



Spatially targeted digital chest radiography to reduce tuberculosis in high-burden settings: A study of adaptive decision making

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ABSTRACT

Background: Spatially-targeted approaches to screen for tuberculosis (TB) could accelerate TB control in high-burden populations. We aimed to estimate gains in case-finding yield under an adaptive decision-making approach for spatially-targeted, mobile digital chest radiography (dCXR)-based screening in communities with varying levels of TB prevalence.

Methods: We used a Monte-Carlo simulation model to simulate a spatially-targeted screening intervention in 24 communities with TB prevalence estimates derived from a large community-randomized trial. We implemented a Thompson sampling algorithm to allocate screening units based on Bayesian probabilities of local TB prevalence that are continuously updated during weekly screening rounds. Four mobile units for dCXR-based screening and subsequent Xpert Ultra-based testing were allocated among the communities during a 52-week period. We estimated the yield of bacteriologically-confirmed TB per 1000 screenings comparing scenarios of spatially-targeted and untargeted resource allocation.

Results: We estimated that under the untargeted scenario, an expected 666 (95% uncertainty interval 522–825) TB cases would be detected over one year, equivalent to 8.9 (7.5–10.3) per 1000 individuals screened. Allocating the screening units to the communities with the highest (prior-year) cases notification rates resulted in an expected 760 (617–926) TB cases detected, 10.1 (8.6–11.8) per 1000 screened. Adaptive, spatially-targeted screening resulted in an expected 1241 (995–1502) TB cases detected, 16.5 (14.5–18.7) per 1000 screened. Numbers of dCXR-based screenings needed to detect one additional TB case declined during the first 12–14 weeks as a result of Bayesian learning.

Conclusion: We introduce a spatially-targeted screening strategy that could reduce the number of screenings necessary to detect additional TB in high-burden settings and thus improve the efficiency of screening interventions. Empirical trials are needed to determine whether this approach could be successfully implemented.

1. Introduction

Tuberculosis (TB) remains a leading infectious cause of death despite the availability of effective treatment. A major obstacle towards reducing transmission and mortality is the failure to detect and treat people with TB. Globally, one-third of the estimated 10 million people who developed TB in 2019 did not have access to high-quality TB

treatment (Harding, 2020).

Levels of undiagnosed TB remain high in many countries and settings, suggesting that conventional diagnostic strategies which rely on self-presentation of symptomatic individuals to health services are not sufficient for limiting transmission. More pro-active strategies to find individuals with TB will thus be needed to achieve population-level impact (Dowdy et al., 2013). Systematic screening among specific

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high-risk populations could help reduce undiagnosed TB. Risk populations to be considered for screening include individuals exposed to TB in the household, people living with human immunodeficiency virus (HIV) infection, and workers exposed to silica, among others (World Health Organization, 2013).

As an alternative to using individual-level risk factors, targeting screening within geographically-defined populations (e.g. communities) could be an attractive approach (Cudahy et al., 2019; Dowdy et al., 2012). The concept of spatially-targeted screening is based on evidence of considerable geographical variation in TB incidence and prevalence reported from numerous studies (Touray et al., 2010; Wang et al., 2012; Yazdani-Charati et al., 2014). Focusing screening towards ‘hotspots’ of undetected TB and associated transmission could lead to more effective allocation of resources than untargeted country-wide efforts (Cudahy et al., 2019). The World Health Organization (WHO) recommends that systematic screening for TB “may be conducted among the general population in areas with an estimated TB prevalence of 0.5% or higher” (World Health Organization, 2021). Studies of spatially-targeted TB screening are limited to date. A recent systematic review identified only three studies in low TB incidence settings, and none had been conducted in high TB incidence countries (Cudahy et al., 2019). A recent modelling study of active TB case finding in Ethiopia suggested that targeting screening towards areas with a high TB burden would be efficient and cost-saving with the potential to significantly reduce the overall burden of TB (Shaweno et al., 2021).

A key challenge for spatially-targeted screening is the identification and prioritization of geographical ‘hotspots’ where such policies could be most effective (Dowdy et al., 2012). Many high TB burden countries struggle to implement high-quality TB surveillance systems at subnational level (van der Werf and Borgdorff, 2007). Where these systems are in place, numbers of diagnosed TB patients might not accurately reflect local variation in the burden of undiagnosed, prevalent TB. As screening for TB demands considerable investments within often resource-constrained healthcare systems, guidance on how to prioritize geographical areas for spatially-targeted screening could help ensure that resources for TB screening are used in the most efficient way.

In this study, we propose the use of an adaptive decision-making algorithm for spatially-targeted screening for TB. Our approach allows for the dynamic allocation of screening resources among multiple geographical areas in the absence of knowledge about variation in the local burden of undiagnosed TB. To investigate this approach, we developed a computer simulation of automated, digital chest radiography (dCXR)-based screening in 24 high TB burden communities in South Africa and Zambia (Ayles et al., 2013, 2008). We used the simulation to estimate gains in TB case-finding yield that would be expected under the spatially-targeted screening approach compared to untargeted (random) allocation of screening resources in the communities.

2. Methods

2.1. Conceptual framework

We propose an adaptive decision-making approach for spatially-targeted TB screening in high TB prevalence settings. The approach is based on Thompson sampling (Russo et al., 2018; Thompson, 1933), a Bayesian probabilistic sampling algorithm that addresses the “exploration-exploitation dilemma” (Auer et al., 2002; Berger-Tal et al., 2014) which has been investigated in a variety of scientific disciplines. Central to this dilemma is the trade-off between the need to obtain new knowledge and to exploit this knowledge to maximize rewards (Berger-Tal et al., 2014); the “exploration” features of these algorithms are potentially attractive for TB because case notifications will not reliably reflect incidence where there are varying levels of health access. The algorithm seeks to guide decision makers in allocating limited resources for screening among multiple geographically-defined populations with the aim to maximize the yield of TB detected over time. A central

assumption of the algorithm is that the number of TB cases detected per screenings performed in a geographically-defined target population follows a distribution around the true prevalence of undetected TB in this population. On average, this screening yield will be higher in populations with a higher background TB prevalence. Details about the decision algorithm are described below and in the [Supplementary material](#) (page 1).

2.2. Screening scenarios investigated

We assumed a hypothetical limited-resource scenario under which a mobile TB screening intervention would be implemented in 24 communities with unknown TB prevalence. No more than four mobile screening units would be available for a period of one year. The units would be placed at public points of interest to offer TB screening to adults walking by. In addition, field teams would be deployed to visit adjacent households to invite adults for screening. In line with WHO recommendations (World Health Organization, 2013), screenings would employ a two-stage screening algorithm consisting of an initial screening test and a subsequent confirmatory bacteriological test. Screening would be offered regardless of TB characteristic symptoms or risk factors and consist of an initial screening test using digital chest radiography (dCXR) with automated, computer-aided detection. Those with a positive initial screening would be offered sputum examination via Xpert Ultra (Dorman et al., 2018). Key assumptions for the screening scenario are summarized in the [Box](#) below.

We defined an *untargeted (base-case) scenario* under which health authorities would randomly allocate the screening units among the communities. At the beginning of the year, four communities, one per screening unit, would be randomly selected; units would be placed in the communities for the entire year. We compared the base-case scenario to two scenarios of spatially-targeted TB screening, a *spatially-targeted case notification-based scenario* under which four screening units would be placed in the four communities with highest prior-year case notification rates and an *adaptive spatially-targeted scenario* which seeks to dynamically deploy the four screening units in four distinct communities with the highest TB prevalence (i.e. 1st to 4th highest) under the adaptive decision-making approach.

2.3. Simulation data sources

We used estimates of population-level TB prevalence in 24 high TB burden communities obtained for the Zambia South Africa Tuberculosis and HIV Reduction (ZAMSTAR) study (Ayles et al., 2013; Marx et al., 2016), a large cluster-randomized trial conducted until 2010. For the primary outcome measure, a total of 64,452 adults were successfully evaluated for culture-positive TB in the 24 communities, irrespective of reporting symptoms, and 894 adults with bacteriologically-confirmed TB were identified (Marx et al., 2016). Estimates of culture-confirmed TB varied among the 24 ZAMSTAR communities between 0.22% and 3.11% (Fig. 1). In addition, we obtained estimates of dCXR and Xpert Ultra sensitivity and specificity from recent (meta-)analyses of diagnostic accuracy (Table 1).

2.4. Simulation approach and data analysis

We developed a Monte-Carlo simulation model to simulate the screening yield expected under the untargeted base-case and the two spatially-targeted scenarios. The simulation was implemented using R statistical application (version: 4.0.2) and consists of 1000 independent model iterations. A detailed description of how we implemented the simulation is provided in the [Supplementary material](#) (page 1).

In brief, the simulation consists of two parts. In the first part, we conducted a series of independent Bernoulli trials to simulate TB cases detected through screening in the communities. Each series is set up with n Bernoulli trials representing the number of individuals screened

Box

Key assumptions for the hypothetical screening scenario.

- Twenty-four communities have been pre-selected for mobile TB screening.
- The prevalence of undetected TB in the communities is not known.
- Resources are available to deploy and operate 4 mobile TB screening units among the communities for a total duration of 52 weeks.
- Every day, between 50 and 70 adults (≥ 18 years) will be screened for TB, equivalent to 300–420 during a 6-day working week; screening will be conducted via digital chest radiography (dCXR); those with a positive dCXR test will undergo sputum testing via Xpert Ultra for bacteriological confirmation.
- The yield of TB patients detected per screenings performed at any time in a community follows a probability distribution around the prevalence of undetected TB at community level.
- To maximize screening yield, health authorities can revise decisions where to deploy the screening units after each week. Resources to move the units between communities are negligible.
- The prevalence of undetected TB at community level decreases with each screening round as a direct result of screening.

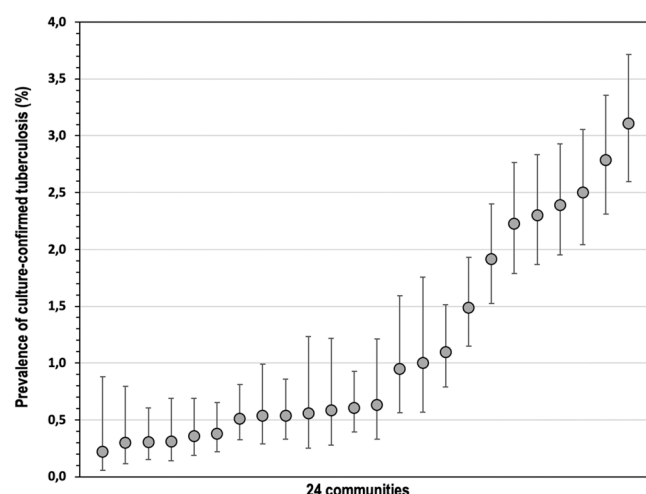


Fig. 1. Estimates of community-level TB prevalence (adults, culture-confirmed TB) used in the simulation

Source: Zambia South Africa TB and HIV Reduction [ZAMSTAR] (Ayles et al., 2013; Marx et al., 2016).

Table 1

Simulation parameters used and their sources.

| Simulation parameters | Best estimate | Uncertainty range | Source |
|--|----------------------|-------------------|---|
| Community TB ^a prevalence | Varying (see Fig. 1) | – | (Ayles et al., 2013; Marx et al., 2016) |
| No. daily dCXR ^b screenings | 60 | 50–70 | Assumption |
| dCXR sensitivity | 95% | – | (Breuninger et al., 2014; Melendez et al., 2016; Murphy et al., 2020; Philipson et al., 2015) |
| dCXR specificity | 55% | 50–60% | (Breuninger et al., 2014; Melendez et al., 2016; Murphy et al., 2020; Philipson et al., 2015) |
| Xpert Ultra sensitivity | 85% | 80–90% | (Boehme et al., 2011; Dorman et al., 2018) |
| Xpert Ultra specificity | 98% | – | (Boehme et al., 2011; Dorman et al., 2018) |

^a Tuberculosis.

^b Digital chest radiography.

per week and the success probabilities, p , are set to simulated ‘true’ TB prevalence values sampled from beta probability distributions that were approximated from TB prevalence survey estimates (Fig. 1). The simulation keeps track of TB prevalence over time to allow for reductions as a

direct effect of TB cases detected through screening (see page 12 for further details). The number of k successes resulting from each Bernoulli experiment represents the simulated ‘true’ number of TB cases detectable through screening each week. We simulated false-positive and false-negative test results based on estimates of diagnostic accuracy obtained from the literature (Table 1). In the second part, we simulated decisions to allocate the screening units among the communities over time. Under the base-case scenario, four distinct communities were randomly sampled for screening. Under the notification-based allocation scenario, four distinct communities with the four highest case notification rates in the previous year were selected for screening. To simulate the spatially-targeted adaptive screening scenario, we implemented a Thompson sampling algorithm (Russo et al., 2018; Thompson, 1933). At the start of the first screening round (week), a prior probability of TB prevalence is sampled for each community from a single prior (beta) distribution. We approximated this prior distribution from a TB prevalence estimate of 2.0% (1.0–3.0%) derived from two pilot studies conducted prior to the ZAMSTAR study (Ayles et al., 2009; Claassens et al., 2013). Sampled estimates of TB prevalence then inform decisions where to allocate screening during the first week of the intervention. Under the adaptive spatially-targeted scenario, the four screening units are allocated to four distinct communities with the (four) highest sampled prevalence estimates. At the end of the first screening round, prior probability distributions in the communities selected for screening are updated based on positive test results, with adjustments to account for the expected number of false-positive and false-negative test results (see the Supplementary material page 9 for further details). Prior to the second week of screening, TB prevalence estimates for each community are then resampled from the updated (posterior) distributions to inform allocation decisions in the following week. The process of sampling, screening allocation, updating of distributions and resampling is repeated for each of the remaining screening rounds.

The principal outcome of this model-based analysis was the number of TB cases detected per 1000 individuals screened under the base-case and each of the two spatially-targeted scenarios during the 52-week intervention period. To investigate trends over time, we calculated weekly numbers of dCXR screenings performed to find one additional TB patient. All outcomes were calculated as the mean, and 95% uncertainty intervals as the 2.5th and 97.5th percentiles of the 1000 model iterations.

2.5. Sensitivity and secondary analysis

We conducted additional analyses to understand how sensitive our findings were to specific assumptions made at primary analysis. We varied the number of screening units available and the number of individuals screened each week. We also increased the underlying population size to reduce the impact of the screening intervention relative to

the estimated prevalent TB burden in the communities. Finally, we investigated the yield of the spatially-targeted approach assuming lower sensitivity of dCXR-based screening, and the effect of increasing the duration of a screening round from one week to one month.

Additionally, we considered an alternative adaptive spatially-targeted scenario that seeks to maximize screening yield by allowing multiple screening units to be placed in the same community. Details of this alternative approach can be found in the [Supplementary material](#) (page 7). Furthermore, we explored an additional decision scenario using case notification rates as prior information to estimate the TB prevalence in the communities under the adaptive decision-making approach ([Supplementary material](#) page 17).

3. Results

3.1. Simulated screening yields

We estimated that under the base-case scenario (random allocation of the four screening units), an expected 666 (95% uncertainty interval 522; 825) bacteriologically-confirmed TB cases would be detected through screening over the one-year intervention period, equivalent to 8.9 (7.5; 10.3) per 1000 screened. Under the case notification-based allocation scenario, an expected 760 (617; 926) bacteriologically-confirmed TB cases would be detected over one year, equivalent to 10.1 (8.6; 11.8) per 1000 screened. The increase in screening yield relative to the base-case scenario would be 14.8% (−4.5%; 36.6%). Adaptive allocation of the screening units would increase this yield. Under the adaptive spatially-targeted scenario, we estimated an expected 1241 (995; 1502) TB cases detected over one year, equivalent to 16.5 (14.5; 18.7) per 1000 screened. The increase in screening yield relative to the base-case scenario would be 87.0% (61.9%; 118.1%). Adaptive spatially-targeted screening also increased the combined positive predictive value (PPV) of the screening algorithm as the background prevalence of TB increased over time. [Table 2](#) shows detailed results of the simulation.

3.2. Trends in numbers needed to screen over time

Under the base-case scenario, we projected a slight increase in numbers needed to screen (NNS) during the intervention period ([Fig. 2a](#)). This is due to the expected reduction in TB prevalence as a result of the impact of the screening intervention on TB prevalence in the communities. Under the spatially-targeted adaptive screening scenario ([Fig. 2c](#)), NNS declined over the first 12–14 screening rounds (weeks) as a result of Bayesian learning.

3.3. Sensitivity and secondary analysis

Lowering the number of individuals screened with dCXR each week ([Fig. 3a](#)) or the number of available screening units ([Fig. 3b](#)) led to slower declines in numbers needed to screen under adaptive spatially-targeted screening due to less optimal learning under the Thompson sampling algorithm. Increasing the population size in the communities reduced the relative impact of the screening intervention on TB prevalence and, hence, the increase in numbers needed to screen over time observed at primary analysis ([Fig. 3c](#)). Finally, lowering the sensitivity of dCXR to detect TB led to decreased numbers of TB cases found and thus higher numbers needed to screen over time for both the base-case (random allocation) and adaptive spatially-targeted screening scenarios ([Fig. 3d](#)). We estimated similar yields and numbers needed to screen for a maximum-targeted scenario, an alternative adaptive approach, under which multiple screening units can be placed in the same community (see: [Supplementary material](#) page 12).

Increasing the duration of a screening round from one week to one month led to slower declines in numbers needed to screen under the adaptive spatially-targeted screening approach due to slower learning.

Table 2

Simulated screening results under the different strategies of allocating 4 mobile screening units in the 24 communities: base-case scenario (untargeted, random allocation), case notification-based scenario and spatially-targeted adaptive scenario. Values are presented as mean estimates over the 1000 simulation iterations and their (95% uncertainty interval).

| Outcome measure | Base-case (random allocation) | Spatially-targeted, case notification-based | Spatially-targeted, adaptive |
|---|-------------------------------|---|------------------------------|
| Total number of dCXR ^a screenings performed | 75,159 (63,024; 86,944) | 75,159 (63,024; 86,944) | 75,159 (63,024; 86,944) |
| % dCXR-positive, referred for Xpert Ultra | 11.8% (10.7%; 12.9%) | 11.9% (10.7%; 13.0%) | 12.3% (11.2%; 13.4%) |
| Total number of TB ^b patients detected | 666 (522; 825) | 760 (617; 926) | 1241 (995; 1502) |
| Yield per 1000 dCXR screenings | 8.9 (7.5; 10.3) | 10.1 (8.6; 11.8) | 16.5 (14.5; 18.7) |
| % increase in yield over base-case scenario | (reference) | 14.8% (−4.5; 36.6) | 87.0% (61.9%; 118.1%) |
| Average no. of dCXR ^a s conducted to identify 1 additional TB case | 113.0 (96.2; 133.0) | 102 (66.3; 192.2) | 60.8 (52.7; 68.9) |
| Total number of relocations of screening units ^c | 4 | 4 | 150 (117; 174) |
| Positive predictive value (%) ^d | 49.9% (44.6%; 54.9%) | 53.3% (48.5%; 58.4%) | 65.3% (60.2%; 70.5%) |
| Negative predictive value (%) ^d | 99.8% (99.7%; 99.8%) | 99.8% (99.7%; 99.8%) | 99.6% (99.5%; 99.7%) |

^a Digital chest radiography.

^b Tuberculosis.

^c Total number of relocations over the 52-week period of all four screening units combined.

^d Combined positive- and negative predictive value of the two-step screening algorithm (dCXR followed by Xpert Ultra).

This is due to a reduction in the total number of relocations of all four screening units from 150 to 38, on average ([Fig. 4](#)). The total number of bacteriologically-confirmed TB cases was reduced by approximately 15%.

4. Discussion

In this study, we simulated an adaptive decision-making approach for spatially-targeted TB screening in high-burden communities. The proposed approach enables decision makers to leverage data obtained during subsequent screening rounds for Bayesian learning to increase the yield of TB detected over time and therefore improve the efficiency of community-based screening.

The value of adaptive (sampling) strategies using spatially explicit and real-time intervention data to inform infectious disease control policies has previously been emphasized, including for interventions against foot-and-mouth disease ([Probert et al., 2018](#)), measles ([Shea et al., 2014](#)), HIV ([Gonsalves et al., 2018](#)) and COVID-19 ([Marecek, 2020](#)). To our knowledge, our study is the first to propose an adaptive strategy for spatially-targeted TB screening. We think that this approach could be readily applied in settings where additional efforts are needed to find and treat people with TB, and where limited resources require allocation decisions to reach the best possible impact.

We propose this approach for spatially-targeted TB screening at a time when evidence is increasing that routine TB healthcare services in many high-burden countries have been seriously impacted by measures to contain the COVID-19 pandemic, resulting in a backlog of undetected TB, potentially with increased transmission, morbidity and mortality

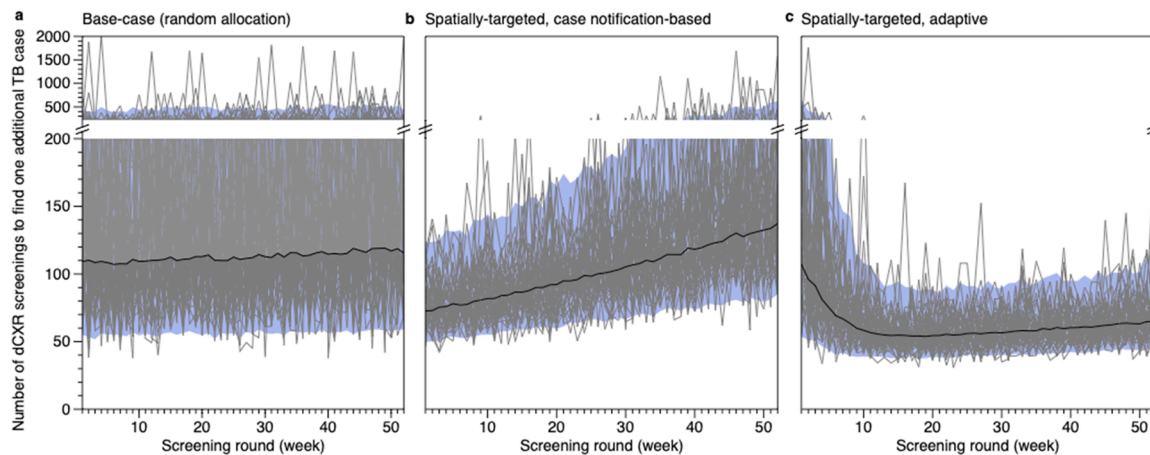


Fig. 2. Performance of different strategies of allocating 4 mobile screening units in the 24 communities over time; left: base-case scenario (untargeted, random allocation), middle: notification-based scenario, right: adaptive spatially-targeted adaptive scenario; a-c: Number of dCXr screenings performed to find one additional TB case over time (weeks); bold black lines shows mean estimates of 1000 simulated trajectories; blue areas show 95% uncertainty intervals; grey lines show 50 randomly sampled model trajectories. Increases in the number of dCXr screenings performed to find one additional TB case over time are observed in later weeks as a result of the impact of the screening intervention. The increase is highest in the case notification-based approach due to lower population size in the selected communities.

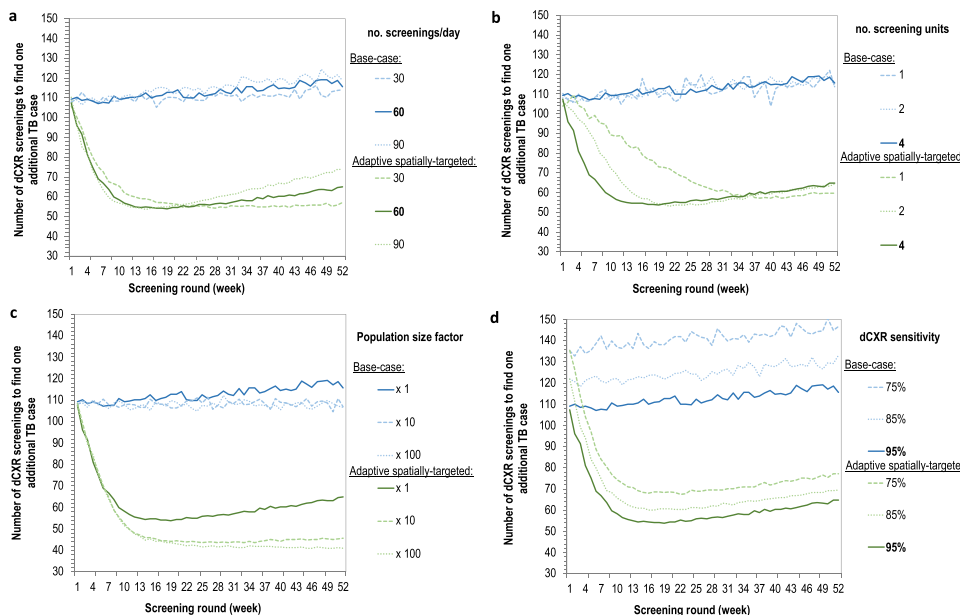


Fig. 3. Sensitivity analysis of simulation parameters. Trends in numbers needed to screen to find one additional person with TB over the 52-week screening period of allocating mobile screening units in the 24 communities over time: base-case scenario (untargeted, random allocation), balanced adaptive spatially-targeted allocation scenario in Fig. 3a,c,d and maximum-targeted allocation scenario in Fig. 3b. Full lines: primary analysis results, dashed lines: sensitivity analysis results. The following parameters were varied for sensitivity analysis: (a) number of screenings conducted per day for each of the 4 screening units (30,60,90); (b) number of screening units available (1,2,4) whilst total numbers of screenings per day was held constant; (c) population sizes increased by orders of magnitude ($10^0, 10^1, 10^2$); (d) sensitivity of digital chest radiography (dCXr) varied (75%,85%,95%) whilst specificity of dCXr remained fixed at 55%.

(Cilloni et al., 2020; Hallett et al., 2020; McQuaid et al., 2020). Spatially-targeted screening could play an important role in accelerating progress in TB control during a COVID-19 recovery phase, particularly in areas with the highest TB burden.

Our simulation of a hypothetical mobile screening intervention in 24 high TB burden communities suggests that dynamic, spatially-targeted allocation of screening units could greatly improve the efficiency of screening as the numbers of dCXr screenings required to detect additional TB could be reduced over time, compared to a random and a case notification-based allocation approach. Our findings are consistent with a recent modelling study which suggested that geographically-targeted allocation of TB active case finding in Ethiopia would be efficient and cost-saving compared to random allocation (Shaweno et al., 2021). They are also consistent with findings from an earlier study about mobile HIV testing in Chicago (Gonsalves et al., 2018), which projected that adaptive allocation nearly doubled the number of HIV infections that could be detected compared to allocation based on historic data.

We considered two different versions of adaptive spatial targeting, which represent options for decision makers to either balance resources among several communities with the highest TB prevalence (balanced-targeted), or allow screening units to be pooled in few communities to maximize screening yield (maximum-targeted; see supplementary). Our results suggest that both compare well in terms of additional TB cases found and screening yield over time. The maximum-targeted version showed marginally better efficiency of learning in the earlier intervention phase. However, placing multiple screening units simultaneously in the same community may be logistically challenging and less efficient especially in smaller communities. We show that the efficiency of spatially-targeted screening increases with the number of screening units available. This is because greater dispersion of available resources leads to improved learning under the adaptive sampling algorithm as each unit shares information about observed TB patients with the other units.

We simulated a spatially-targeted approach that employs chest-

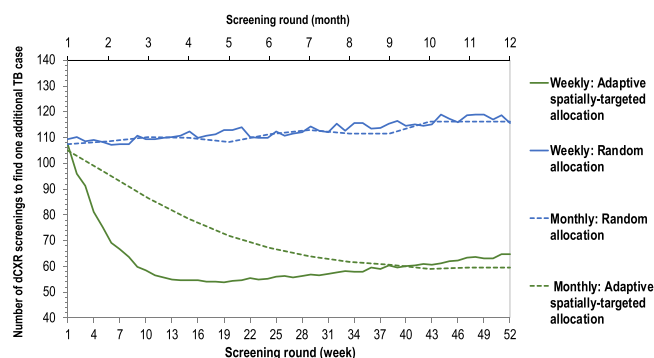


Fig. 4. Trends in numbers needed to screen to find one additional person with TB over the 52-week screening period of allocating mobile screening units in the 24 communities over time: adaptive spatially-targeted screening allocation scenario with weekly and monthly screening rounds; bold lines shows mean estimates of 1000 simulated trajectories.

radiographic screening irrespective of self-reported symptoms. High levels of subclinical TB observed in high-burden settings have raised important questions about the impact of symptom-based case-finding approaches for reducing transmission (Kendall et al., 2021). TB prevalence surveys in the study communities revealed that almost half of individuals with prevalent TB did not report TB-characteristic symptoms (Gunasekera et al., 2020), consistent with findings from a recent meta-analysis of country-level TB prevalence surveys (Frascella et al., 2020) and those from the recent South African national TB prevalence survey (The First National TB Prevalence Survey - South Africa, 2018, 2021). The screening approach we propose would therefore be preferable to symptom-based approaches which are likely to miss a large fraction of TB cases.

We note the following limitations. We applied our simulation to a specific hypothetical screening scenario in 24 communities with significant variation in TB prevalence rates ranging from 0.2% to 3.1%. Absolute case-finding yields under the screening intervention could be lower in communities where TB is less prevalent on average. Relative gains in case-finding yield under the adaptive approach in other settings will depend on the extent to which TB rates vary between geographical areas. However, up to ten-fold differences in TB incidence and prevalence at sub-country level have commonly been reported from several settings (Cudahy et al., 2019); we therefore believe that our approach will be relevant for other settings in need for enhanced strategies to detect TB.

The feasibility of an adaptive approach would also depend on the geographical distance between the communities as screening units will have to be frequently relocated. The proposed adaptive approach may be more easily applied in areas with smaller distances between communities, for example in (sub-) urban areas. We show that the algorithm could be adapted to incorporate screening rounds of longer duration (e.g. to 1 month) which would reduce the total number of relocations. Extending the duration of a screening round leads to fewer relocation decisions which slightly reduces the efficiency of the adaptive algorithm.

We specified screening yield, i.e. the number of TB cases detected per 1000 screenings, as the key target value for the adaptive approach. This parameter does not consider other relevant factors such as the rate at which people in the communities are willing to be screened and to initiate treatment if found to have TB, the overall epidemiological impact and the cost-effectiveness of the intervention. We note that our algorithm could be easily modified to focus on other target values of interest. For example, maximizing the absolute number of individuals in whom TB is detected via screening (or started on treatment) could be sensible if epidemiological impact was the priority. This target value would also take variation in participation rates between communities

into account. Minimizing the costs per TB case detected could be specified to prioritize communities where screening was highly cost-effective. The latter approach would also need to consider the costs associated with moving screening units and teams between communities.

Further challenges related to bacteriological confirmation of TB could lead to lower absolute case-finding yields. For example, sputum scarcity and reduced sensitivity of Xpert ultra among individuals who tested positive at the initial screening test could lower the yield of TB detectable through the intervention. Other, novel diagnostic tools could be considered for spatially-targeted case finding to mitigate losses in TB diagnosis.

Finally, our simulation is based on community-level TB prevalence as the key underlying determinant for weekly screening yield and does not consider other determinants such as the temporal and spatial variation in TB prevalence within communities. These other determinants would add to variation in screening yield observed in real life. However, they would unlikely eliminate the benefits of a spatially-targeted screening approach per se.

In conclusion, we propose an adaptive approach for spatially-targeted screening which could be implemented in settings with a high burden of undetected TB, where enhanced case-finding strategies are urgently needed (Burke et al., 2021). Empirical trials are needed to assess the feasibility and effectiveness of this approach. Transmission-dynamic modelling could help to determine the epidemiological impact and cost-effectiveness of this strategy for accelerating TB control in settings with a high TB burden. We emphasize that this approach could form part of dynamic case-finding policies (Yaesoubi and Cohen, 2013) that aim to make better use of data and observations to decide where additional investments for TB control are warranted, to reduce TB in populations most severely affected by the disease.

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CRediT authorship contribution statement

Abigail K. de Villiers: Conceptualization, Methodology, Model implementation, Data analysis, Visualization, Writing – original draft. **Christopher Dye:** Conceptualization, Methodology, Writing – review & editing. **Reza Yaesoubi:** Conceptualization, Methodology, Writing – review & editing. **Ted Cohen:** Conceptualization, Methodology, Writing – review & editing. **Florian Marx:** Conceptualization, Methodology, Supervision, Visualization, Writing – original draft, Writing – review & editing.

Previously presented work

Preliminary findings of this work were presented at the 51st Union World Conference on Lung Health, Virtual, October 2020 through a virtual poster presentation (abstract number: EP24–332–23).

Conflicts of interest

The authors do not have any commercial or other association that

might pose a conflict of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.epidem.2022.100540](https://doi.org/10.1016/j.epidem.2022.100540).

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