$459	$367	$611
S8	MAPIN	$589	$441	$736	$589	$471	$785
A8	LSTMN	$691	$518	$863	$691	$553	$921
A6	CHEAS	$1,937	$1,453	$2,422	$1,937	$1,550	$2,583
A9	FUNDA	$3,094	$2,321	$3,868	$3,094	$2,475	$4,126
A10	IRDSA	$10,497	$7,873	$13,122	$10,497	$8,398	$13,996

a. Low and high values represent 25% adjustment in total costs reported by each project, where lower costs correspond to low ratio value.
b. Low and high values represent 25% adjustment in total number of case detection reported by each project, where lower costs correspond to high ratio value.

Table S9. Sensitivity analysis of assessing the effects of total cost, number change on the cost-effectiveness ratio per case diagnosed in projects with multiple objectives.

Project with treatment		Total Cost +/- 25%[a]			Number Diagnosed +/- 25%[b]			Number Treatment Initiated +/- 25%[c]			Number Treatment Completed +/- 25%[d]		
#	Code	Base Value	Low Value	High Value	Base Value	Low Value	High Value	Base Value	Low Value	High Value	Base Value	Low Value	High Value
S4	ASHAK	$103	$77	$128	$103	$79	$143	$123	$98	$163	-	-	-
W1	CATAC	$141	$105	$176	$141	$111	$190	$155	$124	$207	$8	$6	$11
W2	KHANA	$152	$114	$190	$152	$115	$214	$196	$157	$261	$84	$68	$113
S5	INNOV	$160	$120	$200	$160	$125	$219	$188	$151	$251	$29	$23	$39
A1	HEAAI	$272	$204	$340	$272	$209	$378	$326	$261	$435	$160	$128	$213
A5	LSTME	$280	$210	$350	$280	$217	$385	$321	$257	$428	-	-	-
A4	SHDEP	$303	$227	$378	$303	$239	$409	$343	$274	$457	$137	$109	$182
S9	RUMAH	$311	$234	$389	$311	$242	$428	$362	$290	$483	-	-	-
E3	BRICF	$356	$267	$444	$356	$280	$482	$387	$310	$516	$28	$23	$38
S7	OPASH	$415	$311	$518	$415	$336	$571	$497	$397	$662	-	-	-
A3	CIDRZ	$420	$315	$525	$420	$325	$579	$486	$389	$648	-	-	-
S6	BNMTN	$424	$318	$530	$424	$319	$577	$453	$363	$604	$28	$23	$38
A7	GLRAN	$438	$328	$547	$438	$344	$595	$495	$396	$660	-	-	-
W3	VNTPV	$511	$383	$639	$511	$407	$684	$638	$510	$851	-	-	-
W4	FITVT	$739	$554	$924	$739	$587	$992	$789	$631	$1,052	-	-	-
A11	NAANK	$2,056	$1,542	$2,570	$2,056	$1,627	$2,770	$2,147	$1,718	$2,863	$146	$117	$195
P1	ASOCI	$3,233	$2,425	$4,041	$3,233	$2,576	$4,329	$4,294	$3,435	$5,725	$92	$73	$122
A12	GLOHI	$9,913	$7,435	$12,391	$9,913	$7,803	$13,437	$10,608	$8,486	$14,144	-	-	-

a. Low and high values represent 25% adjustment in total costs reported by each project, where lower costs correspond to low ratio value.
b. Low and high values represent 25% adjustment in total number of case detection reported by each project, where lower costs correspond to high ratio value.
c. Low and high values represent 25% adjustment in total number of case initiated treatment by each project, where lower costs correspond to high ratio value.
d. Low and high values represent 25% adjustment in total number of case completing treatment by each project, where lower costs correspond to high ratio value.

Fig S1. Sensitivity Analysis on the Cost Effectiveness Ratio per Case Diagnosed with Total Cost +/- 25% for case-finding only projects. For each case-finding only project, the blue diamond reflects the base value of the CE ratio, and line represents the range of ratio when total costs fluctuates +/- 25% (from the upper bar to the bottom bar). Letters of the codes on x-axis represent the geographic region in which the projects were performed, and numbers order projects from largest (1) to smallest within each region (e.g. S1 represents the project with the largest size in SEAR). The y-axis describes the scope and direction of the effect of the total costs change on the CE ratio of each projects. Cost per case diagnosed is calculated as respective case-finding costs divided by a number of patients diagnosed. Projects FUNDA, IRDSA were removed from the figure due to extremeness.

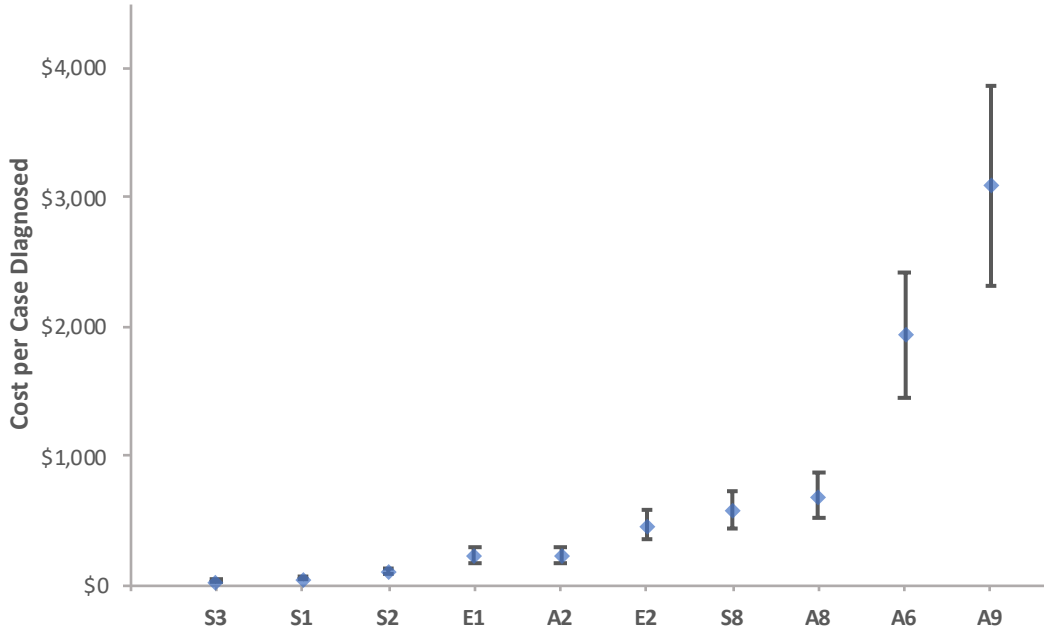


Fig S2. Sensitivity Analysis on the Cost Effectiveness Ratio per Case Diagnosed with Total Cost +/- 25% for projects with case-finding and treatment. For each dual-purpose project, the blue diamond reflects the base value of the CE ratio, and line represents the range of ratio when total costs fluctuates +/- 25% (from the upper bar to the bottom bar). Letters of the codes on x-axis represent the geographic region in which the projects were performed, and numbers order projects from largest (1) to smallest within each region (e.g. A1 represents the project with the largest size in AFR). The y-axis describes the scope and direction of the effect of the total costs change on the CE ratio of each projects. Cost per case diagnosed is calculated as respective case-finding costs divided by a number of patients diagnosed. Projects NAANK, ASOCI, GLOHI were removed from the figure due to extremeness.

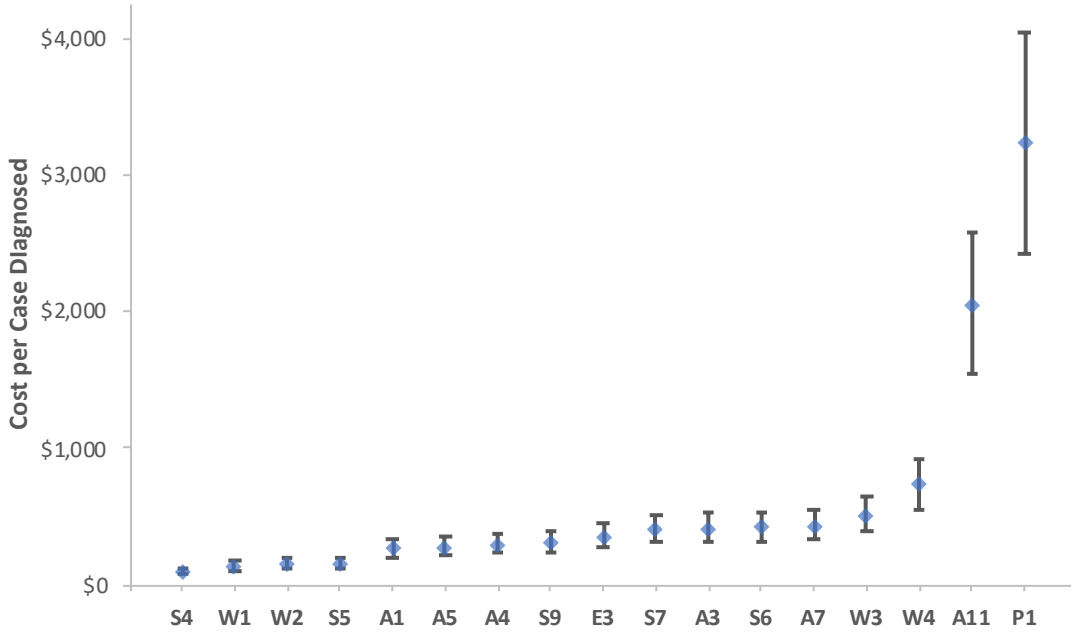


Fig S3. Sensitivity Analysis on the Cost Effectiveness Ratio per Case Diagnosed with Number Diagnosed +/- 25% for case-finding only projects. For each case-finding only project, the blue diamond reflects the base value of the CE ratio, and line represents the range of ratio when number of patients diagnosed fluctuates +/- 25% (from the bottom bar to the upper bar). Letters of the codes on x-axis represent the geographic region in which the projects were performed, and numbers order projects from largest (1) to smallest within each region (e.g. S1 represents the project with the largest size in SEAR). The y-axis describes the scope and direction of the effect of the number of patients diagnosed change on the CE ratio of each projects. Cost per case diagnosed is calculated as respective case-finding costs divided by a number of patients diagnosed. Projects FUNDA, IRDSA were removed from the figure due to extremeness.

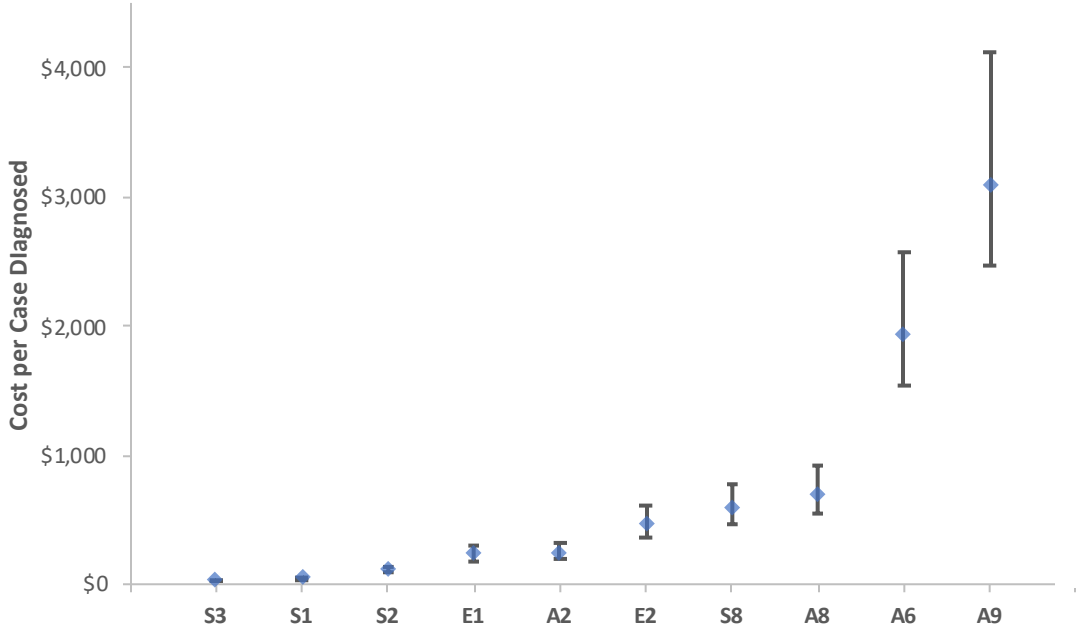


Fig S4. Sensitivity Analysis on the Cost Effectiveness Ratio per Case Diagnosed with Number Diagnosed +/- 25% for projects with case-finding and treatment. For each dual-purpose project, the blue diamond reflects the base value of the CE ratio, and line represents the range of ratio when number of patients diagnosed fluctuates +/- 25% (from the bottom bar to the upper bar). Letters of the codes on x-axis represent the geographic region in which the projects were performed, and numbers order projects from largest (1) to smallest within each region (e.g. A1 represents the project with the largest size in AFR). The y-axis describes the scope and direction of the effect of the number of patients diagnosed change on the CE ratio of each projects. Cost per case diagnosed is calculated as respective case-finding costs divided by a number of patients diagnosed. Projects NAANK, ASOCI, GLOHI were removed from the figure due to extremeness.

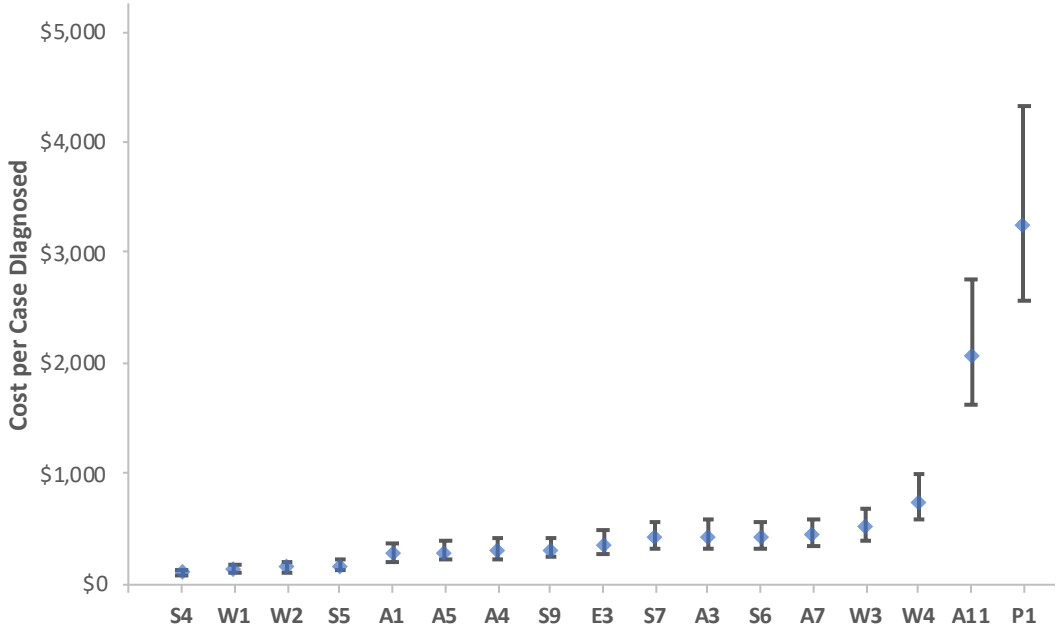


Fig S5. Sensitivity Analysis on the Cost Effectiveness Ratio per Treatment Initiated with Number Initiated +/- 25% for projects with case-finding and treatment. For each dual-purpose project, the blue diamond reflects the base value of the CE ratio, and line represents the range of ratio when number of patients initiated on treatment fluctuates +/- 25% (from the bottom bar to the upper bar). Letters of the codes on x-axis represent the geographic region in which the projects were performed, and numbers order projects from largest (1) to smallest within each region (e.g. A1 represents the project with the largest size in AFR). The y-axis describes the scope and direction of the effect of the number of patients change on the CE ratio of each projects. Cost per treatment initiation is calculated as total project costs divided by a number of patients initiated on treatment. Projects NAANK, ASOCI, GLOHI were removed from the figure due to extremeness.

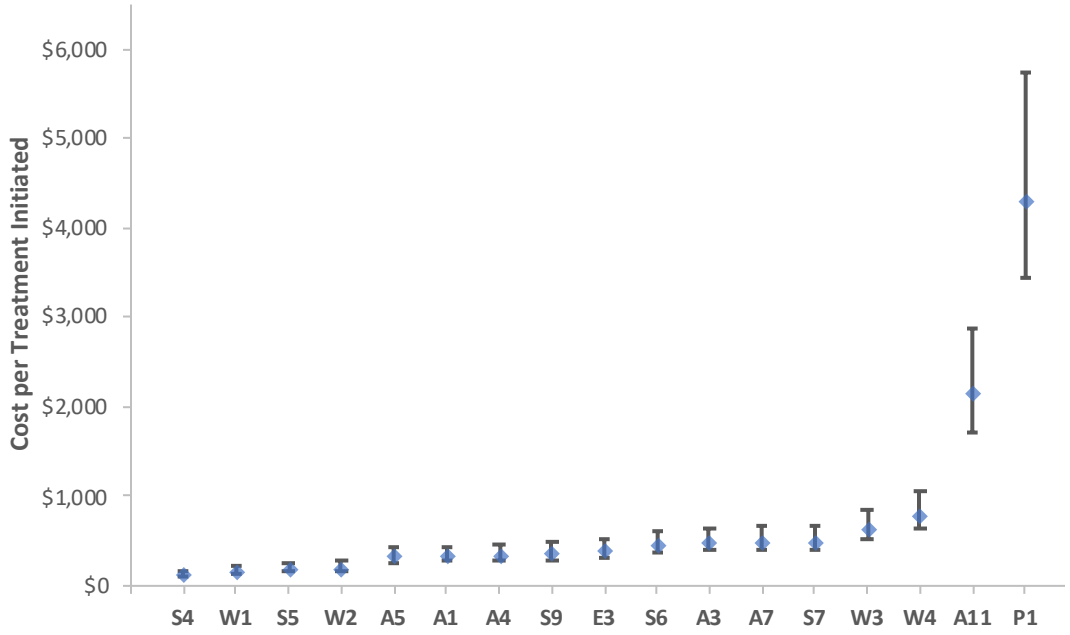


Fig S6. Sensitivity Analysis on the Cost Effectiveness Ratio per Treatment Completed with Number Completed +/- 25% for projects with case-finding and treatment. For each dual-purpose project, the blue diamond reflects the base value of the CE ratio, and line represents the range of ratio when number of patients completed treatment fluctuates +/- 25% (from the bottom bar to the upper bar). Letters of the codes on x-axis represent the geographic region in which the projects were performed, and numbers order projects from largest (1) to smallest within each region (e.g. A1 represents the project with the largest size in AFR). The y-axis describes the scope and direction of the effect of the number of patients change on the CE ratio of each projects. Cost per treatment completed is calculated as total project costs divided by a number of patients completed treatment. Projects NAANK, ASOCI, GLOHI were removed from the figure due to extremeness.