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Original Article

Is tuberculosis elimination a feasible goal in Colombia by 2050?

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Abstract

Colombia has an underreporting of 30% of the total cases, according to World Health Organization (WHO) estimations. In 2016, successful tuberculosis (TB) treatment rate was 70%, and the mortality rate ranged between 3.5% and 10%. In 2015, Colombia adopted and adapted the End TB strategy and set a target of 50% reduction in incidence and mortality by 2035 compared with 2015. The aims of this study were: To evaluate whether Colombia will be able to achieve the goals of TB incidence and mortality by 2050, using the current strategies; and whether the implementation of new screening, diagnosis and TB treatment strategies will allow to achieve those WHO targets. An ecological study was conducted using TB case-notification, successful treatment and mortality rates from the last 8 years (2009–17). System dynamics analysis was performed using simulated scenarios: (1) continuation with the same trends following the trajectory of the last 8 years (Status quo) and (2) modification of the targets between 2017 through 2050, assuming the implementation of multimodal strategies to increase the screening, to improve the early diagnosis and to improve the treatment adherence. Following the current strategies, it is projected that Colombia will not achieve the End TB strategy targets. Achieving the goal of TB incidence of 10/100 000 by 2050 will only be possible by implementing combined strategies for increasing screening of people with respiratory symptoms, improving access to rapid diagnostic tests and improving treatment adherence. Therefore, it is necessary to design and implement simultaneous strategies according to the population needs and resources, in order to stride towards the End TB targets.

Keywords: Tuberculosis, dynamic systems, End TB strategy, targets, incidence, mortality, successful treatment

Introduction

System dynamics analysis helps to understand public health problems and predict the effects of interventions. The main advantages of this analysis lay in the systemic approach to health problems, allowing to interrogate the interactions between actors, to evaluate multiple causes and consequences and to analyse how each element influences the problem using the published evidence. The above is useful to guide policymakers towards decisions and to generate public policies with optimal impact (Sterman, 2006; Trochim *et al.*, 2006). This strategy has been applied to the development of human immunodeficiency virus (HIV) epidemic control strategies (Dangerfield *et al.*, 2001; Fleßa, 2003), as well as to guide public health decisions for the following conditions: dental caries (Hirsch *et al.*, 2012), prostate cancer (Palma *et al.*, 2016), poliomyelitis

Key Messages

- World Health Organization (WHO) launched End tuberculosis (TB) strategy with ambitious goals in order to attain TB elimination by 2050.
- Colombia has the following challenges: (1) case detection mainly relies on passive case finding. (2) Only approximately 3% of people with respiratory symptoms are screened for TB. (3) Colombia has an estimated rate of underreporting of 30% of the total cases according to WHO. (4) In 2016, successful TB treatment rate was 70%, and a mortality rate ranging between 3.5% and 10% (15, 16 and 18).
- We found with simulated results for the current scenario (status quo), i.e. continuing with the current practices, it is anticipated that no changes will occur, with stable percentage of mortality and successful treatment of TB rather than decreasing incidence.
- We simulated the following strategies: (1) to increase the screening through active case finding. (2) To improve the early diagnosis through the improvement of laboratory network and use of molecular test (point of care) in primary healthcare institutions. (3) To improve successful treatment through the implementation of community-based directly observed therapy short course (DOTS) programmes, universal DOTS coverage message reminders and cash transfer interventions. Our results indicate that implementation of a single strategy will not be enough for Colombia to achieve the End TB strategy targets. The combination of TB screening, diagnosis and treatment adherence strategies will produce the highest increase in the TB incidence rate during the first 11 years, to decrease later up to 10/100 000 by 2050.

eradication (Duintjer Tebbens *et al.*, 2005), and to evaluate outcomes and costs of chronic diseases (Homer *et al.*, 2004), among other conditions.

The World Health Organization (WHO) aims to end the global tuberculosis (TB) epidemic by 2050, and proposed to reduce the incidence and mortality rates (20% and 35% by 2020, 80% and 90% by 2030 and 90% and 95% by 2050, respectively), and to ensure that no TB-affected families face catastrophic costs (WHO, 2015, 2017a). Achieving these goals will require investment in improved access to diagnostics and treatment, research and innovation. The WHO reported in 2018 that the mortality rate is decreasing 3% per year, with a higher decline in the last 5 years in European region (11%) and South-East Asia (4%). The TB incidence has shown a decline of 2% per year, and in the Americas region the decline between 2010 and 2016 has been 1.6% per year, and in 2017 an increase has been seen (WHO, 2017a, 2018).

Colombia has implemented multiple strategies proposed by the WHO: directly observed therapy short course (DOTS) since 2000; the strategic plan 'Colombia free of TB' in 2006, and the strategic plan 'Colombia towards the End of TB' in 2015. In an evaluation conducted in 2016 in 25 municipalities of Colombia to report the progress since 2006 until 2015, some of the positive findings were: (1) the improvement of the laboratory network, 22 out of 210 laboratories for diagnosis use liquid culture (mycobacteria growth indicator tube), 27 out of 34 laboratories that perform susceptibility test implemented GenXpert® and 22 line probe assay (LPA) test. (2) Colombia centralized the procurement of TB treatment. (3) The government guarantees individualized access through the health insurance companies for the majority of the population. (4) Community DOTS programmes have been implemented in seven cities with the highest burden of TB (Ministerio de Salud y Protección Social *et al.*, 2016). However, the main persistent challenges are: (1) case detection relies mainly on passive case finding. (2) Only around 3% of people with respiratory symptoms are screened for TB. (3) Underreporting rate is estimated at 30% of the total cases according to WHO. (4) In 2016, rate of successful TB treatment was 70%, and a mortality rate ranged between 6.5% and 12.3% (INS, 2017a; Ministerio de Salud y Protección Social *et al.*, 2016; Pérez, 2018). Colombia's strategic plan to End TB included a section about a 'Gap analysis for the fulfilment of the objectives of the tuberculosis programme'. The strategy outlined gaps that constitute barriers that have not allowed fulfilment of each aspect of the strategic plan. Gaps persist in the accessibility to conventional tests and new technologies that are being introduced in the country for an earlier diagnosis, especially in high-risk populations. No diagnostic algorithms have been implemented that guide and facilitate timely and reliable diagnosis and access to new technologies. Barriers to full adherence include difficulty in accessing (distance and cost) treatment administration sites and complex social conditions. The implementation of community DOT and social protection interventions, centred on the affected person and his/her family, is partial and with wide regional variation.

These findings reflect some improvement attributed to implementation of multiple strategies; however, Colombia has not been able to achieve the goals set by the WHO. The 2018 WHO report mentions that the mortality rate in Colombia has a slight decline, but it has not been stable over time, and the TB incidence has been stable until 2014, where it started to increase. Colombia has not been able to achieve the successful treatment goal of 85%, and then the new goal of 90% over the last 17 years, and since 2014 the successful treatment percentage has been decreasing to 61%, being lower in HIV infected and those infected with multidrug-resistant (MDR)/rifampicin-resistant TB (RR-TB).

In this article, we used the information collected over the last 8 years, capturing TB incidence, successful treatment and mortality with the aim to evaluate whether Colombia will be able to achieve the goals of TB incidence and mortality by 2050, under different scenarios using system dynamics simulation. In addition, we evaluated the impact of implementation of enhanced screening, diagnosis and TB treatment strategies on the ability to achieve those WHO targets.

Materials and methods

Context of TB programme in Colombia

Colombia has two types of health insurance, contributive for people with formal employment or with payment capacity, and subsidized for people without employment or low income. WHO classifies the country as a medium TB burden country, with 14 480 TB cases reported with a TB incidence of 26.5 cases per 100 000 inhabitants in 2017 (INS, 2017b). Antioquia and Valle departments contributed

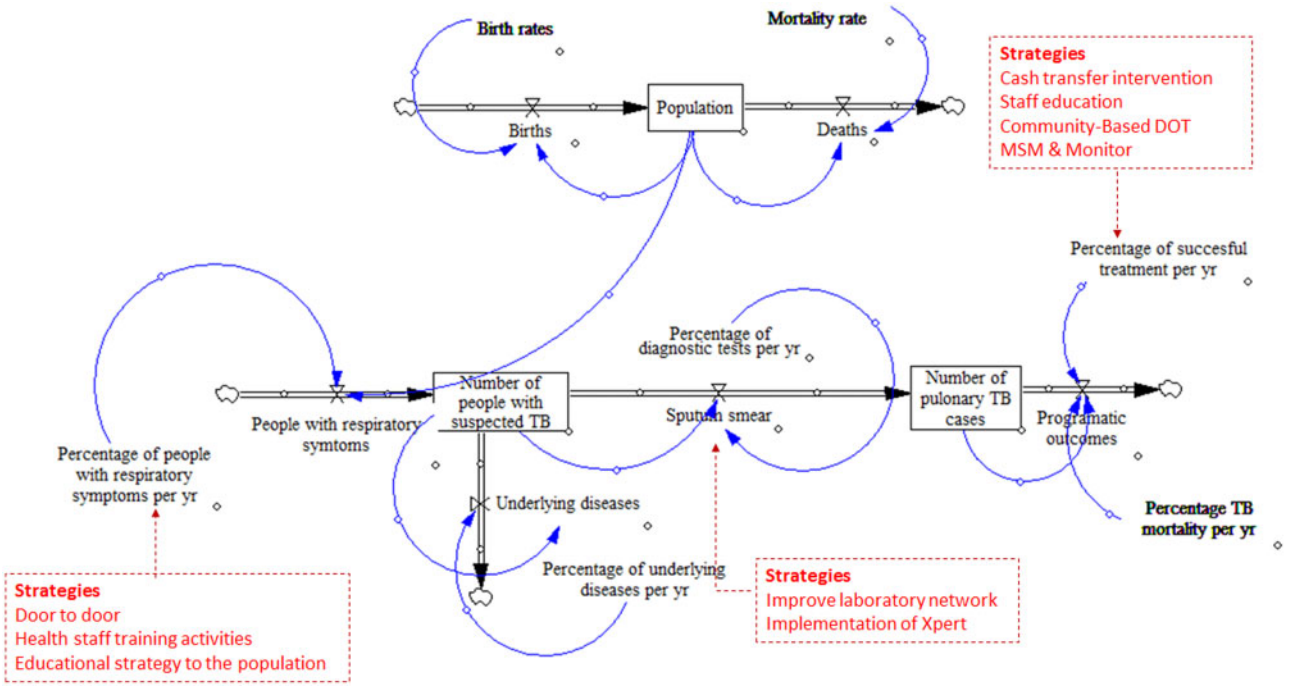

Figure 1 System dynamics diagram of tuberculosis in Colombia. Stocks are boxes that show the number of people with suspected TB and the number of TB cases. A flow (arrow) represents the rate of change in a stock based on those variables that are used in the equations, to estimate the values that cause changes in the stocks like percentage of births, percentage of general mortality, percentage of people in high-risk groups, percentage of people with respiratory symptoms, percentage of people diagnosed by sputum smear, culture or Xpert, percentage of successful TB treatment and percentage of TB mortality. In addition, we modelled the influence of the following strategies: (1) increasing the screening through ACF, (2) improving early diagnosis and (3) improving successful treatment.

with 31.8% of the cases. TB diagnosis is covered under the health benefits plan and treatment is paid by the government.

Study type

This is an ecological study using a system dynamics simulation model to predict what will happen to the numbers of people with suspected TB and in pulmonary TB cases if the national TB programme (NTP) implements 'a specific' or multiple 'strategies', and to predict the feasibility of the Colombian TB Programme to attain the targets established by WHO in 2050.

System dynamics requires understanding of how each part of a problem is connected, and how factors that impact risk, rates and outcomes interact (flow diagram). Figure 1 depicts the approach to TB and the variables that influence the diagnosis and outcomes of the disease.

The stocks (boxes) mean 'number of people with suspected TB', and 'number of pulmonary TB cases', and can go up and down based on the flows or rate of change (Figure 1). The flows (arrows) are the variables that increase or decrease the stocks. The variables that affect the number of people with suspected TB are the percentage of births/year, percentage of deaths/year, percentage of high-risk groups among the total population, percentage of general population without specific risk factors and percentage of people screened, all of them per year. We assumed that 100% of people in high-risk groups should be screened every year, in Colombia represents 19.2% among the total population (Table 1).

The variables that increase or decrease the stock of number of pulmonary TB cases are the percentage of people with suspected TB per year, the percentage of TB cases diagnosed by sputum smear, sputum culture or Xpert, the percentage of people with successful treatment and died during TB treatment, all of them per year. The time variables used were: initial time: 2017, final time: 2050, time step: every year.

Using existing data (Table 1) from the Colombian National Health Institute (INS, 2017c), World Bank Group (World Bank Group, 2017), WHO (WHO, 2017b) and PAHO (WHO, 2018), we modelled the number of people with suspected TB and number of pulmonary TB cases between 2018 and 2050 if we continue with the same TB programme.

Then, we searched the published literature using PubMed to identify strategies for screening, diagnosis and treatment that have been successful to increase the percentages of people with respiratory symptoms that are screened for TB, percentage of TB cases, and percentage of successful treatment. In addition, how these strategies decreased the percentage of people who died (Table 1). We chose studies that reported programmatic strategies instead of clinical trials, as we wanted to have information regarding the impact of those strategies in real world more than in a controlled environment.

Based on the information of published papers, we modified the variables of the flows (Table 1) assuming the implementation of different strategies reported in literature in the following areas:

1. To increase the screening through active case finding (ACF; Supplementary Table S1). On each strategy, we took the percentage of people with suspected TB per year that was reported in published papers as we briefly summarize (Table 1):
   a. Health staff training activities: Chaisson *et al.* (2015) conducted a quasi-experimental study. Initially they did qualitative interviews in order to understand barriers to TB evaluation and inform intervention design. Then, they designed, focused on feasibility and impact of two interventions:

Table 1 Information used for system dynamics modelling of tuberculosis in Colombia 2017–50

Constant information for all scenarios		
Percentage of births/year (DANE, 2018): 1%	Diabetes (CAC, 2017b): 1 099 471	Children >15 years (5%) (DANE, 2019): 1 392 108
Percentage of deaths/year (DANE, 2018): 0.45%	COPD (Caballero *et al.*, 2008): 1 500 000	Indigenous peoples (DANE, 2019): 1 378 884
Healthcare personnel (Monsalve *et al.*, 2013): 466 822	Arthritis (CAC, 2017c): 72 478	Homeless (Ministerio de Salud y Protección Social, 2013): 34 417
Immigrants (DANE, 2005): 915 478	Cancer (CAC, 2017d): 229 374	Prisoners (INPEC, 2017): 119 179
Malnutrition <5 years (ICBF, 2016): 520 000	Kidney disease (CAC, 2017b): 1 406 364	Household contacts: 43 440
HIV (CAC, 2017a): 82 856		
Total population in high-risk groups: 9 260 864 (a)	Total population (DANE, 2006): 48 258 000 (b)	Percentage of people to screen (a/b): 19.2% per year
Screening strategies	Diagnosis strategies	Treatment strategies
Percentage of successful treatment (WBG, 2018): 72% per year	Percentage of people with suspected TB under educational strategy to the population: 28% in 2018, and from 2019 to 2050: 20% per year (Oshi *et al.*, 2017)	Percentage of people with suspected TB under educational strategy to the population: 28% in 2018 and since 2019–50: 20% year (Oshi *et al.*, 2017)
Percentage of TB mortality (WBG, 2018): 10.2% per year	Percentage of successful treatment (WBG, 2018): 72% per year	Implementation of Xpert: diagnosis of TB cases: 82% per year (Reechaipichitkul *et al.*, 2017)
TB incidence rate 2017 (WHO, 2017a): 30/100 000 population	Percentage of TB mortality (WBG, 2018): 10.2% per year	TB incidence rate 2017 (WHO, 2017a): 30/100 000 population
Percentage of cases with TB in 2018 (OIM, 2017; Aye *et al.*, 2018): 12.5%	TB incidence adjusted by underreporting or under-diagnosis (30%; WHO, 2017a): 40/100 000 at 2017	Percentage of cases with TB in 2018 (OIM, 2017; Aye *et al.*, 2018): 12.5%
Mean of TB incidence decline from 2019 to 2050 (WHO, 2018): 1.6% per year	Percentage of cases with TB in 2018 (OIM, 2017; Aye *et al.*, 2018): 12.5%	Staff education[a] (Lewin *et al.*, 2005) Successful treatment: 2017 (72%), from 2018 to 2050: 79.5% per year Mortality: 2017: 10.2%, from 2018 to 2050: 9.24% per year TB incidence decline since 2019: 1.7%
Health staff training activities[a] People with suspected TB: (Chaisson *et al.*, 2015) 15.7% in 2018, and from 2019 to 2050: 11.4% per year	Mean of TB incidence decline since 2019 (WHO, 2018): 1.6% per year	Community-based DOT[a] (Zhang *et al.*, 2016) Successful treatment: 2017 (72%), from 2018 to 2050: 90.1% per year Mortality: 2017: 10.2%, from 2018 to 2050: 8.16% per year TB incidence decline, from 2019 to 2050: 2% per year
Door to door[a] People with suspected TB: 39% in 2018, and from 2019 to 2050: 19% per year (Morishita *et al.*, 2017)	Improve laboratory network[a] 100% of TB cases are diagnosed using liquid culture per year Conventional diagnosis with sputum smear[a] (Reechaipichitkul *et al.*, 2017): 47.6% per year compared to sputum culture	M&M and Monitor[a] (Liu *et al.*, 2015) Successful treatment: 2017 (72%), from 2018 to 2050: 86.9% per year Mortality: 2017: 10.2%, from 2018 to 2050: 8.57% per year TB incidence decline, from 2019 to 2050: 1.91% per year
Educational strategy to the population[a] People with suspected TB: 28% in 2018, and from 2019 to 2050: 20% per year (Oshi *et al.*, 2017)	Implementation of Xpert[a] (Reechaipichitkul *et al.*, 2017): TB cases detection: 84% per year compared with sputum culture	Cash transfer intervention[a] (Torrens *et al.*, 2016) Successful treatment: 2017 (72%), from 2018 to 2050: 82.1% per year Mortality: 2017: 10.2%, from 2018 to 2050: 8.57% per year TB incidence decline from 2019 to 2050: 1.9% per year
Combined strategies		
Screening strategy: Educational strategy to the population. People with suspected TB: 28% in 2018, and from 2019 to 2050: 20% per year (Oshi *et al.*, 2017) Diagnosis strategy: Implementation of Xpert (Reechaipichitkul *et al.*, 2017). TB cases detection: 82% per year Treatment strategy: Community-based DOT (Zhang *et al.*, 2016): Successful treatment: 2017: 72%, from 2018 to 2050: 90.1% per year Mortality: 2017: 10.2%, from 2018 to 2050: 8.16% per year Status quo: TB incidence decline from 2019 to 2050: 1.6% per year TB incidence rate in 2017: % (WHO, 2017a): 30/100 000 population Combined A[a]: TB incidence decline from 2019 to 2050 (Floyd *et al.*, 2018): 4% per year Combined B[a]: TB incidence decline from 2019 to 2050 (Floyd *et al.*, 2018): 10% per year		

[a]It means the strategies and values we used for each model.
M&M, Text messaging only.

performance feedback and same-day microscopy. For the first intervention, they delivered a monthly Report Card, which displayed: (1) a health centre's performance on each International Standard of TB Care indicator for the current month and for the previous 6 months and (2) performance data averaged across all six health centres. After staff introduced the Report Card at each health centre, it was sent electronically each month to the health centre in-charge or TB focal person. Health centre staff were asked to review the Report Card at monthly staff meetings to devise a performance. The second intervention was same-day microscopy that involves collection and analysis of two sputum samples at a patient's initial visit to the health centre using light-emitting diode fluorescence microscopy, facilitating same-day diagnosis and treatment initiation for smear-positive TB cases.

b. Door to door: Morishita *et al.* (2017) conducted a project that delivered the TB screening and diagnostic services to all target populations through a mobile unit. Each mobile team was composed of two physicians, one nurse, one medical technologist and one radiologic technologist, and it was equipped with a digital chest X ray (CXR) machine, light-emitting diode fluorescence microscope (LED-FM), and Xpert machine for molecular diagnosis. People aged 15 or above were interviewed for TB symptoms and the known risk factors for TB, then underwent CXR examination and the results were read by the physician in the mobile team. People with suspected TB were requested to provide two spot sputum specimens for diagnostic tests, at least 1 -h apart. Both specimens were examined for sputum smear microscopy using LED-FM, and for Xpert. The test results were released on the same day. Individuals with positive result or those who had negative results but with a high clinical index of suspicion for active TB were treated for TB.

c. Educational strategy to the population: Oshi *et al.* (2017) conducted training for all health workers within the NTP and laboratory staff; for political, community, and religious leaders and other stakeholders; and the appointment of one project supervisor per local government area to support and supervise field activities. The suite of educational activities included advocacy, communication and social mobilization component delivering messages about TB and the availability of the services during community meetings, campaigns and the local radios. In addition, roadside shows were carried out to further increase awareness about TB. ACF strategies included the following: (1) Community outreach: Community mobile health teams conducted TB screening outreaches and house-to-house visits in the intervention area to identify the individuals with chronic cough, inform symptomatic individuals how to produce sputum and collect three (spot–morning–spot) sputum specimens for smear microscopy; (2) ACF for TB among women attending antenatal care clinics; (3) ACF for TB among women attending mother and child health clinics; (4) ACF for TB among people living with HIV attending antiretroviral clinics; (5) ACF for TB among people attending general outpatient department; and (6) Active screening, at their homes, of contacts of registered smear-positive TB patients. Anyone with a cough for 2 weeks or more, previous history of TB or a family member currently/previously with disease was suspected of having TB. Individuals that were flagged based on the above questions were asked to submit three sputum samples for smear microscopy: A spot sample was obtained from all presumptive TB cases, a second sputum sample the next morning, and another spot sputum sample when patients delivered the second sample. A similar approach was used for the evaluation of contacts of TB patients in the intervention area. Among people identified for further testing, the screener captured information on other TB-associated symptoms, including haemoptysis, fever, weight loss and night sweats.

2. To improve the early diagnosis through the improvement of laboratory network and use of molecular tests (point of care: GeneXpert® and molecular LPAs) in primary healthcare institutions. We chose articles that reported the implementation of molecular tests in primary healthcare institutions that allows for same-day diagnosis (Supplementary Table S2). We took the percentage of TB cases diagnosed by sputum smear, sputum culture or Xpert (Table 1) reported by Reechaipichitkul *et al.* (2017).
   a. In brief, they collected information from patients with (1) clinical signs and symptoms, including cough and/or prolonged fever of more than 2 weeks, (2) age ≥15 years, (3) abnormal chest radiograph, (4) available of sputum acid-fast bacilli (AFB) smear, GeneXpert *Mycobacterium tuberculosis* (*MTB*)/rifampicin (RIF) assay and mycobacterium culture results, (5) received treatment at Srinagarind Hospital and (6) definite final diagnosis of pulmonary TB. They took demographic and clinical data of patients including sputum AFB smear, sputum GeneXpert MTB/RIF assay, sputum mycobacterium culture, MTB drug susceptibility, treatment and outcome. Diagnosis of pulmonary TB was based on MTB positive sputum culture.
3. To improve successful treatment (Supplementary Table S3). We took the percentage of people with successful treatment and deaths during TB treatment in each study (Table 1).
   a. Staff education: Lewin *et al.* (2005) reported a training intervention focused on concentrating the attention of all nurse-managed primary care clinic on (1) equipping clinic staff to understand the barriers to improving client relations; (2) encouraging patient-centred care, including the provision of support to patients and sharing control of the consultation with them; (3) empowering clinic staff to implement changes at their clinic; and (4) continuous quality improvement, self-evaluation and critical reflection on practice. They took places that the overall successful treatment completion rate for all adult patients with smear-positive pulmonary TB was <70% in the year preceding the trial.
   b. Community-based DOT (CB-DOT): We took a systematic review published by Zhang *et al.* (2016) of studies in which CB-DOT, defined as DOT that was delivered by lay healthcare personnel (including village health workers)/community health workers or voluntary lay individuals from the community (not including family or workplace individuals).
   c. M&M Monitor: Liu *et al.* (2015) evaluated two strategies by separated and the combination of both. The strategies were: (1) Text messaging only: Up to three SMS reminders were sent to the patient on the day of medication, depending on whether the patient replies or not. These reminders were sent at the agreed time medication was to be taken and subsequently at 12 noon and 6 P.M. if no reply was received. SMS text was 'please take the medication on time' and was the same for each reminder. (2) Medication monitor only: If the box was not opened at that time, there are up to eight further reminders (bleep), taking place at 5 min, 20 min, 30 min, 1 h, 2 h, 4 h, 6 h and 8 h after the agreed time. Once the box had been opened, the reminders stop for that day. (3) Combined:

Table 2 Tuberculosis case-notification, mortality and successful tuberculosis treatment in Colombia between 2009 and 2017

Year	TB case-notification[a]	Mortality rate per 100 000 inhabitants[a]	Mortality among those within TB treatment programme[b] (%)	Successful TB treatment[b]
2009	10 913	0.86	6.33	75
2010	10 622	0.85	7.10	74
2011	10 895	1.32	7.35	73
2012	10 956	1.31	8.08	72
2013	10 849	1.34	8.98	71
2014	11 571	1.80	10.61	76
2015	11 647	1.92	12.03	75
2016	12 439	2.58	12.52	61
2017	14 408	2.99	9.9[a]	ND

ND, no data.
[a]Data taken from the Colombian NIH reports https://www.ins.gov.co/buscador-eventos/Paginas/Info-Evento.aspx.
[b]Data taken from the indicators from WHO https://www.who.int/tb/country/data/download/en/.

a combination of the SMS and medication monitor reminders.

Treatment adherence was evaluated by a physician at the monthly dispensing visits. Depending on the number of missed doses, the patient was switched to intensive management, implying that the village or community care provider visited the patient once a week for the rest of the treatment; or switched to DOT.

d. Cash Transfer: Torrens *et al.* (2016) evaluated in one group of patients newly diagnosed with TB who benefitted from Bolsa Familia Programme (BFP) transfers during TB treatment. The unexposed group was composed of patients newly diagnosed with TB who were eligible for BFP benefits but only started to receive them after the end of treatment.

System dynamic simulation

System dynamics model uses differential equations to predict data over the time. We simulated model 1 to predict how different screening strategies can increase the number of people with suspected TB and the number of TB cases. Model 2 was used to assess different diagnostic strategies and their impact on the number of TB cases, we took the strategy of model 1 that reported the highest percentage of people with suspected TB. The third model evaluated different treatment strategies and their impact on the number of TB cases. We took the strategy identified in model 1 to have the highest percentage of people with suspected TB, and from model 2 the strategy that used Xpert for diagnosis. We then generated model 4 that incorporated the best strategies taken from models 1–3 to evaluate the impact of combined interventions on the number of pulmonary TB cases.

We compared within the models 3 and 4 each strategy vs 'Status quo'. Status quo reflects what is expected to happen to TB prevalence if current strategies and same trends of 2009–17 are continued going forward (Table 2).

We kept constant: percentage of births/year, percentage of deaths/year and percentage of high-risk groups among the total population per year (Table 1). The analysis of system dynamics and simulation was done using Vensim® programme.

Results

Using ACF strategies will allow to identify more TB cases (up to 70 cases/100 000) but none of the single strategies will be sufficient to achieve the goal of <10/100 000 inhabitants by 2050 (Figure 2).

Using ACF plus liquid culture or Xpert will increase the TB prevalence up to 120/100 000 but to improve the screening and diagnosis alone will not allow to achieve the End TB strategy Goal by 2050 (Figure 3).

Implementation of a single strategy for successful treatment will not allow Colombia to achieve the End TB targets that were set, and the use of treatment adherence strategy in isolation, without implementing early diagnosis, will maintain a stable trend of TB prevalence over time (Figure 4).

Figure 5 shows that modifications in the screening, diagnosis and treatment will increase the TB incidence during the first 5 years after implementation. The initial increase will be followed by a dramatic decrease in the TB incidence rate that would reach rates within the End TB strategy targets by 2050 if the screening, diagnosis and treatment strategies are maintained every year.

Discussion

In this article, we show how the implementation of a unique strategy that impact individually screening, diagnosis or treatment in TB programme is not adequate to achieve the targets of End TB strategy of <10 cases/100 000. Based on the pertaining to TB case-notification, mortality and successful treatment in Colombia between 2009 and 2017, the first strategy that should be implemented needs to be directed to increase the TB treatment success. Currently, the treatment success falls short of international standards and alarmingly, rates have been decreasing since 2014, along with increasing mortality rates among TB cases. It is essential to collect, report and analyse disaggregate information about public health and clinical responses especially among high-burden populations. Understanding the demographic, geographic, socio-economic and co-morbid conditions that underlie poor treatment outcomes is critical in order to identify gaps and provide targeted interventions (WHO, 2014).

The TB case-notification, successful treatment and mortality have been variable in Colombia. As have been reported in other countries, the rates have been stable over time, and in some parameters like TB incidence and mortality rates have shown small increases. A possible explanation for those increasing in TB case-notification could be related to the implementation and execution of Global Fund for the TB, malaria and HIV epidemic control strategies project conducted in eight cities with the highest burden of TB in Colombia. In this project, strategies including GenXpert® implementation, improvement in information systems and reporting, as

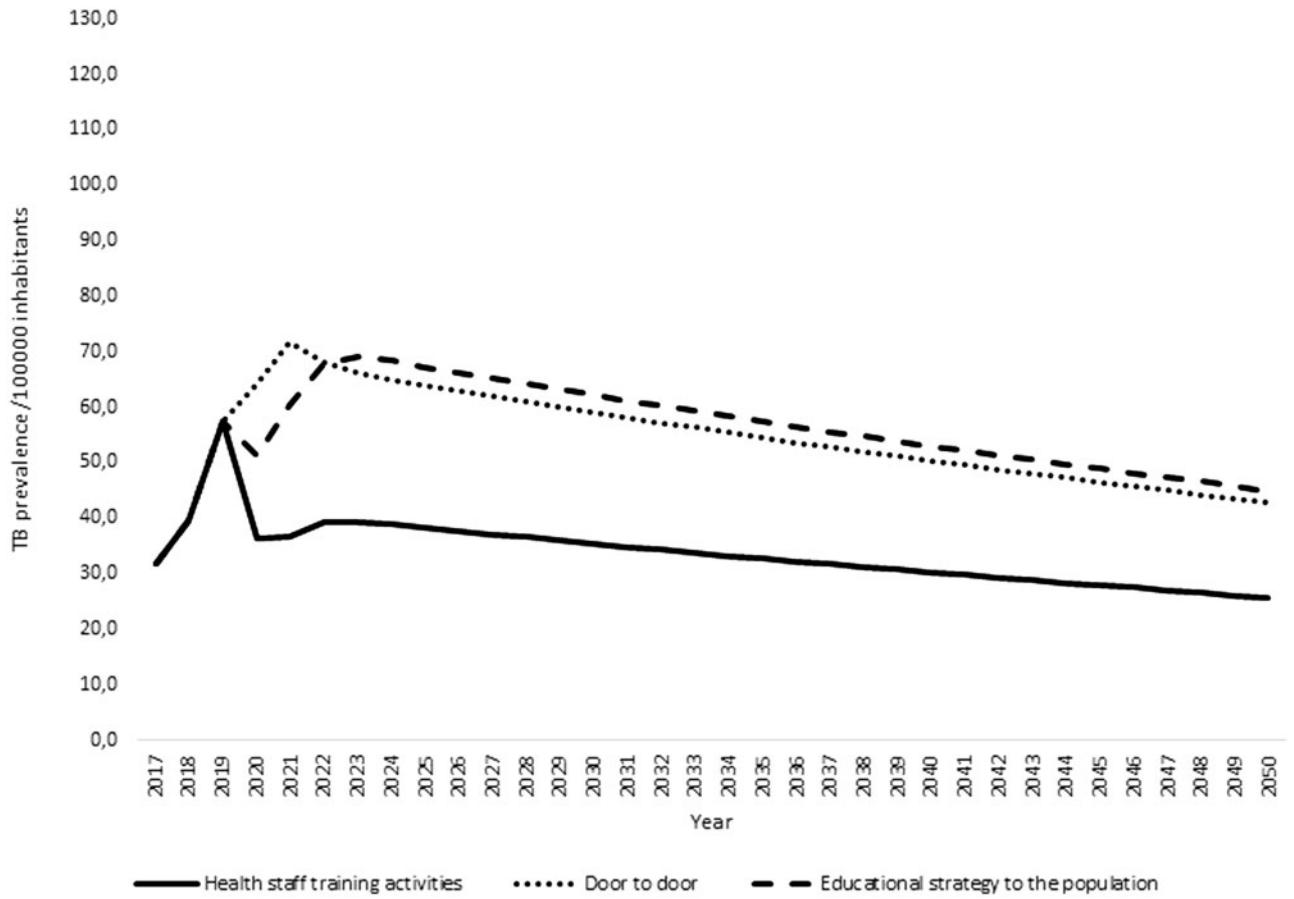

Figure 2 Simulation of tuberculosis prevalence from 2017 to 2050 using three strategies to identify people with suspected TB. Health staff training activities (black line). Door to door activities (dot line). Education strategy to the population (dashed line).

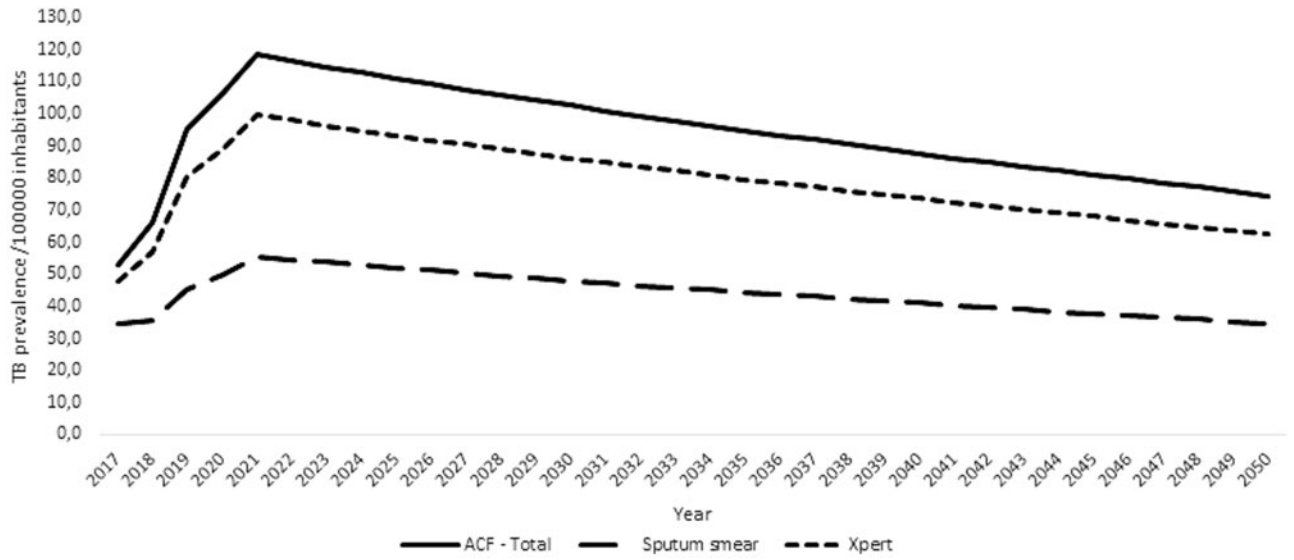

Figure 3 Simulation of tuberculosis prevalence from 2017 to 2050 using three strategies to diagnose TB. ACF—total (black line): using liquid culture to make the TB diagnosis, sensitivity of 100%. Sputum smear sensitivity of 47.6% (dashed line). Xpert sensitivity of 84% (short dashed line).

well as community strategies like ACF or community DOTS, may have accounted for the observed increases.

When analysing the simulated results for maintaining current scenario (status quo), presuming no change in practices, no projected changes are to be expected. This scenario will result in stable rather than decreasing the prevalence, percentage of mortality and successful treatment of TB. The findings are similar to a study that summarizes global data in which they compared the trends of

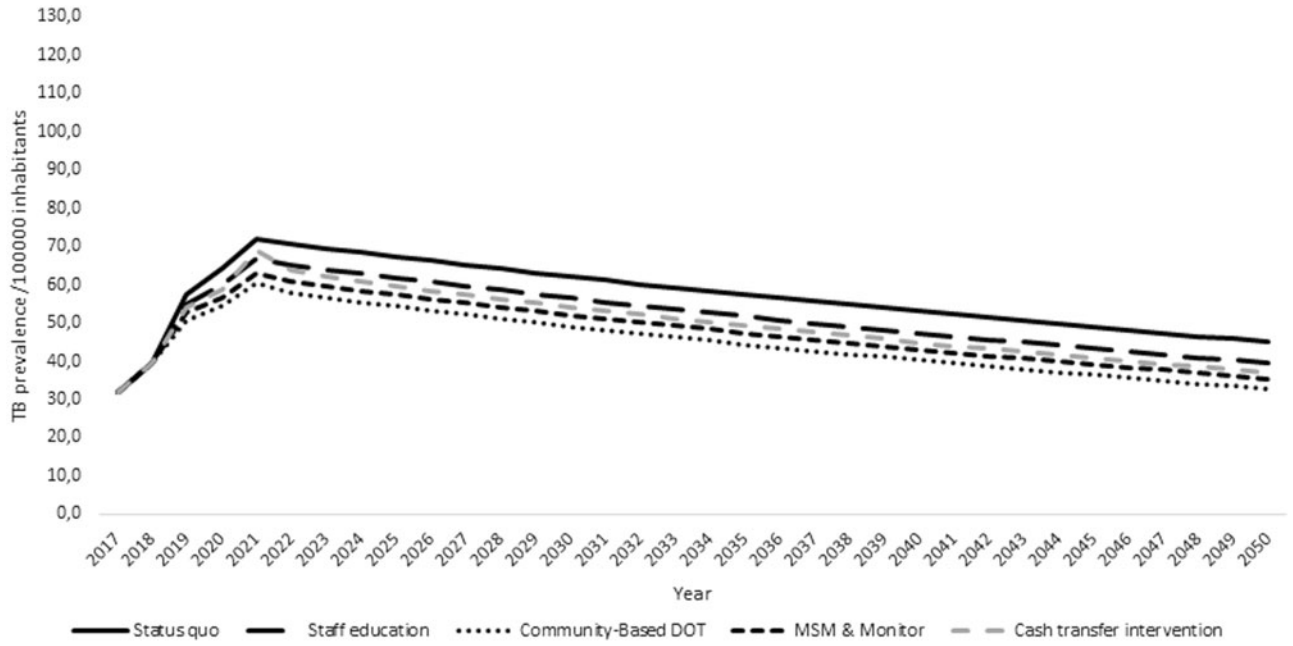

Figure 4 Simulation of tuberculosis prevalence from 2017 to 2050 using four strategies to increase successful treatment. Status quo (black line): To keep the successful treatment on 72% as the previous years in Colombia, with a decline in TB incidence of 1.6% per year. Staff education (dashed line). Community-based DOT (dot line). M&M and monitor (short dashed line). Cash transfer intervention (gray dashed line).

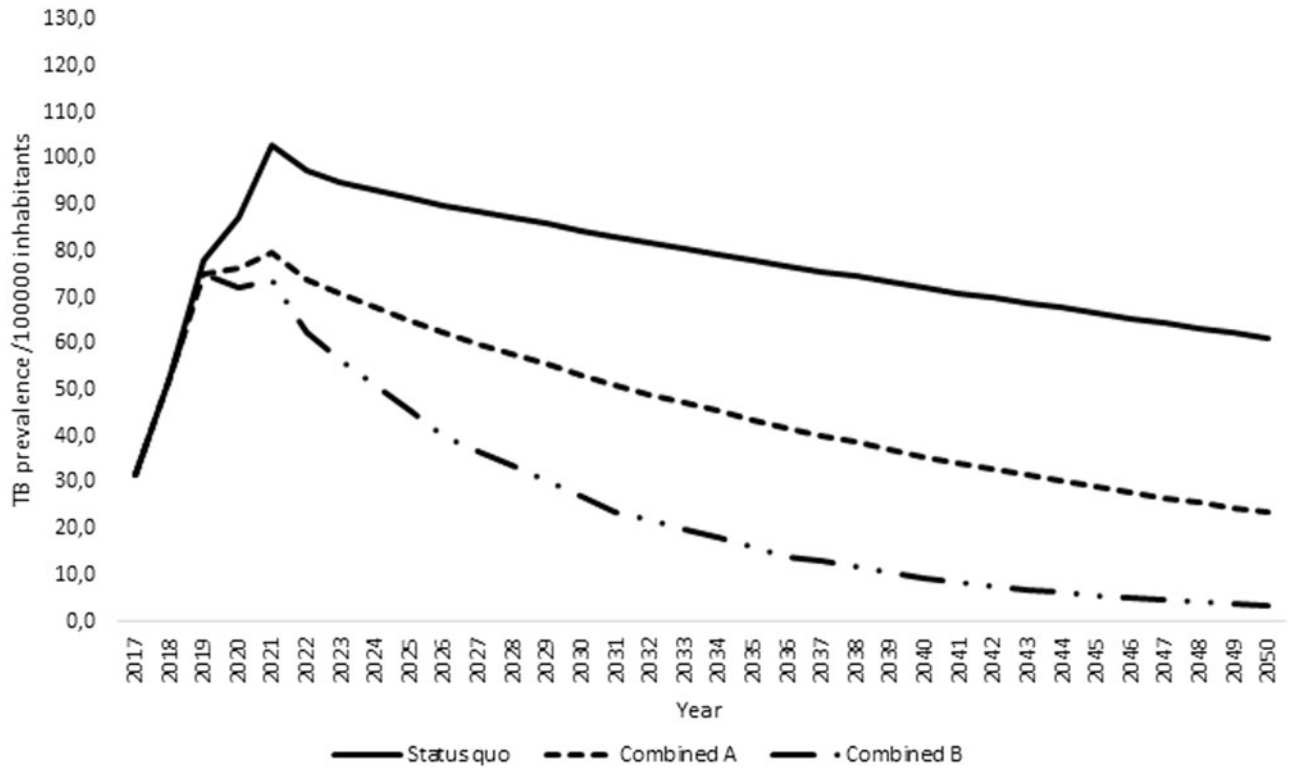

Figure 5 Simulation of tuberculosis prevalence from 2017 to 2050 using combined strategies to improve screening, diagnosis and treatment. Status quo (black line): To keep the successful treatment on 72% as the previous years in Colombia, with a decline in TB incidence of 1.6% per year. Combined A (dashed line): the combination of TB screening, diagnosis and successful treatment will have a decline in the TB incidence of 4% per year. Combined B (dot and dashed line): the combination of TB screening, diagnosis and successful treatment will have a decline in the TB incidence of 10% per year.

20 years (Kazemnejad *et al.*, 2014), and another conducted in Brazil between 2013 and 2016 where the incidence remain almost constant (Pinto *et al.*, 2017). In China, Huynh *et al.* modelled TB incidence and mortality by analysing the projection of data with the current trend, and although they found a downward trend for the years 2025 and 2035, the anticipated reductions fall short of approaching

the goals proposed by WHO. In the case of TB incidence, they found a decrease of 25% by 2025 and 42% by 2035, and mortality was projected to decrease by 28% by 2025 and 41% by 2035 (Huynh *et al.*, 2015). A simulation conducted in South Africa, focused on evaluation of the expected trends of the incidence and mortality of TB in HIV-positive people, and found that the rates would remain constant if current strategies were to continue unaltered (Chindelevitch *et al.*, 2015). Another simulation conducted in India compared the impact of universal use of GenXpert® vs to no implementation of GenXpert®, and they found that the TB of all forms and MDR-TB incidences will decrease after the universal implementation of GenXpert® (Sachdeva *et al.*, 2015).

Our simulation shows the impact of combining strategies on decreasing TB prevalence. Colombia needs to implement multimodal interventions to improve the screening, rapid diagnosis and successful treatment in order to achieve End TB strategy goals instead of using individualized strategies, as has been reported by other authors. Other simulations performed with mathematical models using different scenarios changing the discrete and sustained ACF rates in China, India and South Africa, have shown that sustained ACF programmes over 10 years hold promise to achieve a dramatic population-level impact on both incidence (22–27% reduction) and mortality (40–44% reduction). In addition, they found that ACF interventions that increased the number of cases diagnosed and treated by 25% in their first year reduced the average duration of untreated disease from 15.2 to 12.7 months in South Africa, 20.0 to 17.3 months in India and 20.4 to 17.0 months in China (Azman *et al.*, 2014). Houben *et al.* also simulated provision of continuous access to treatment for latent TB for people on antiretroviral therapy, expanded facility-based screening for symptoms of TB at health centres and improved TB care (access, diagnosis of TB and MDR-TB, improve post-diagnosis, ACF in general population followed by treatment of latent TB). Combining the above interventions could lead to a decrease of 55% in the TB incidence and 72% reduction in mortality rates (Houben *et al.*, 2016). In China, Huynh *et al.* modelled several interventions, including expansion of DOTS to all patients, reduced time to treatment, improved treatment success, ACF in elders, preventive therapy in elders (>65 years old). Applying individual interventions failed to achieve the proposed goals, but when all the strategies are integrated and offered as a suite, it would be possible to achieve the goals, decreasing the TB incidence by 71% by 2025 to 84% by 2035 compared with 2015; resulting in decreased mortality from 85% by 2025 to 92% by 2035 (Huynh *et al.*, 2015).

One of the pillars of the strategy for ending TB is patient-centred care. In Colombia, this pillar has been directed to identify populations at risk and their needs (Ministerio de Salud y Protección Social *et al.*, 2016). Therefore, the strategies that would be chosen to impact the TB incidence, such as enhancing the time of diagnoses, will depend on the conditions of the populations. For example, in remote regions with barriers or difficulties to access health services, community agents trained in symptoms detection and how to collect the samples can be a good alternative to improve screening and diagnosis and thus have an impact on TB incidence (Gabriel and Mercado, 2011; OIM, 2017). In areas with high HIV and MDR rates having access to GenXpert® would allow faster diagnoses and detection of resistant mycobacteria (Sachdeva *et al.*, 2015).

Interventions aimed at improving adherence to treatment and thereby increasing successful treatment such as economic incentives and subsidies in the form of money or food for populations with very low incomes have shown to be promising (Boccia *et al.*, 2016; Torrens *et al.*, 2016), but these programmes must be tightly linked to compliance with treatment. In addition, members selected from the community who receive training and economic compensation for monitoring, treatment provision and counselling have been demonstrated to have significant impact (Gabriel and Mercado, 2011; OIM, 2017).

The interventions must be comprehensive, in order to control transmission, reduce the prevalence of the disease, reduce mortality and increase treatment success. In Colombia, the strategies must be designed and adapted for each region, because the country is heterogeneous in the rates of the disease, in the availability of resources, in population structures, in possibilities of access to diagnostic tools. Disaggregated data regarding treatment outcomes as mentioned earlier will be necessary for optimal resource allocation to regions and populations with the greatest need. For example, recently we reported that the successful treatment in non-HIV and non-homeless group was 80.7%, in HIV + non-homeless group was 62.6%, in HIV− homeless group was 38.5% and in HIV + homeless group 29.7% (Gomez *et al.*, 2019). The model imply that political will and leadership will need to understand and accept the anticipated initial increases in TB incidence in order to continue to provide sustainable funding for implementation of the strategies. Such sustained engagement is of paramount importance to fully realize the benefits of the interventions. For example, GenXpert® was designed to provide a cheaper and faster result within hours, but unfortunately in Colombia there are laboratories where the prices of GenXpert® range between 150 and 300 USD (information collected from phone calls we did), and the health insurance companies take between 1 and 2 months to approve the GenXpert® procedure. In this context, the excessive cost makes this technology less useful for general implementation.

Whichever intervention is implemented, there must be allocation of resources, because many of the strategies found in the literature are funded by different institutions, in most cases, these are external organizations (NGOs, USAID, Global Fund, etc.). Dependence on external funding may lead to strategies that are not sustainable over time unless they become an integral part of the budget, and involve community capacity building.

In conclusion, our results show that the current strategies are insufficient and will not allow Colombia to achieve the End TB strategy targets, and even alarmingly witness an increase the incidence and mortality rates. This system dynamic simulation modelling exercise has suggested that a combination of multiple, simultaneous interventions that aim to improve screening, diagnosis and treatment adherence are needed to achieve the targets. These data can be used to inform and advocate with leadership for resource allocation, and guided evidence-based decisions for choosing simultaneous interventions to improve screening, diagnosis and treatment adherence. Such multimodal interventions can position Colombia to decrease the TB incidence by 2050 to 10/100 000. It is necessary to evaluate the implementation of those strategies altogether over time to determine the impact of each one. It is important to design individualized strategies according to the problems and needs of each region, as well as geographical and cultural aspects.

Supplementary data

Supplementary data are available at *Health Policy and Planning* online.

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