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Research paper

Tuberculosis in the Western Pacific Region: Estimating the burden of disease and return on investment 2020–2030 in four countries

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ABSTRACT

Background: We aimed to estimate the disease burden of Tuberculosis (TB) and return on investment of TB care in selected high-burden countries of the Western Pacific Region (WPR) until 2030.

Methods: We projected the TB epidemic in Viet Nam and Lao People's Democratic Republic (PDR) 2020–2030 using a mathematical model under various scenarios: counterfactual (no TB care); baseline (TB care continues at current levels); and 12 different diagnosis and treatment interventions. We retrieved previous modeling results for China and the Philippines. We pooled the new and existing information on incidence and deaths in the four countries, covering >80% of the TB burden in WPR. We estimated the return on investment of TB care and interventions in Viet Nam and Lao PDR using a Solow model.

Findings: In the baseline scenario, TB incidence in the four countries decreased from 97•0/100,000/year (2019) to 90•1/100,000/year (2030), and TB deaths from 83,300/year (2019) to 71,100/year (2030). Active case finding (ACF) strategies (screening people not seeking care for respiratory symptoms) were the most effective single interventions. Return on investment (2020–2030) for TB care in Viet Nam and Lao PDR ranged US$4-US$49/dollar spent; additional interventions brought up to US$2•7/dollar spent.

Interpretation: In the modeled countries, TB incidence will only modestly decrease without additional interventions. Interventions that include ACF can reduce TB burden but achieving the End TB incidence and mortality targets will be difficult without new transformational tools (e.g. vaccine, new diagnostic tools, shorter treatment). However, TB care, even at its current level, can bring a multiple-fold return on investment.

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Research in context

Evidence before this study

We searched MEDLINE through PubMed for mathematical modelling studies evaluating the TB burden and/or cost-effectiveness or return on investment of TB care or interventions in any country of the WHO Western Pacific Region until 11 August 2020 without any language restriction. Among the 56 records revealed by the search, seven studies were relevant including TB burden estimates (three studies from China and one from each of Cambodia, Fiji, Papua New Guinea and the Philippines), of which three reported cost-effectiveness estimates comparing TB care strategies. None of the studies however attempted to estimate the total economic burden of TB or the return on investment for spending on TB services.

Added value of this study

This study reports TB incidence and mortality projections for four countries in the WHO Western Pacific Region under a broad range of future scenarios and interventions until 2030, and estimates the return on investment for spending on TB care and implementing selected TB interventions in these countries. The four countries covered 90% of new incident cases and 82% of TB related deaths in 2019 in the Western Pacific Region.

Implications of all the available evidence

Investments in TB care can be expected to bring a multiple-fold return through gains in productivity. If the standard of TB care remains at present levels, TB incidence and mortality are expected to decrease only moderately over the next decade in the highest-burden countries of the Western Pacific Region. Further interventions that intensify the identification of active TB cases are expected to be cost-effective and contribute substantially to ameliorating TB burden.

1. Introduction

Tuberculosis (TB) is the leading cause of death from a single infectious agent [1]. About 10 million people fell ill and 1•4 million people, including those living with HIV, died of TB in 2019 [1]. In 2014, the World Health Organization (WHO) launched the End TB Strategy, aiming to reach by 2035 a global incidence and mortality similar to those of low-burden countries today and ultimately eliminate TB as a public health threat by 2050 [2]. The 2030 incidence and mortality targets are also part of the Sustainable Development Goal (SDG) 3 to “ensure healthy life and promote well-being for all at all ages” [3]. Interventions to prevent and treat TB have been estimated to be extremely cost-effective, providing up to a 43-fold return on investment if 95% reduction in TB deaths is achieved [4].

The Western Pacific Region (WPR) of the WHO covers 37 countries and areas, and almost one fourth of the world’s population. The region is diverse in population density, demographics, economy, and TB burden. Estimated TB incidence rates in 2019 ranged from <10 to >500 per 100,000 population across the countries, and the trends over recent years also range from stable decrease to increase [5]. Many countries are undergoing demographic and economic transitions that also impact TB. To guide progress towards the End TB targets in WPR, the WHO Western Pacific Regional Office published in 2016 a Regional Framework for Action and Implementation for the period 2016–2020 [6]. The purpose of this study is to inform the development of the next Regional Framework (2020–2030) by estimating the disease and economic burden of TB between 2020 and 2030 in selected high-burden countries of the WPR. Specifically, we project TB incidence, TB mortality, TB-related healthcare costs and economic growth in the selected countries under various scenarios of TB diagnosis, treatment and prevention; and estimate the return on investments in TB care and prevention.

2. Methods

2.1. Study design and setting

We searched for applicable mathematical models and completed modelling studies for the highest-burden countries of the region. We intended to use TIME Impact, an established mathematical model which is also a part of the Spectrum/OneHealth framework [7,8]. We retrieved the TIME calibration files for Viet Nam and Lao People’s Democratic Republic (PDR), the two countries in WPR for which a calibration exists, from the respective National TB programmes. Next, we reviewed the literature to find modelling studies for China and the Philippines, the two countries with highest absolute TB burden (Fig. 1). In 2019, 90% of the incident TB cases in the WPR were in the four included countries [1].

2.2. Model structure

TIME Impact is a dynamic deterministic compartmental model [8]. Model calibrations for Viet Nam and Lao PDR were informed by national TB programme data. Selected parameters are listed in Supplementary Tables 1 and 2.

For China, we used results from a review of five models, harmonized to project TB incidence and deaths between 2015 and 2025 under six intervention scenarios [9]. For the Philippines, we referred to an analysis from 2017 covering eight scenarios until 2030 [10].

2.3. Policy scenarios

We ran TIME Impact for Viet Nam and Lao PDR for a range of policy scenarios (Table 1). First, we modeled a baseline scenario (TB care and control, including the rates and pathways of case detection, treatment linkage and success, remaining as they were in 2019 until 2030), and a counterfactual scenario (all TB-related care and control efforts, including diagnosis and treatment, ceasing in 2020). Second, we simulated single-intervention scenarios, implemented gradually from 2020, reaching target coverage in 2025 and remaining at these levels until 2030: (i) use of GeneXpert in all diagnostic pathways (improving net sensitivity and specificity); (ii) preventive therapy (PT) for children aged <5 years in households of TB patients; (iii) patient support (to improve treatment success); (iv) active case finding (ACF) defined as screening persons not seeking care for respiratory symptoms either randomly, systematically or based on risk factors (realized in the model by increasing the diagnosis rates and numbers of tests); and (v) ACF followed by latent TB screening and PT. We modeled two ACF screening rates: moderate (2% of the population screened annually; without PT) or intensive (7% of the population screened annually; both with and without PT). We assumed either that ACF was conducted randomly in the population (i.e. the yield of testing was equal to national prevalence; untargeted ACF), or that specific high-risk populations were targeted (yield set seven times higher than national prevalence; targeted ACF). PT was modeled with two coverages among people with latent TB infection: 20% (only untargeted ACF) or 90%. Finally, we modeled two combination scenarios: one comprising all the above-mentioned interventions (including the most intensive and effective of the ACF-PT strategies); and one with all interventions and a further scale-up of ACF and improvement of net sensitivity and specificity beyond 2025, calibrated to reach the 2030 End TB incidence and mortality targets.

We calculated pooled results for the four included countries by summing the annual incident TB cases and TB-related deaths.

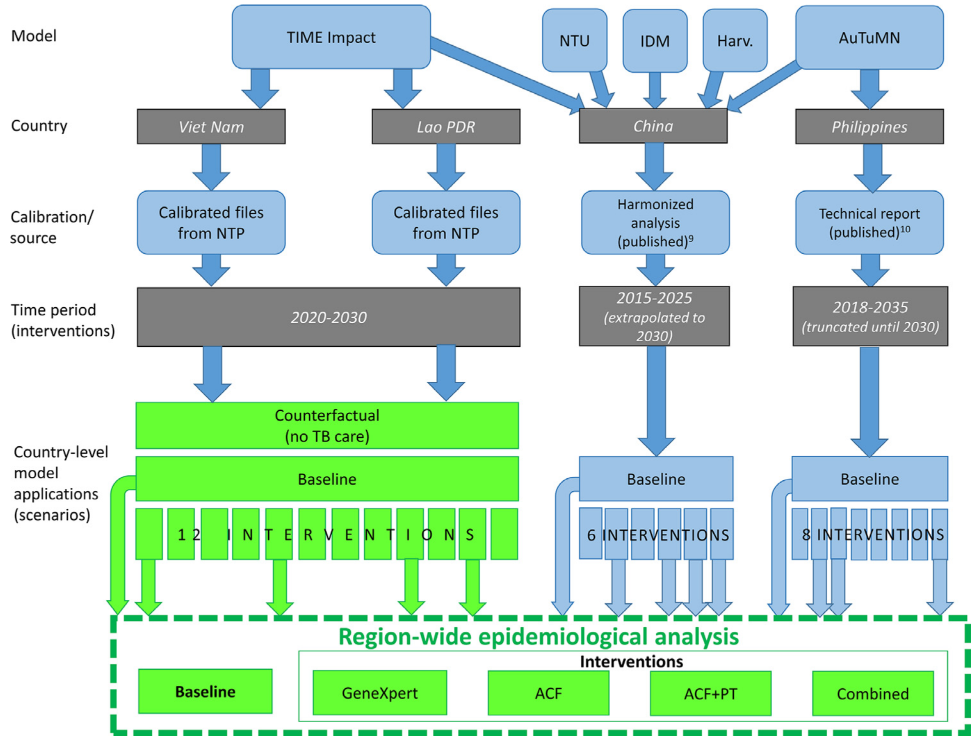

Fig. 1. Schematic representation of the study: models, countries, data sources, time periods, and analyzed scenarios. Blue boxes show tools, data and analyses that were developed earlier (as part of published studies or unpublished evaluations); green boxes show analyses that were done within the present study. ACF, active case finding; AuTuMN, Australian Tuberculosis Modelling Network; Harv., Harvard University; IDM, Institute for Disease Modelling; NTP, National Tuberculosis Programme; NTU, National Taiwan University; PDR, People's Democratic Republic; PT, preventive therapy.

Table 1
Description of modeled scenarios for Viet Nam and Lao People's Democratic Republic, and the scenarios for the combined regional analysis. All scenarios were modeled as scaling up gradually from 2020, reaching target coverage in 2025. The columns for China and the Philippines indicate if the corresponding models had a comparable (but not necessarily equivalent) scenario.

Scenario	Explanation	Target coverage	China[9]	Philippines[10]	Included in the combined WPR analysis
Counterfactual	All TB care stopped in 2020	n/a	n/a	n/a	No
Baseline	TB care continues on 2019 level	n/a	Yes	Yes	Yes
GeneXpert	GeneXpert used in all diagnostic pathways	100%	Yes	Yes	Yes
Patient support	Decreasing treatment non-success from 8% to 5% by patient support	100%	Yes	No	No
Paediatric PT	PT for household contact aged <5	59%	No	Yes	No
ACF: moderate untargeted	Testing of population randomly	2%	No	No	No
ACF: intensive untargeted	Testing of population randomly	7%	No	No	Yes*
ACF: moderate targeted	Testing of known high-risk populations	2%	Yes	No	No
ACF: intensive targeted	Testing of known high-risk populations	7%	No	Yes	No
ACF: intensive untargeted with limited PT	Testing of population randomly, PT for latently infected	7% (ACF), 20% (PT)	No	No	No
ACF: intensive untargeted with PT	Testing of population randomly, PT for latently infected	7% (ACF), 90% (PT)	No	No	Yes*
ACF: intensive targeted with PT	Testing of known high-risk populations, PT for latently infected	7% (ACF), 90% (PT)	Yes	No	No
Combination strategy	All interventions combined	n/a	Yes	Yes	Yes
End TB combination strategy	All interventions combined, and if necessary, further intensified to reach End TB incidence/mortality target by 2030	n/a	No	No	No

ACF, active case finding; PT, preventive therapy; SDG, sustainable development goals; WPR = WHO Western Pacific Region; n/a, not applicable.
* For China and the Philippines, the closest possible available scenarios were taken (i.e. targeted moderate or intensive, for China including PT if applicable).

We included a baseline and five intervention scenarios: universal GeneXpert, improved treatment success, targeted ACF, targeted ACF with PT, and a combination strategy (Table 1, Supplementary Table 3). For China, we used the mean over all five included models, and extrapolated the relative reduction in incidence and deaths between 2020 and 2025 to the period 2026–2030. For the Philippines, because the model published in 2017 was calibrated to incidence estimates that were likely too low given the latest prevalence survey results that became available subsequently, we used the relative impact of each intervention assuming that incidence and mortality in the baseline scenario remain constant [1]. In addition to the point estimates, we present an interval that covers the full range across the estimates of the five models for China.

2.4. Economic analysis

We report disability-adjusted life years (DALY) and incremental cost-effectiveness ratios (ICER) for each intervention compared with baseline in Viet Nam and Lao PDR. The broader economic impact of TB disease and care was assessed following the WHO-EPIC approach, based on a human capital augmented Solow model [11,12]. (Supplementary Text 1) We explored two alternatives regarding the elasticity in respect to physical capital (the relative impact of labor versus physical capital on the outcome; Supplementary Text 1): 0•1 (economic growth dominated by labor), or 0•5 (physical capital and labor contribute equally to economic growth). Healthcare costs were deducted from the savings, whereas the averted morbidity and mortality contributed to the labor.

We conducted economic analyses explicitly for Viet Nam and Lao PDR. Input costs were obtained from the National TB Programmes in local currency and converted into US dollars. Discounting and inflation were not taken into account. We compared the counterfactual with the baseline scenario, and the baseline scenario with two interventions: moderate targeted ACF, and the combination scenario. TB investments were defined as the total TB expenditure, including both domestic and international funding; only domestic funding was deducted from the economic output. We also made similar calculations for China and the Philippines comparing no TB care with baseline, assuming that the relative labor gain due to TB care would be the same as in either Viet Nam or Lao PDR, and that TB expenditure would stay on the level of 2018 thereafter.

2.5. Role of the funding source

This funders had no role in the study design, collection, analysis or interpretation of the data, in the writing of the report, or in the decision to submit for publication.

3. Results

3.1. Incidence and TB deaths

Unless additional interventions were implemented, TB incidence in the four countries decreased from 97•0 in 2019 to 90•1 (range across different models for China: 79•2–96•0) per 100,000 per year in 2030 (Fig. 2A). Universal GeneXpert for detection and care decreased the projected incidence in 2030 to 86•2 (75•3–92•1)/100,000/year, ACF to 77•7 (63•9–86•7)/100,000/year, ACF with PT for latently infected persons to 37•9 (37•9–37•9)/100,000/year by 2030, and a combination of all modeled interventions to 29•6 (29•6–29•6)/100,000/year in 2030. TB deaths decreased in the baseline strategy from 83,300 in 2019 to 71,100 (64,600–73,600) in 2030 (Fig. 2B). The numbers of TB deaths in 2030 in the GeneXpert, ACF, ACF-PT and combination strategies were 62,400 (51,400–67,200), 47,500 (35,100–60,400), 28,600

Fig. 2. Annual pooled TB incidence per 100,000 population (panel A) and TB related deaths (panel B) in four countries of the Western Pacific Region (China, Lao People's Democratic Republic, the Philippines, Viet Nam) 2015–2030 in five scenarios. The red diamonds in 2025 and 2030 show the End TB milestones and Sustainable Development Goals TB incidence/mortality targets, respectively. ACF, active case finding; PT, preventive therapy; combined, combination of all included strategies.

(28,600–28,600) and 15,900 (15,900–15,900), respectively. The End TB 2025 incidence milestone (50% reduction from 2015 level) was reached by the combination strategy, but no strategy could achieve the End TB 2030 incidence target (80% reduction from 2015), nor the TB mortality 2025 milestone or 2030 target (75% and 90% reduction from 2015, respectively).

TB care on the current level (baseline) could prevent 812,000 TB related deaths and 5,444,000 new TB cases in Viet Nam and 87,000 deaths and 221,000 incident cases in Lao PDR between 2020 and 2030, compared with the counterfactual scenario without any TB care. Increasing access to GeneXpert was more efficient in Viet Nam (6% reduction in incidence compared with baseline scenario in 2025) and the Philippines (9% reduction) than in Lao PDR (1% reduction) or China (minimal reduction; Table 2; Supplementary Figs. 1 and 2). However, the baseline coverage differed substantially between the countries, being highest in Lao PDR (72%). Paediatric PT had minimal impact in Viet Nam and the Philippines, but resulted in 2% reduction from baseline in 2025 in Lao PDR. Increased treatment success had similar impacts in Viet Nam and Lao PDR (3–4% reduction); in China its impact differed between the models. The impact of ACF varied across the alternative intensity and targeting scenarios in Viet Nam and Lao PDR. In Viet Nam "moderate untargeted" ACF reduced incidence in 2025 by 4% compared with baseline, and "intensive targeted" ACF by 34%. In Lao PDR the range was slightly narrower (3–28% reduction); in China and the Philippines, ACF reduced incidence by up to 17%. The incremental impact of latent TB screening and PT compared with ACF alone was moderate in Viet Nam, but substantial in Lao PDR and China. In Lao PDR, the End TB 2030 target was reached with the combination of all interventions, whereas in Viet Nam a further scale-up of diagnosis beyond 2025 was needed.

In Viet Nam, incidence was projected to decrease most rapidly in children and young people, approximately halving in people aged under 20 between 2015 and 2030 (Supplementary Fig. 3). The smallest reduction (about 30%) was among people aged ≈65 years. In Lao PDR, the distribution of TB incidence between age groups was not projected to change during the coming years. These results

Table 2

The relative impact of the modeled scenarios for TB incidence and TB related deaths in four countries of the Western Pacific region. Results for Viet Nam and Lao People's Democratic Republic were based on the TIME Impact model, and the results for China and the Philippines were extracted from modelling estimates extracted from the literature [9],[10]. The scenarios are defined in Table 1.

Scenario	Viet Nam			Lao People's Democratic Republic			China	Philippines
	Incidence in 2030 per 100,000 (relative reduction from baseline)	Total TB deaths 2020–30 (relative reduction from baseline)	Cost-effectiveness (US$/DALY averted)	Incidence in 2030 per 100,000 (relative reduction from baseline)	Total TB deaths 2020–30 (relative reduction from baseline)	Cost-effectiveness (US$/DALY averted)	Reduction in incidence in 2025 (relative from baseline)	Reduction in incidence in 2025 (relative from baseline)
Counterfactual	1162	943,600	n/a	655	119,400	n/a	n/a	n/a
Baseline	100	131,500	n/a	138	32,500	n/a	n/a	n/a
GeneXpert	88 (12%)	120,400 (8%)	$81	134 (3%)	30,900 (5%)	$118	0%	9%
Patient support	97 (3%)	128,000 (3%)	c/s	130 (6%)	30,900 (5%)	$929	0%–11%	n/a
Paediatric PT	100 (0%)	131,300 (0%)	c/s	132 (4%)	31,200 (4%)	$6	n/a	n/a
ACF: moderate untargeted	90 (10%)	122,300 (7%)	$1209	131 (5%)	30,600 (6%)	$1491	n/a	n/a
ACF: intensive untargeted	77 (23%)	109,800 (17%)	$2267	123 (11%)	28,500 (12%)	$675	n/a	n/a
ACF: moderate targeted	71 (29%)	102,500 (22%)	$537	116 (16%)	26,600 (18%)	$182	2%–17%	n/a
ACF: intensive targeted	55 (45%)	82,900 (37%)	$1476	103 (25%)	22,100 (32%)	$404	n/a	16%
ACF: intensive untargeted, limited PT	72 (28%)	105,200 (20%)	$1849	66 (52%)	23,700 (27%)	$273	n/a	n/a
ACF: intensive untargeted with PT	63 (37%)	99,000 (25%)	$1603	10 (93%)	16,800 (48%)	$135	n/a	n/a
ACF: intensive targeted with PT	52 (48%)	84,100 (36%)	$1415	6 (96%)	14,100 (57%)	$210	51%–80%	n/a
Combination strategy	40 (60%)	67,600 (49%)	$1257	5 (96%)	13,300 (59%)	$322	56%–80%	34%
End TB combination strategy	25 (75%)	47,600 (64%)	$3016	5 (96%)	13,300 (59%)	$322	n/a	n/a

ACF, active case finding; DALY, disability-adjusted life year; PT, preventive therapy; n/a, not applicable.

need to be interpreted with caution: TIME does not include an age structure and assumes homogenous mixing (demographic projections were taken from the DemProj module of the OneHealth tool) [8]

3.2. Economic analysis

Most interventions were likely cost-effective or even cost-saving. In Viet Nam the combination strategy set to reach the End TB incidence and mortality targets was the least cost-effective strategy compared with baseline (ICER US$3016/DALY averted), but in Lao PDR, the combination strategy was more cost-effective than some individual interventions (ICER US$322/DALY averted compared with baseline; Table 2). Among the four ACF strategies, the moderate targeted strategy was the most cost-effective in both countries. In Lao PDR, adding PT to ACF improved cost-effectiveness; in Viet Nam, the ICER of ACF strategies was approximately the same with or without PT.

Viet Nam's GDP has recently grown annually by about 6%, and was US$245 billion in 2018 (US$2567 per capita). With this growth rate, total GDP would more than double by 2030, to US$529 billion (labor-dominated scenario)-US$538 billion (equal contribution of labor and capital). In the hypothetical counterfactual scenario with all TB care stopped in 2020, GDP would continue to grow, as the effective labor force will also keep increasing despite the rapidly increasing TB burden. Under the baseline scenario, the total cost of TB services was 34–36 million US$ per year. In 2018, about US$17 million of Viet Nam's TB expenditure was covered by the Global Fund and 1 million by other grant funds for TB care, so about half of the total programmatic costs were deducted from the annual domestic economic output. In 2020, TB care (baseline scenario) contributed approximately 30,000 experience-adjusted additional work years due to averted deaths and morbidity (Table 3). In 2025, the difference was expected to be 279,400 work-years, and in 2030, 846,700 work-years, totaling 3•8 million work-years between 2020 and 2030. This results in an incremental gain of US$18•4 billion (labor-dominated) or US$10•7 billion (equal contribution of labor and capital) by 2030. The corresponding returns on investment in TB care were US$49 and US$28 per dollar spent, respectively.

In Lao PDR, the return on investment was lower. In 2018, the GDP of Lao PDR was US$18•0 billion (US$2542 per capita). Of the total cost of TB care (US$2•0 million in 2018), 23% was paid from domestic sources [1]. TB care added 188,000 work-years between 2020 and 2030 (Table 3), corresponding to a GDP gain of US$92 million (labor-dominated) or US$549 million (equal contribution of labor and capital). The corresponding returns on investment were US$4 and US$24 per dollar spent in TB care, respectively.

In China, the returns per dollar spent were US$6 (labor-dominated) and US$8 (equal contribution of labor and capital) using the labor gain from the Viet Nam analysis, and US$96 (labor-dominated) and US$72 (equal contribution) with labor gain estimates from Lao PDR (Supplementary Table 4). For the Philippines, the corresponding values were US$2, US$1, US$25 and US$12, respectively.

The return on investment for further interventions compared with the baseline strategy was projected to be higher in Viet Nam than Lao PDR. In Viet Nam, targeted moderate ACF provided a return of US$1•40–$2•70 and the combination strategy a return of US$0•90–$1•80 on every dollar spent. In Lao PDR, the return on investment for moderate targeted ACF was $0•40–$2•90, and in the

Table 3
Return on investment for TB care, active case finding and a combination intervention in Viet Nam and Lao People's Democratic Republic. The results are calculated from the TIME Impact epidemiological and economic projections using a human capital augmented Solow model. Elasticity α refers to the exponent of the contribution of human capital (labor) to the economic growth; we assumed that the corresponding exponent for physical capital is $1 - \alpha$. All values are cumulative over the period 2020–2030.

	Viet Nam		Lao People's Democratic Republic	
Elasticity (labor)	$\alpha = 0.1$	$\alpha = 0.5$	$\alpha = 0.1$	$\alpha = 0.5$
TB care (baseline) compared with no TB care (counterfactual)				
Total cost	$ 378,000,000		$ 23,000,000	
Financed by savings*	$ 185,000,000		$ 5300,000	
Gain in labor	3795,200		188,500	
Gain in GDP	$ 18.4 billion	$ 10.7 billion	$ 92 million	$ 549 million
Return on investment	$ 49	$ 28	$ 4	$ 24
ACF (moderate, targeted) compared with baseline				
Total cost	$ 218,611,000		$ 9197,000	
Gain in labor	126,300		10,100	
Gain in GDP	$ 586 million	$ 297 million	$ 3.9 million	$ 26.2 million
Return on investment	$ 2•70	$ 1•40	$ 0•40	$ 2•90
Combination strategy compared with baseline				
Total cost	$ 989,568,000		$ 49,096,000	
Gain in labor	417,500		56,000	
Gain in GDP	$ 1.82 billion	$ 890 million	$ 356,000	$ –4.5 million**
Return on investment	$ 1•80	$ 0•90	$ 0•00	$ –0•10**

ACF, active case finding; GDP, gross domestic product. *Return on investment is calculated for the total investment including international spending. **Negative values indicate that the gain in GDP was less than the investment spent in the intervention.

combination strategy the costs were as high as the economic benefit.

4. Discussion

Our analysis predicted that TB incidence and TB-related deaths will decrease in the countries with the highest absolute TB burden in the WPR during the coming decade, but only modestly unless further interventions are introduced. Between 2015 and 2025, TB incidence is projected to decrease by 9%, showing that the End TB milestone of 50% decrease is unattainable without extensive new interventions. In China, Viet Nam and Lao PDR the decrease is expected to be faster regardless of interventions. In the Philippines, the situation is less clear: the trend over recent years shows that TB incidence remains constant [1]. Nevertheless, TB care will likely bring a multiple-fold return for the investments within the coming decade. Interventions to improve the effectiveness of TB care along the continuum of care are also likely to be cost-effective.

ACF was shown to result in the greatest reduction in TB incidence and TB-related deaths among the interventions. However, we did not consider how screening would be applied in practice: ACF needs either to have extremely high coverage of the total population, or target groups of individuals with high TB prevalence. Both approaches have their limitations. Mass screening among the general population would be time consuming, expensive, and operationally difficult [13],[14]. For example, the modeled ACF strategy in China assumed 100% population coverage [9], implying screening hundreds of millions of people.

Reaching the End TB 2025 milestone and 2030 target for TB incidence and mortality will be challenging. In Viet Nam, the 2025 incidence milestone could be reached with ACF if the coverage and yield are sufficiently high, requiring at least three-fold increase in the total number of tests. Continuing the decrease towards the 2030 End TB target requires a combination of intensive interventions. The 2030 target was set assuming new transformational tools, such as a new vaccine that is effective both pre- and post-exposure, new diagnostic techniques able to detect infection and disease quickly and at the point of care, and shorter and highly efficacious treatment regimens, would be available by 2025 [2]. High-coverage ACF together with such interventions could keep the TB epidemic on track towards this target. The results from the Philippines were similar: even a combination intervention could only reduce incidence by one third. This is particularly worrying as the baseline assumptions for the Philippines may have been too optimistic.

The WPR is undergoing major demographic and economic transitions. The demographic transition will increase the contribution of the elderly to total TB burden, as was seen in our results in Viet Nam. The role of this age group in the economy may also become greater: in China the 60–64 year-old are predicted to become the second-largest five-year age group within the next decade [15]. In contrast, in the Philippines the youngest generations are predicted to remain by far the largest age groups. This demonstrates how the TB epidemic in WPR is driven by two opposing trends: the rapid demographic transition and a steadily declining epidemic in China and Viet Nam, and the less dramatic demographic and epidemiological changes in the Philippines.

Based on the Viet Nam and Lao PDR models, the current standard of TB care was estimated to return US$4–49 on each dollar spent within an 11-year time window. The calculation of a region-level estimate is however challenging. Under extreme assumptions, the return on investment could reach almost US$100 in China, whereas in the Philippines the overall TB care would not generate a return equal to the outlay. But based on demography and economy, the Viet Nam results may be broadly applicable to China and the Lao PDR model to the Philippines, suggesting a range of US$6–25 per dollar spent in these two countries. A weighted mean value for the four modeled countries, based on the three highest-burden countries would be US$13 per dollar spent.

Additional interventions are likely to bring net benefit by increasing productivity. For example, a moderate but targeted ACF campaign in Viet Nam could bring at least a 1•4-fold return on investment. For very intensive combination interventions, the results are unclear. In particular in Lao PDR the GDP gained by an intensive combination strategy was not necessarily greater than the outlay for interventions, despite the substantial projected epidemiological impact. A likely reason is related to the decreasing physical capital according to the model. Therefore, the response needs to take in to account the context of each country.

The four countries included in our analysis cover 90% of the new incident cases of TB and 82% of TB related deaths in the WPR in 2019. Despite the high relative TB burden in some countries not included in our analysis, their contribution to the absolute disease burden remains very limited, and our results can thus be expected to broadly reflect the development of the TB epidemic in the entire region. Our results were also approximately in line with two further previous modelling studies from the region [16,17]. In Fiji, where the prevalence is relatively low (54/100,000 in 2018), only moderate decrease in incidence and mortality were predicted, even after additional interventions [16]. A study from the Western province of Papua-New-Guinea, one of the highest-incidence countries of the WPR, predicted a stable trend under a status quo scenario, with the potential for decreases through interventions that increase detection and treatment [17]. The analysis from Fiji also demonstrated how ACF has a particularly limited role in settings with a high contribution of latent TB to the overall epidemic, and PT needs consideration. However, some caution is needed when generalizing the findings of our study to the entire region, particularly the economic projections. The impact of countries such as Japan and South Korea with high per-capita GDP is likely to be higher than their proportion of the epidemic burden would suggest.

4.1. Limitations

Our study has several limitations. We combined the results of several models that differ in structure, approach and recency of the data used for calibration. The economic evaluation was based essentially on two countries, and the return on investments should be seen as an estimate of the magnitude rather than providing exact values. The study addresses the overall situation in the included countries with the aim of approximating the epidemic and economic burden in the entire WPR, and the results should not be applied directly to any individual country. The economic evaluation was based on a comparison of the GDP projections, which takes the perspective of the society, but does not consider factors that are of importance to the affected individuals, like the consequences of the catastrophic costs that the TB affected households still face in many parts of the WPR [18]. The analysis also did not take into account the impact of the COVID-19 pandemic. The economic projections will almost certainly overestimate the true situation in the coming years, and the influence of the pandemic on TB care and mortality may act as cofactors of the TB epidemic. However, although COVID-19 is expected to have a major impact on the entire society in the next years, our findings remain a useful indication of the trends over the 11-year time window. Finally, our analysis did not take into account the numerous distal determinants of TB burden and access to TB services [19].

5. Conclusions

In the heterogeneous Western Pacific region, TB incidence is expected to continue to decrease, albeit slowly, based on modelling projections from countries that together cover >80% of the burden of TB in the region. A slow transition of the epicenter of the epidemic from the Asian mainland towards the Philippines and towards older age groups in countries with an ageing population is expected. The targets set for TB incidence and mortality reduction by 2030 will be difficult to reach without large-scale, coordinated and sustained policy shift and implementation efforts, along with transformational new tools. However, TB care in the WPR is an extremely profitable investment, providing a multiple-fold return on investments. The situation in each country needs to be reviewed in detail to select efficient, context-appropriate and acceptable interventions that can together put the Western Pacific Region on a path towards eliminating TB as a public health threat.

6. Contributors

TI, KR, FM, KO and MR planned the concept of the study, and JE, TI, MR and OK the study design. JE, RH, JT and AN collected and verified the data. JE, RH, JR, RR, EM and JT developed and applied the mathematical models. JE and EO planned and conducted the economic analyses. JE wrote the first version of the manuscript. All authors contributed to interpretation of the results and revision of the manuscript, and approved the final version of the manuscript.

Declaration of Competing Interest

This study was funded by the World Health Organization Western Pacific Regional Office and the Swiss National Science Foundation (Grant 163878). We declare no competing interests. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of the WHO.

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Data sharing statement

No data were specifically collected for this study. The results for China and the Philippines are publicly available through the respective publications. The baseline model calibrations for Viet Nam and Lao PDR were received from the respective National TB Programmes. The exact parameters of the intervention scenarios (Viet Nam, Lao PDR), region-level extrapolations and all economic analyses will be available on request from the corresponding author.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lanwpc.2021.100147.

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