

RESEARCH ARTICLE

Optimizing community screening for tuberculosis: Spatial analysis of localized case finding from door-to-door screening for TB in an urban district of Ho Chi Minh City, Viet Nam

Luan Nguyen Quang Vo^{1*}, Thanh Nguyen Vu², Hoa Trung Nguyen³, Tung Thanh Truong⁴, Canh Minh Khuu⁴, Phuong Quoc Pham⁴, Lan Huu Nguyen⁵, Giang Trung Le², Jacob Creswell⁶

1 Friends for International TB Relief, Ho Chi Minh City, Viet Nam, **2** Ho Chi Minh City Public Health Association, Ho Chi Minh City, Viet Nam, **3** Go Vap District Preventive Health Center, Ho Chi Minh City, Viet Nam, **4** Ho Chi Minh City Department of Science & Technology, Center for Applied Geographic Information Systems (HCMGIS), Ho Chi Minh City, Viet Nam, **5** Pham Ngoc Thach Hospital, Ho Chi Minh City, Viet Nam, **6** Stop TB Partnership, Geneva, Switzerland

* luan.vo@tbhelp.org



OPEN ACCESS

Citation: Vo LNQ, Vu TN, Nguyen HT, Truong TT, Khuu CM, Pham PQ, et al. (2018) Optimizing community screening for tuberculosis: Spatial analysis of localized case finding from door-to-door screening for TB in an urban district of Ho Chi Minh City, Viet Nam. PLoS ONE 13(12): e0209290. <https://doi.org/10.1371/journal.pone.0209290>

Editor: Daniel Gemechu Datiko, Management Sciences for Health, ETHIOPIA

Received: August 7, 2018

Accepted: December 3, 2018

Published: December 18, 2018

Copyright: © 2018 Vo et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files.

Funding: LNQV received an award for conducting this study. The grant number is STBP/TBR/GSA/2016-06. The funder's full name is Stop TB Partnership (<http://www.stoptb.org/>). The funder reviewed and provided suggested edits for the final manuscript.

Abstract

Background

Tuberculosis (TB) is the deadliest infectious disease globally. Current case finding approaches may miss many people with TB or detect them too late.

Data and methods

This study was a retrospective, spatial analysis of routine TB surveillance and cadastral data in Go Vap district, Ho Chi Minh City. We geocoded TB notifications from 2011 to 2015 and calculated theoretical yields of simulated door-to-door screening in three concentric catchment areas (50m, 100m, 200m) and three notification window scenarios (one, two and four quarters) for each index case. We calculated average yields, compared them to published reference values and fit a GEE (Generalized Estimating Equation) linear regression model onto the data.

Results

The sample included 3,046 TB patients. Adjusted theoretical yields in 50m, 100m and 200m catchment areas were 0.32% (95%CI: 0.27,0.37), 0.21% (95%CI: 0.14,0.29) and 0.17% (95%CI: 0.09,0.25), respectively, in the baseline notification window scenario. Theoretical yields in the 50m-catchment area for all notification window scenarios were significantly higher than a reference yield from literature. Yield was positively associated with treatment failure index cases ($\beta = 0.12$, $p = 0.001$) and short-term inter-province migrants ($\beta = 0.06$, $p = 0.022$), while greater distance to the DTU ($\beta = -0.02$, $p < 0.001$) was associated with lower yield.

Competing interests: The authors have declared that no competing interests exist.

Conclusions

This study is an example of inter-departmental collaboration and application of repurposed cadastral data to progress towards the end TB objectives. The results from Go Vap showed that the use of spatial analysis may be able to identify areas where targeted active case finding in Vietnam can help improve TB case detection.

Introduction

Tuberculosis (TB) is one of the most intractable public health challenges and a leading cause of avoidable deaths worldwide. In 2016, there were an estimated 10.4 million incident cases of TB worldwide and 1.7 million TB deaths.[1] Despite advances in treatment and prevention programs, TB incidence is declining only at 1.65% per annum.[2] At this rate, global TB elimination may only be achieved near the end of the 22nd century.[3] A major cause for the slow decline is the estimated 4 million people who develop TB annually who are missed by national TB control programs (NTPs). For this reason, early detection and improved diagnosis of TB is a vital component of WHO's End TB strategy.[4]

Community-based screening for TB can detect more people with TB than passive case finding alone and detect them earlier.[5] However, strategies to improve case detection and their results will differ by setting.[6] As a result, the population-level impact of these activities remains poorly understood.[7] For example, screening of household contacts and people living with HIV is efficient and recommended in all settings[5], but due to the limited size of these high-risk populations the impact on additional cases identified, i.e., cases detected over baseline[8], is limited. Contacts and PLHIV also have a higher likelihood of detection through routine case finding activities.[9,10] Active screening in other high-risk groups such as mine workers, prisons, refugees and diabetics has also been recommended, but these strategies suffer from similar limitations in coverage and lower yields than contacts and PLHIV.[11–15] Facility-based screening can produce a high yield, but depends on patient-initiated health-seeking usually in advanced stages of disease progression and thereby may have limited impact on transmission.[16–19] Conversely, indiscriminate population-wide screening and mass chest x-ray screening produce broad coverage, but have traditionally produced a low yield of newly diagnoses tuberculosis.[20] Driven by a confluence of complexities and risk heterogeneities, and the associated high marginal cost of detection[21,22], WHO has recommended to avoid the pursuit of resource-intensive, unfocussed strategies, particularly involving mass radiography.[23] Identifying “middle-ground” solutions between high yield activities such as contact investigation and high coverage ones including community screening or active case finding (ACF) often mark successful approaches.[24–26]

Considerable evidence has shown that proximity and prolonged exposure to a source case, for example in households, among community contacts, places of mass congregation or other disease clusters, greatly raises the risk of TB infection and progression to active disease.[27–34] With the advance of Global Positioning Systems (GPS), precision vector cartography and mobile communication technology, there is a growing body of evidence on the spatial heterogeneity of tuberculosis prevalence to establish the value of Geographic Information Systems (GIS) in TB surveillance and to elucidate transmission dynamics in such disease “hot-spots.”[35–39] Many studies and approaches further incorporate molecular genetic, demographic,[40] socioeconomic or other subnational data to contextualize these disease clusters.[41,42] However, there remains limited quantitative evidence on the potential localized TB

burden in geographic proximity to index patients, possible cluster size of such TB hotspots or the number needed to screen to find a TB case within these disease clusters.[43,44] We similarly lack evidence on targeting proximal neighbor(hood) contacts for TB screening.[5,45,46] This opens up the avenue to explore “catchment areas” as means to quantify the number needed to screen (NNS) and theoretical yield from targeted ACF. However, to apply spatial restrictions methods such as catchment areas using the concentric circle approach will require the ability to quantify the potential effectiveness and to assess the associated resource implications.[47–49]

The advent of GIS and mobile communications technology in low- and middle-income countries warrants applying them to screening activities. We conducted an exploratory analysis of spatial and temporal relations of notified TB cases in an urban district of Ho Chi Minh City, Viet Nam, to quantify the search parameters, i.e., size of the area and incubation time after notification, and propose a pragmatic neighborhood contact screening strategy that could improve coverage while maintaining an acceptably high yield.

Methods

Study design & aims

This study was a retrospective cross-sectional, spatial analysis of routine TB surveillance and digital cadastral data. The aim of this study was to determine the existence and size of a catchment area around an index case, in which door-to-door screening could theoretically yield significantly more cases compared to population-wide screening. Our objectives were to assign individual GPS coordinates to all index cases in our sample and calculate the average theoretical yield from simulated door-to-door screening in three catchment area sizes, which we then compared to a published reference value. Lastly, we identified secondary index case parameters that were positively and negatively associated with theoretical yield.

Study setting

The study took place in Go Vap district, Ho Chi Minh City (HCMC). Go Vap is an urban district with a population of 650,000 people in an area of $\sim 21\text{km}^2$ for a population density of approximately 31,000 persons per km^2 . As such, Go Vap is one of the most densely populated areas in HCMC (4,020 persons/ km^2) and Viet Nam (290 persons/ km^2) overall. In 2014, 768 TB cases were notified in Go Vap for a notification rate of 136.7 per 100,000 people compared to 188.3 in HCMC and 112.8 in Vietnam.[50]

Data sources & processing

The Center for Applied GIS of Ho Chi Minh City within the HCMC Department of Science and Technology has a GIS database of the city with detailed geospatial vector data (shapefiles) of real estate property lots.[51] In this study, we repurposed this database, which typically informs urban planning and construction projects, for public health use. We included all drug-sensitive and drug-resistant TB cases notified in Go Vap between 1 November 2011 and 30 November 2015 with a recorded address in the district. These patients served as index cases for analysis throughout the study. We excluded patients re-enrolled immediately, i.e., within 1 month subsequent to a recorded treatment failure. We automated geocoding of patient addresses using a matching algorithm, manually geocoded addresses that did not produce an exact match. We excluded patients from the sample for whom automated and manual geocoding was unsuccessful. Using the GIS software, we then calculated concentric catchment areas around each patient’s residence with radii of 50m, 100m and 200m. We selected these discrete

radii as they corresponded to the amount of time (a week, a month and a quarter, respectively) an outreach worker needed to screen all households based on prior experience.[52] A catchment area with radius 50m included on average 74.5 (IQR: 49–95) households, while areas of 100m and 200m included an average of 250.5 (IQR: 184–311) and 873.9 (IQR: 696–1062) households, respectively.

For each index case, we counted the number of TB cases who resided inside the three catchment areas and who were notified after the index case within three predefined notification windows (one, two and four quarters). We used the total number of real estate property lots as a proxy for households in each catchment area. We counted a property lot to lie within the catchment area, if it included any part of the property boundary vectors. We multiplied the national average urban household size with the number of property lots to enumerate the estimated population in each catchment area.[53] We calculated the theoretical yield from door-to-door screening in these areas as the proportion of notified TB cases over the estimated number of residents in each catchment area (S1–S4 Figs).

Data analysis

We calculated summary statistics for the counts of notifications and households, and descriptive statistics for the patient covariates in the sample. The dataset consisted of multidimensional panel data with nine repeated measures for each index case (three catchment areas and three notification windows). The response variable, theoretical yield for each index case and catchment area-notification window combination, showed a semi-continuous, negative binomial distribution. We used generalized estimating equation (GEE) methods to adjust standard errors for non-normality and within-subject correlation of the repeated measures.[54,55] We chose GEE methods over mixed effects models due to the time-invariant nature of the study and its parameters, the large sample with limited repeated measures and the population-level nature of the response variable.[56] Given its continuous nature and the lack of missing data in the primary exposure and response variables, the analyses were not exposed to typical GEE limitations.[57] We used univariate regression to describe the association of theoretical yield (primary response) and catchment area size and notification window (primary exposures), and secondary covariates. Aside from age and gender, secondary covariates with a p-value of less than 0.2 in the univariate GEE regression model were fitted in the multivariate model. The model accounted for interaction between the two primary exposure variables. Based on the Quasi-likelihood Information Criterion (QIC) we used an exchangeable correlation structure and a Gaussian variance function as model specifications and calculated localized, theoretical detection yields from the model's coefficients.[58,59] We expressed these theoretical TB detection yields in terms of number needed to screen (NNS), which was calculated as the inverse of the theoretical yield.

Ethical considerations

We obtained written permission for analysis of the TB patient data from the Go Vap District Preventive Health Center, the administrative authority of the District TB Unit and legal owner of the data. The ethics committee of the Ho Chi Minh City Provincial HIV/AIDS Committee provided ethical approval for this study.

Results

In the period from 2011 to 2015, the Go Vap District TB Unit notified 3,133 TB people with TB. Among these, 79 people were retreatment cases who enrolled immediately after treatment failure and did not meet the inclusion criteria. We geocoded 2,513 (82%) cases automatically

and 533 (18%) manually locating them at the nearest main street and primary alley. We were unable to geocode 8 addresses, so the final sample size included 3,046 people (99% of those notified).

Table 1 shows descriptive statistics of the sample. About one-third (n = 976) of notified cases were female and median age was 40 years (IQR: 28–52) years. People with TB/HIV coinfection comprised 6% (198) of cases, while 5% (145) reported comorbid diabetes. The majority of the sample was unemployed (42%, 1,275) or employed as unskilled or semi-skilled labor (44%, 1,320). Temporary residents comprised 29% (869) of the sample, among whom the majority (675) consisted of short-term, inter-province migrants, defined as persons whose household registration is in a district or province different from the one in which they currently reside. The median distance to the DTU was 2.8km (IQR: 1.5, 3.5). Smear-positivity characterized 54% (1,631) of cases, among whom 2% (39) were diagnosed with MDR-TB while about a quarter of the cases were extra-pulmonary TB. Previously untreated cases

Table 1. Patient characteristics of notified TB cases at the Go Vap district TB Unit, Ho Chi Minh city, Viet Nam (n = 3,046[‡]).

	Total N (%)	(cont.) Total	Total N (%)
Total	3,046 (100)	Total	3,046 (100)
Sex		Type of TB [§]	
Female	976 (32)	AFB(+)	1,631 (54)
Male	2,057 (68)	AFB(-)	679 (22)
Age		EP	736 (24)
<25 years	500 (16)	Drug-resistant	
25–34 years	707 (23)	No	3,007 (99)
35–44 years	582 (19)	Yes	39 (1)
45–54 years	599 (20)	Patient type	
≥55 years	645 (21)	New	2,377 (78)
HIV/AIDS [¶]		Relapse	304 (10)
No/Unknown	2,848 (94)	Failure	39 (1)
Yes	198 (6)	LTFU retreatment#	32 (1)
Diabetes mellitus		Transfer In [†]	294 (10)
No/Unknown	2,901 (95)	Treatment outcomes	
Yes	145 (5)	Success	2,607 (85)
Employment		Cure	1,344 (44)
Unemployed	1,275 (42)	Complete	1,263 (41)
Un-/semi-skilled	1,320 (44)	LTFU#	121 (4)
Skilled	411 (14)	Failure	99 (3)
Residency		Death	114 (4)
Permanent	2,177 (71)	Transfer out	102 (3)
Long-term intra-province	184 (6)	Proximity to TB Unit	
Long-term inter-province	10 (0)	Close	1,002 (34)
Short-term inter-province	675 (22)	Medial	1,028 (35)
		Distant	927 (31)

Notes

‡ Individual parameters may include missing data, which were excluded from the regression analysis

¶ Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome

§ AFB(+) = Sputum smear positive; AFB(-) = Sputum smear negative; EP = Extra-pulmonary TB

LTFU = Loss to Follow-up

† Inbound transfers and referrals with prior uncertain exposure to anti-TB drugs.

<https://doi.org/10.1371/journal.pone.0209290.t001>

Table 2. Adjusted theoretical yield by catchment area size and notification window based on the GEE linear regression model (n = 3,046).

	Radius = 50m	Radius = 100m	Radius = 200m
<i>Theoretical yield† in all catchment areas (mean %, 95%CI)</i>			
1 Quarter	0.23 (0.17, 0.30)	0.12 (0.04, 0.21)	0.08 (0.00, 0.17)
2 Quarters¶	0.32 (0.27, 0.37)	0.21 (0.14, 0.29)	0.17 (0.09, 0.25)
4 Quarters	0.47 (0.40, 0.53)	0.36 (0.27, 0.45)	0.32 (0.22, 0.41)
<i>Number needed to screen† in all catchment areas (mean NNS, 95%CI)</i>			
1 Quarter	435 (333, 588)	833 (476, 2500)	1250 (-, 10000)
2 Quarters¶	313 (270, 370)	476 (345, 714)	588 (400, 1111)
4 Quarters	213 (189, 250)	278 (222, 370)	313 (244, 455)
<i>Zero-yield catchment areas (proportion %, 95%CI)</i>			
1 Quarter	78.6 (77.1, 80.0)	55.9 (54.1, 57.6)	22.1 (20.6, 23.6)
2 Quarters¶	65.7 (64.0, 67.4)	37.6 (35.9, 39.3)	10.6 (9.6, 11.8)
4 Quarters	53.0 (51.1, 54.7)	24.2 (22.7, 25.8)	6.0 (5.2, 6.9)
<i>Theoretical yield† in non-zero catchment areas§ (mean %, 95% CI)</i>			
1 Quarter	0.69 (0.60, 0.77)	0.20 (0.05, 0.35)	0.09 (0.00, 0.25)
2 Quarters¶	0.77 (0.70, 0.85)	0.28 (0.15, 0.42)	0.18 (0.03, 0.32)
4 Quarters	0.93 (0.84, 1.02)	0.44 (0.29, 0.59)	0.33 (0.17, 0.49)
<i>Number needed to screen† in non-zero catchment areas§ (mean NNS, 95% CI)</i>			
1 Quarter	145 (130, 167)	500 (286, 2000)	1111 (-, 1428)
2 Quarters¶	130 (118, 143)	357 (238, 667)	556 (312, 3333)
4 Quarters	108 (98, 119)	227 (169, 345)	303 (204, 588)

Notes
 † Based on the national average urban household size of 3.66 persons per household; stratified by notification windows of 1, 2 and 4 quarters subsequent to the index case
 ¶ Base case scenario
 § Refers to catchment areas that have at least one notification in addition to the index cases in any of the three radii and notification windows

<https://doi.org/10.1371/journal.pone.0209290.t002>

comprised 78% (2,377) of the sample. Treatment outcomes were high with 85% (2,607) having documented treatment success.

Based on the fitted model, the adjusted theoretical yield of localized door-to-door screening in the base scenario with a notification window of 2 quarters was 0.32% (95%CI: 0.27, 0.37) in a catchment area with radius 50m. For catchment areas with radii of 100m and 200m, the theoretical yields were 0.21% (95%CI: 0.14, 0.29) and 0.17% (95%CI: 0.09, 0.25), respectively (Table 2). This corresponds to NNS of 313 (95%CI: 270–370), 476 (95%CI: 345–714) and 588 (95%CI: 400–1,111), respectively.

The majority of scenarios had a high proportion of zero-yield catchment areas, i.e., contained no other notification in the catchment area aside from the index case. The proportion of zero-yield catchment areas ranged from 53.0%-78.6% for catchment areas of radius 50m and declined to ranges of 24.2%-55.9% and 6.0%-22.1% for radii of 100m and 200m, respectively. The theoretical yield in non-zero yield catchment areas increased to 0.77% (95%CI: 0.70%-0.85%), 0.28% (95%CI: 0.15%-0.42%), and 0.18% (95%CI: 0.03%-0.32%) for catchment areas of 50m, 100m and 200m, respectively. This corresponds to NNS of 130 (95%CI: 118–143), 352 (95%CI: 237–683) and 571 (95%CI: 313–3,225), respectively.

In addition to the strong association between theoretical yield and the two primary exposures, catchment area size and notification window, results from the fitted GEE linear regression model in Table 3 displayed associations between theoretical yield and other index patient

Table 3. GEE linear regression model of theoretical yield of door-to-door screening adjusted for primary and secondary index patient characteristics (n = 3,046).

	Coefficient	95% CI	p-value
Constant	0.32**	0.27,0.37	<0.001
Catchment area (CA)			
100m	-0.11**	-0.13,-0.08	<0.001
200m	-0.15**	-0.18,-0.12	<0.001
Notification window (NW)			
1 quarter	-0.09**	-0.10, -0.08	<0.001
4 quarter	0.15**	0.14, 0.16	<0.001
Female	0.02	-0.02, 0.06	0.340
Age	0.00	-0.00, 0.00	0.462
Patient type			
Relapse	0.01	-0.03, 0.05	0.683
Retreatment after failure	-0.05	-0.10, 0.00	0.059
LTFU retreatment#	0.09	-0.13, 0.31	0.428
Inbound transfer†	0.04	-0.09, 0.18	0.530
Unknown prior treatment	-0.03	-0.06, 0.09	0.140
Residency status			
Long-term intra-province	0.01	-0.05, 0.06	0.832
Long-term inter-province	-0.05	-0.15, 0.05	0.328
Short-term inter-province	0.06**	0.01, 0.11	0.022
Treatment outcome			
Treatment success	-0.01	-0.04, 0.02	0.515
Failure	0.12**	0.05, 0.18	0.001
Death	0.00	-0.04, 0.04	0.897
Loss to follow-up	0.13	-0.05, 0.31	0.148
Transfer out	-0.03	-0.09, 0.02	0.205
Distance to DTU‡	-0.02**	-0.03, -0.01	<0.001

Notes

** Reject the null hypothesis at a 95% confidence level

‡ Wald test

LTFU = Loss to Follow-up

† Inbound transfers and referrals with prior uncertain exposure to anti-TB drugs

‡ Continuous variable with distance in kilometers.

<https://doi.org/10.1371/journal.pone.0209290.t003>

characteristics. The model showed a significant negative association between theoretical yield and distance to DTU (beta = -0.02, p<0.001) higher theoretical yield among short-term inter-province migrants (beta = 0.06, p = 0.022) and among people for whom treatment failed (beta = 0.12, p = 0.001).

Discussion

This was an exploratory study using the combination of routine TB surveillance and urban planning data to explore opportunities to optimize active case finding for TB. We found no other studies that have attempted this enumeration at the level of index patient household or individual catchment area.

It is clear that ACF will be needed to reach the people with TB that are currently missed by facility-based case finding NTPs use since their reach is limited.[1,4,7,9,60] However, ACF is inherently more expensive and indiscriminate measures are not productive.[61–64]

Approaches that improve the yield of ACF interventions are needed. We used estimated localized notification rates, i.e., TB cases notified over the total estimated population in a catchment area, to illustrate spatial heterogeneity and the existence of TB disease clusters in our sample as an alternative to standard spatial autocorrelation methods, which may be included in further analyses.[65,66] In a review of ACF interventions, the weighted mean NNS for community and population-wide screening was 603 corresponding to a detection yield of 0.17%.[67] The theoretical yields in the 50m catchment area size across all notification window scenarios were significantly higher (S5 Fig), but on their own, are unlikely to merit community screening. Our results suggest that hotspots may be identified even in catchment areas with 100m and 200m radii in densely populated urban settings, if a sufficiently long notification window were permitted.

An important consideration for the economic viability of this type of spatially restricted door-to-door screening involves the identification and avoidance of zero-yield catchment areas. Our results showed that neighborhood contact screening in a catchment area of 50m within a quarter of notification would have yielded no additional case in almost four-fifths of index patients. Targeting the correct index cases and avoiding zero-yield catchment areas increased yield in our study 2–3 times. Given the rudimentary nature of the routine surveillance data available for this study, we identified only three index patient covariates that were significantly associated with theoretical yield and may improve targeting of the right catchment areas. One of these parameters was treatment failure of the index patient. This parameter was positively associated with yield, possibly linked to prolonged transmission. Short-term, temporary residency status was also associated with non-zero community cases which may be a function of the propensity of economic migrants to reside in boarding homes and urban slum communities upon arrival in the city.[68–72] Concordant with other studies, temporary residency may be an appropriate indicator for the higher likelihood of finding a TB hotspot.[73–77] The third significantly, albeit negatively, associated parameter was index case distance to the District TB Unit. This finding may relate to our use of routine notifications, which evidence has shown to be lower at greater distances from the TB treatment facility.[78,79] As such, this result may imply a localized under-detection rather than under-representation of TB patients.

In summary, the results of this study suggest that conducting door-to-door screening in a 50m radius around an index case with temporary residency status and history of treatment failure may be an economically viable strategy to expand coverage at acceptable case detection yields. In concordance with our results, studies have similarly evaluated and identified neighborhood contacts [80], and specifically those within 50m of an index case [43], to comprise a viable target population for intensified screening with productive yields.

While the government of Viet Nam passed legislature with the goal of reducing TB prevalence to 20 per 100,000 by 2030, the current prevalence and rate of reduction of 4.6% suggest that the country may miss the projected deadline by over three decades.[81,82] Implementing neighborhood screening in 50m catchment areas around retreatment and migrant index cases may be one rapidly implementable strategy to bend the curve. This strategy may also be applicable outside of Viet Nam in other high-burden countries with similar urbanization trends and sociocultural attributes. Studies have shown that proximal clustering of first-degree relatives and high degrees of social interaction in the immediate neighborhood and neighborhood establishments, e.g., bars, cafes, karaoke shops, are significant contributors to tuberculosis transmission, particularly in high burden settings.[83–86]

However, given the limited geographic scope and retrospective nature of the study, further research on this topic seems warranted. A follow-up study on this subject could aim to validate prospectively the theoretical yields obtained from our analysis. Such a prospective study may

employ rapid molecular diagnostics instead of smear microscopy for diagnosis of TB in the neighborhood contact and genotypic fingerprinting for validation of the index case as the source of transmission. The prospective study could further evaluate interventions with different types of intensity. For example, the study could evaluate the effectiveness and cost effectiveness of screening a catchment area using an approach based on mobile radiography units rather than door-to-door screening by community health workers.

An inherent inaccuracy of this study is that theoretical yield should be discounted for cases notified through routine case finding over time. In our sample of routine notification data from 2011–2015 in Go Vap, we identified a total of 356 (12% of total notifications) household contacts living in 170 households. Of the 170 households, 155 (91%) included the index case and one other notified household contact. In 14 (8%) households there were three notified patients and one household contained four notified cases. Identifying households with multiple notified cases may help identify “super-spreaders” for whom more intensified outbreak investigation may be warranted.[87,88]

A nationally representative cluster-randomized controlled trial on facility-based household contact investigation conducted in Viet Nam reported a relative risk between active and routine household contact investigation of 2.5, suggesting that approximately 40% of household contacts may be notified through routine case finding, while the remainder would have been missed or detected later.[9] We re-analyzed the dataset excluding all 356 household contact notifications. The theoretical yields of this subset across all nine catchment area-notification window scenarios did not change significantly. This suggests that household contact investigation may not affect the yield of catchment area screening at a population level, likely due to the limited proportion of TB cases stemming from intra-household transmission compared to other community sources in moderate and high prevalence settings.

This study has several limitations. The theoretical yields are based on passive notification in the public sector, primarily detected with microscopy, all factors associated with under-detection of incident cases[1,89,90], meaning the yields are likely underestimates. One of the variables explaining lack of community cases was distance to the health facility, which may also mean that people with TB were missed by the passive system rather than a true association with fewer community cases since other studies measuring this have shown similar results.[75] In addition, we did not differentiate between residential and commercial property lots. We were also not able to differentiate between property lots with single-family or congregate housing, particularly informal boarding home communities. The analysis did not take into consideration property lot sizes for the population estimate of the catchment areas. These factors may have contributed to an over- or underestimation of the total number of residents in a catchment area and subsequently theoretical yield. However, uncertainties may have been mitigated by the large sample size of index cases and high granularity in the cadastral data. Transmission patterns via genotyping of notified cases and health-seeking behaviors through additional primary data collection as used in similar spatial analysis studies may help our understanding of the results.[91,92]

Conclusions

To reach the people with TB currently missed by NTPs, we need new strategies that detected people with TB earlier and in greater numbers. There is strong agreement that eliminating TB will require intensified TB case finding beyond the status quo. Using geospatial mapping to create models to enhance theoretical case finding yields may be useful to optimize active case finding approaches.

Supporting information

S1 Data. Dataset. Go Vap index case dataset 2011–2015 with counts and proportions of households and TB notifications by catchment area and notification windows, and secondary index case parameters.

(CSV)

S1 Fig. TB notifications in Go Vap district, 2011–2015. Visualization of geocoded index patients with residency in Go Vap district notified at the district TB unit from 2011–2015.

(TIF)

S2 Fig. TB notifications in a sub-segment of Go Vap district. Visualization of a select number of geocoded index patients in several wards in Go Vap district.

(TIF)

S3 Fig. TB notifications layered onto cadastral property lot data. Visualization of households and incident TB cases within specified catchment areas and notification window (here: $r = 100\text{m}$, $t = 1$ quarter).

(TIF)

S4 Fig. Sample localized household and patient density by the primary study exposure parameters. Cross-tabulation of the total count of property lots as well as the count and proportion of TB notifications around a sample index case. These data are tabulated by catchment area and by time window, specifically the full timeframe, 2011–2015, and the three notification window scenarios.

(TIF)

S5 Fig. Theoretical yield comparison with literature. Theoretical yield of door-to-door screening by catchment area and notification window compared to pooled estimates from literature ($n = 3,046$).

(TIF)

Author Contributions

Conceptualization: Luan Nguyen Quang Vo, Thanh Nguyen Vu, Tung Thanh Truong, Canh Minh Khuu, Phuong Quoc Pham, Lan Huu Nguyen, Giang Truong Le, Jacob Creswell.

Data curation: Luan Nguyen Quang Vo, Thanh Nguyen Vu, Hoa Trung Nguyen, Tung Thanh Truong, Canh Minh Khuu.

Formal analysis: Luan Nguyen Quang Vo, Tung Thanh Truong, Canh Minh Khuu.

Funding acquisition: Luan Nguyen Quang Vo, Jacob Creswell.

Investigation: Luan Nguyen Quang Vo, Jacob Creswell.

Methodology: Luan Nguyen Quang Vo, Tung Thanh Truong, Canh Minh Khuu, Giang Truong Le, Jacob Creswell.

Project administration: Luan Nguyen Quang Vo, Thanh Nguyen Vu, Hoa Trung Nguyen, Phuong Quoc Pham, Lan Huu Nguyen, Jacob Creswell.

Resources: Luan Nguyen Quang Vo.

Software: Tung Thanh Truong, Canh Minh Khuu, Phuong Quoc Pham.

Supervision: Luan Nguyen Quang Vo, Phuong Quoc Pham, Lan Huu Nguyen, Giang Truong Le, Jacob Creswell.

Validation: Luan Nguyen Quang Vo, Hoa Trung Nguyen, Jacob Creswell.

Visualization: Luan Nguyen Quang Vo, Tung Thanh Truong, Canh Minh Khuu.

Writing – original draft: Luan Nguyen Quang Vo.

Writing – review & editing: Luan Nguyen Quang Vo, Jacob Creswell.

References

1. World Health Organization. Global Tuberculosis Report 2017. 2017. WHO/HTM/TB/2017.23.
2. Ortblad KF, Lozano R, Murray CJ. An alternative estimation of tuberculosis incidence from 1980 to 2010: methods from the Global Burden of Disease 2010. *Lancet* 2013; 381:S104. [https://doi.org/10.1016/S0140-6736\(13\)61358-6](https://doi.org/10.1016/S0140-6736(13)61358-6).
3. Yuen CM, Amanullah F, Dharmadhikari A, Nardell EA, Seddon JA, Vasilyeva I, et al. Turning off the tap: Stopping tuberculosis transmission through active case-finding and prompt effective treatment. *Lancet* 2015; 386:2334–43. [https://doi.org/10.1016/S0140-6736\(15\)00322-0](https://doi.org/10.1016/S0140-6736(15)00322-0) PMID: 26515675
4. World Health Organization. Implementing the End TB Strategy: The Essentials. World Heal Organ 2015:1–130. <https://doi.org/10.1017/CBO9781107415324.004>
5. World Health Organization. Systematic screening for active tuberculosis: Principles and Recommendations. 2013. WHO/HTM/TB/2013.04.
6. Creswell J, Sahu S, Blok L, Bakker MI, Stevens R, Ditiu L. A multi-site evaluation of innovative approaches to increase tuberculosis case notification: Summary results. *PLoS One* 2014; 9. <https://doi.org/10.1371/journal.pone.0094465> PMID: 24722399
7. Kranzer K, Afnan-Holmes H, Tomlin K, Golub JE, Shapiro AE, Schaap A, et al. The benefits to communities and individuals of screening for active tuberculosis disease: A systematic review. *Int J Tuberc Lung Dis* 2013; 17:432–46. <https://doi.org/10.5588/ijtld.12.0743> PMID: 23485377
8. Blok L, Creswell J, Stevens R, Brouwer M, Ramis O, Weil O, et al. A pragmatic approach to measuring monitoring and evaluating interventions for improved tuberculosis case detection. *Int Health* 2014; 6:181–8. <https://doi.org/10.1093/inthealth/ihu055> PMID: 25100402
9. Fox GJ, Nhung N V., Sy DN, Hoa NLP, Anh LTN, Anh NT, et al. Household-Contact Investigation for Detection of Tuberculosis in Vietnam. *N Engl J Med* 2018; 378:221–9. <https://doi.org/10.1056/NEJMoa1700209> PMID: 29342390
10. Blok L, Sahu S, Creswell J, Alba S, Stevens R, Bakker MI. Comparative meta-analysis of tuberculosis contact investigation interventions in eleven high burden countries. *PLoS One* 2015; 10:1–18. <https://doi.org/10.1371/journal.pone.0119822> PMID: 25812013
11. Khanal S, Baral S, Shrestha P, Puri M, Kandel S, Lamichanne B, et al. Yield of intensified tuberculosis case-finding activities using Xpert MTB/RIF among risk groups in Nepal. *Public Heal Action* 2016; 6:136–41. <http://dx.doi.org/10.5588/pha.16.0015>.
12. Morishita F, Garfin AMCG, Lew W, Oh KH, Yadav RP, Reston JC, et al. Bringing state-of-The-Art diagnostics to vulnerable populations: The use of a mobile screening unit in active case finding for tuberculosis in Palawan, the Philippines. *PLoS One* 2017; 12:1–21. <https://doi.org/10.1371/journal.pone.0171310> PMID: 28152082
13. Stuckler D, Basu S, McKee M, Lurie M. Mining and risk of tuberculosis in sub-saharan Africa. *Am J Public Health* 2011; 101:524–30. <https://doi.org/10.2105/AJPH.2009.175646> PMID: 20516372
14. Liu Y, Weinberg MS, Ortega LS, Painter JA, Maloney SA. Overseas Screening for Tuberculosis in U.S.-Bound Immigrants and Refugees. *N Engl J Med* 2009; 360:2406–15. <https://doi.org/10.1056/NEJMoa0809497> PMID: 19494216
15. Zhao Q, Xiao X, Lu W, Qiu L-X, Zhou C-M, Jiang W-L, et al. Screening diabetes in tuberculosis patients in eastern rural China: a community-based cross-sectional study. *Int J Tuberc Lung Dis* 2016; 20:1370–6. <https://doi.org/10.5588/ijtld.16.0045> PMID: 27725050
16. Bonadonna LV, Saunders MJ, Zegarra R, Evans C, Alegria-Flores K, Guio H. Why wait? The social determinants underlying tuberculosis diagnostic delay. *PLoS One* 2017; 12:1–18. <https://doi.org/10.1371/journal.pone.0185018> PMID: 28945782
17. Hoa NB, Tiemersma EW, Sy DN, Nhung N V., Vree M, Borgdorff MW, et al. Health-seeking behaviour among adults with prolonged cough in Vietnam. *Trop Med Int Heal* 2011; 16:1260–7. <https://doi.org/10.1111/j.1365-3156.2011.02823.x> PMID: 21692960

18. Cai J, Wang X, Ma A, Wang Q, Han X, Li Y. Factors associated with patient and provider delays for tuberculosis diagnosis and treatment in Asia: A systematic review and meta-analysis. *PLoS One* 2015; 10:1–22. <https://doi.org/10.1371/journal.pone.0120088> PMID: 25807385
19. Getnet F, Demissie M, Assefa N, Mengistie B, Worku A. Delay in diagnosis of pulmonary tuberculosis in low-and middle-income settings: Systematic review and meta-analysis. *BMC Pulm Med* 2017; 17:1–15. <https://doi.org/10.1186/s12890-016-0353-7>
20. Hagood TM. Chest Screening and Tuberculosis in the United States. *Radiographics* 1994;1–16.
21. Gomes MGM, Barreto ML, Glaziou P, Medley GF, Rodrigues LC, Wallinga J, et al. End TB strategy: The need to reduce risk inequalities. *BMC Infect Dis* 2016; 16:1–4. <https://doi.org/10.1186/s12879-015-1330-0>
22. Jenkins HE, Plesca V, Ciobanu A, Crudu V, Galusca I, Soltan V, et al. Assessing spatial heterogeneity of MDR-TB in a high burden country. *Eur Respir J* 2013; 42. <https://doi.org/10.1183/09031936.00111812> PMID: 23100496
23. World Health Organization. World Health Organization. WHO Technical Report Series No. 552. Geneva, Switzerland: WHO; 1974. WHO Expert Committee on Tuberculosis: Ninth Report. 1974.
24. Corbett EL, Bandason T, Duong T, Dauya E, Makamure B, Churchyard GJ, et al. Comparison of two active case-finding strategies for community-based diagnosis of symptomatic smear-positive tuberculosis and control of infectious tuberculosis in Harare, Zimbabwe (DETECTB): A cluster-randomised trial. *Lancet* 2010; 376:1244–53. [https://doi.org/10.1016/S0140-6736\(10\)61425-0](https://doi.org/10.1016/S0140-6736(10)61425-0) PMID: 20923715
25. Datiko DG, Lindtjorn B. Health extension workers improve tuberculosis case detection and treatment success in southern Ethiopia: A community randomized trial. *PLoS One* 2009; 4:1–7. <https://doi.org/10.1371/journal.pone.0005443> PMID: 19424460
26. Eang MT, Satha P, Yadav RP, Morishita F, Nishikiori N, Van-Maaren P, et al. Early detection of tuberculosis through community-based active case finding in Cambodia. *BMC Public Health* 2012; 12:1. <https://doi.org/10.1186/1471-2458-12-1>
27. Churchyard G, Kim P, Shah NS, Rustomjee R, Gandhi N, Mathema B, et al. What We Know about Tuberculosis Transmission: An Overview. *J Infect Dis* 2017; 216:S629–35. <https://doi.org/10.1093/infdis/jix362> PMID: 29112747
28. Uys P, Marais BJ, Johnstone-Robertson S, Hargrove J, Wood R. Transmission elasticity in communities hyperendemic for tuberculosis. *Clin Infect Dis* 2011; 52:1399–404. <https://doi.org/10.1093/cid/cir229> PMID: 21628479
29. World Health Organization. Toman's Tuberculosis. Second. Geneva: World Health Organization; 2004.
30. Menzies D. Issues in the management of contacts of patients with active pulmonary tuberculosis. *Can J Public Heal Rev Can Santé Publique* 1997; 88:197–201.
31. Rouillon A. Survey Transmission of Tubercle Bacilli: the Effects of Chemotherapy *. *Tubercle* 1976; 57:275–99. [https://doi.org/10.1016/S0041-3879\(76\)80006-2](https://doi.org/10.1016/S0041-3879(76)80006-2) PMID: 827837
32. Festenstein F. Spread of tuberculosis within a family. *Lancet* 1970; 317:603–5.
33. Fox GJ, Schaaf HS, Mandalakas A, Chiappini E, Zumla A, Marais BJ. Preventing the spread of multi-drug-resistant tuberculosis and protecting contacts of infectious cases. *Clin Microbiol Infect* 2017; 23:147–53. <https://doi.org/10.1016/j.cmi.2016.08.024> PMID: 27592087
34. Dodd PJ, Looker C, Plumb ID, Bond V, Schaap A, Shanaube K, et al. Age- and Sex-Specific Social Contact Patterns and Incidence of Mycobacterium tuberculosis Infection. *Am J Epidemiol* 2016; 183:156–66. <https://doi.org/10.1093/aje/kwv160> PMID: 26646292
35. Tadesse T, Demissie M, Berhane Y, Kebede Y, Abebe M. The Clustering of Smear-Positive Tuberculosis in Dabat, Ethiopia: A Population Based Cross Sectional Study. *PLoS One* 2013; 8:1–6. <https://doi.org/10.1371/journal.pone.0065022> PMID: 23717686
36. Shah L, Choi HW, Berrang-Ford L, Henostroza G, Krapp F, Zamudio C, et al. Geographic predictors of primary multidrug-resistant tuberculosis cases in an endemic area of Lima, Peru. *Int J Tuberc Lung Dis* 2014; 18:1307–14. <https://doi.org/10.5588/ijtld.14.0011> PMID: 25299862
37. Munch Z, Van Lill SWP, Booyesen CN, Zietsman HL, Enarson DA, Beyers N. Tuberculosis transmission patterns in a high-incidence area: a spatial analysis. *Int Union Against Tuberc Lung Dis* 2003; 7:271–277(7).
38. Cook VJ, Shah L, Gardy J, Bourgeois A. Recommendations on modern contact investigation methods. *Int J Tuberc Lung Dis* 2011; 16:297–305. <https://doi.org/10.5588/ijtld.11.0350> PMID: 22136695
39. Izumi K, Ohkado A, Uchimura K, Murase Y, Tatsumi Y, Kayebeta A, et al. Detection of tuberculosis infection hotspots using activity spaces based spatial approach in an urban Tokyo, from 2003 to 2011. *PLoS One* 2015; 10:1–16. <https://doi.org/10.1371/journal.pone.0138831> PMID: 26382251

40. Bakker M, Rood E, Mergenthaler C, Blok L, van Gorp M, Straetemans M, et al. MATCH: Mapping and Analysis for Tailored disease Control and Health system strengthening. Amsterdam: 2017.
41. Ratovonirina NH, Rakotosamimanana N, Razafimahatratra SL, Raheison MS, Refrégier G, Sola C, et al. Assessment of tuberculosis spatial hotspot areas in Antananarivo, Madagascar, by combining spatial analysis and genotyping. *BMC Infect Dis* 2017; 17:562. <https://doi.org/10.1186/s12879-017-2653-9> PMID: 28806916
42. Kolifarhood G, Khorasani-Zavareh D, Salarilak S, Shoghli A, Khosravi N. Spatial and non-spatial determinants of successful tuberculosis treatment outcomes: An implication of Geographical Information Systems in health policy-making in a developing country. *J Epidemiol Glob Health* 2015; 5:221–30. <https://doi.org/10.1016/j.jegh.2014.11.001> PMID: 26231398
43. Fatima R, Qadeer E, Yaqoob A, UI Haq M, Majumdar SS, Shewade HD, et al. Extending “contact tracing” into the community within a 50-metre radius of an index tuberculosis patient using Xpert MTB/RIF in urban, Pakistan: Did it increase case detection? *PLoS One* 2016; 11:1–11. <https://doi.org/10.1371/journal.pone.0165813> PMID: 27898665
44. Crampin AC, Floyd S, Ngwira BM, Mwinuka V, Mwaungulu JN, Branson K, et al. Assessment and evaluation of contact as a risk factor for tuberculosis in rural Africa. *Int J Tuberc Lung Dis* 2008; 12:612–8. PMID: 18492326
45. Yadav RP, Nishikiori N, Satha P, Eang MT, Lubell Y. Cost-effectiveness of a tuberculosis active case finding program targeting household and neighborhood contacts in Cambodia. *Am J Trop Med Hyg* 2014; 90:866–72. <https://doi.org/10.4269/ajtmh.13-0419> PMID: 24615134
46. Gashu Z, Jerene D, Ensermu M, Habte D, Melese M, Hiruy N, et al. The yield of community-based “retrospective” tuberculosis contact investigation in a high burden setting in Ethiopia. *PLoS One* 2016; 11:1–13. <https://doi.org/10.1371/journal.pone.0160514> PMID: 27483160
47. Veen J. Microepidemics of tuberculosis: the stone-in-the-pond principle. *Tuber Lung Dis* 1992; 73:73–6. [https://doi.org/10.1016/0962-8479\(92\)90058-R](https://doi.org/10.1016/0962-8479(92)90058-R) PMID: 1643300
48. Cruz AT, Starke JR. Pediatric Tuberculosis. *Pediatr Rev* 2010; 31.
49. Pisu M, Gerald J, Shamiyeh JE, Bailey WC, Gerald LB. Targeted Tuberculosis Contact Investigation Saves Money Without Sacrificing Health. *J Public Heal Manag Pr* 2009; 15:319–27. <https://doi.org/10.1097/PHH.0b013e31819c3ef2> PMID: 19525776
50. Viet Nam National TB Control Programme. NTP Year-end report 2016. Hanoi: 2016.
51. Center for Applied Geographic Information Systems, Department of Science and Technology. HCMGIS Maps 2017. <https://maps.hcmgis.vn> (accessed August 6, 2018).
52. Nguyen TH, Vo Nguyen Quang L, Le TG, Vu NT, Nguyen HD. Results of the community-based intervention for the prevention and control of TB in Go Vap district, Ho Chi Minh city, 2014 [vietnamese]. *Viet Nam J Public Heal* 2015; 38:6–12.
53. General Statistics Office. Age-sex structure and marital status of the population in Vietnam. 2009.
54. Agresti A. *Categorical Data Analysis*. vol. 45. Second Edi. Gainesville, FL: John Wiley & Sons, Inc.; 2002. <https://doi.org/10.1198/tech.2003.s28>
55. Liang KYEE, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986; 73:13–22.
56. Hubbard AE, Ahern J, Fleischer NL, Laan M Van Der, Lippman SA, Jewell N, et al. To GEE or not to GEE: Comparing population average and mixed models for estimating the associations between neighborhood risk factors and health. *Epidemiology* 2010; 21:467–74. <https://doi.org/10.1097/EDE.0b013e3181caeb90> PMID: 20220526
57. Kirkwood BR, Sterne JAC. Medical statistics. *Med Stat* 2003; 513. <https://doi.org/10.1002/sim.1961>
58. Pan W. Akaike’s Information Criterion in Generalized Estimating Equations. *Biometrics* 2004; 57:120–5. <https://doi.org/10.1111/j.0006-341X.2001.00120.x>
59. Cui J. QIC program and model selection in GEE analyses. *Stata J* 2007; 7:209–20. <https://doi.org/10.3760/cma.j.issn.1003-9406.2011.02.007>
60. Lönnroth K, Corbett E, Golub J, Godfrey-Faussett P, Uplekar M, Weil D, et al. Systematic screening for active tuberculosis: Rationale, definitions and key considerations. *Int J Tuberc Lung Dis* 2013; 17:289–98. <https://doi.org/10.5588/ijtld.12.0797> PMID: 23407219
61. Supramaniam V. Is chest X-ray screening for pulmonary tuberculosis by mass radiography: A cost-effective tool in a military population? *Med J Malaysia* 1980; 34:301–6. PMID: 6774221
62. Van Rie A, Hanrahan C. Active case finding for tuberculosis: What is the most informative measure for policy makers? *Int J Tuberc Lung Dis* 2014; 18:377. <https://doi.org/10.5588/ijtld.13.0924> PMID: 24670579
63. Vassall A. Health Tuberculosis Perspective Paper. Copenhagen Consens 2014: 28.

64. Blok L, Bakker MI, Straetemans M, Gerstel L, Brouwer M, Stevens R, et al. Should active case-finding projects increase the number of tuberculosis cases notified at national level? *Int J Tuberc Lung Dis* 2017; 21:474–5. <https://doi.org/10.5588/ijtld.17.0025-2>
65. Zelner JL, Murray MB, Becerra MC, Galea J, Lecca L, Calderon R, et al. Identifying hotspots of multi-drug-resistant tuberculosis transmission using spatial and molecular genetic data. *J Infect Dis* 2016; 213:287–94. <https://doi.org/10.1093/infdis/jiv387> PMID: 26175455
66. Tiwari N, Adhikari CMS, Tewari A, Kandpal V. Investigation of geo-spatial hotspots for the occurrence of tuberculosis in Almora district, India, using GIS and spatial scan statistic. *Int J Health Geogr* 2006; 5:1–11. <https://doi.org/10.1186/1476-072X-5-1>
67. Shapiro A, Akande T, Lonroth K, Golub J, Chakravorty R. A systematic review of the number needed to screen to detect a case of active tuberculosis in different risk groups. 2013.
68. Benyoussef A, Cutler L, Levine A, Mansourian P, Phan-tan T. Health Effects of Rural-Urban Migration in Developing Countries—Senegal. *Soc Sci Med* 1974; 8:243–54. PMID: 4852227
69. Nguyen LD, Raabe K, Grote U. Rural-Urban Migration, Household Vulnerability, and Welfare in Vietnam. *World Dev* 2015; 71:79–93. <https://doi.org/10.1016/j.worlddev.2013.11.002>
70. Kontgis C, Schneider A, Fox J, Saksena S, Spencer JH, Castrence M. Monitoring peri-urbanization in the greater Ho Chi Minh City metropolitan area. *Appl Geogr* 2014; 53:377–88. <https://doi.org/10.1016/j.apgeog.2014.06.029>
71. Le BD, Tran GL, Nguyen TPT. Social protection for rural-urban migrants in Vietnam: current situation, challenges and opportunities. *CSP Res Rep* 2011; 08:1–20. <https://doi.org/10.1353/dem.2004.0010>
72. The World Bank. Vietnam Urbanization Review: Technical Assistance Report 2011:263. <https://doi.org/10.1017/CBO9781107415324.004>
73. Tomás BA, Pell C, Cavanillas AB, Solvas JG, Pool R, Roura M. Tuberculosis in migrant populations. A systematic review of the qualitative literature. *PLoS One* 2013; 8:1–12. <https://doi.org/10.1371/journal.pone.0082440> PMID: 24349284
74. Wei X, Chen J, Chen P, Newell JN, Li H, Sun C, et al. Barriers to TB care for rural-to-urban migrant TB patients in Shanghai: A qualitative study. *Trop Med Int Heal* 2009; 14:754–60. <https://doi.org/10.1111/j.1365-3156.2009.02286.x> PMID: 19392747
75. Li X, Yang Q, Feng B, Xin H, Zhang MX, Deng Q, et al. Tuberculosis infection in rural labor migrants in Shenzhen, China: Emerging challenge to tuberculosis control during urbanization. *Sci Rep* 2017; 7:1–8. <https://doi.org/10.1038/s41598-016-0028-x>
76. Bocquier P, Collinson MA, Clark SJ, Gerritsen AAM, Kahn K, Tollman SM. Ubiquitous burden: the contribution of migration to AIDS and Tuberculosis mortality in rural South Africa. *Etude Popul Afr* 2014; 28:691–701. <https://doi.org/10.11564/28-0-525> PMID: 25574071
77. Duc L V., Vree M, Sy DN, Co N V., Borgdorff MW, Cobelens FGJ. Steep increases in tuberculosis notification among young men in the industrialised districts of Danang, Vietnam. *Int J Tuberc Lung Dis* 2007; 11:567–70. PMID: 17439683
78. Lorent N, Choun K, Malhotra S, Koeut P, Thai S, Khun KE, et al. Challenges from tuberculosis diagnosis to care in community-based active case finding among the urban poor in Cambodia: A mixed-methods study. *PLoS One* 2015; 10:1–15. <https://doi.org/10.1371/journal.pone.0130179> PMID: 26222545
79. Bui LV, Mor Z, Chemtob D, Ha ST, Levine H. Use of Geographically Weighted Poisson Regression to examine the effect of distance on Tuberculosis incidence: A case study in Nam Dinh, Vietnam. *PLoS One* 2018; 13:e0207068. <https://doi.org/10.1371/journal.pone.0207068> PMID: 30419051
80. Becerra MC, Pachao-Torreblanca IF, Bayona J, Celi R, Shin SS, Kim JY, et al. Expanding tuberculosis case detection by screening household contacts. *Public Health Rep* 2005; 120:271–7. <https://doi.org/10.1177/003335490512000309> PMID: 16134567
81. Office of the Prime Minister. Approval of the National Strategy for TB prevention and control until 2020 with vision to 2030 [vietnamese]. Viet Nam: 2014.
82. Viet Nam National TB Control Programme. NTP Year-end report 2015. Hanoi: 2015.
83. Classen CN, Warren R, Richardson M, Hauman JH, Gie RP, Ellis JHP, et al. Impact of social interactions in the community on the transmission of tuberculosis in a high incidence area. *Thorax* 1999; 54:136–40. PMID: 10325918
84. Chheng P, Nsereko M, Malone LL, Okware B, Zalwango S, Joloba M, et al. Tuberculosis case finding in first-degree relative contacts not living with index tuberculosis cases in Kampala, Uganda. *Clin Epidemiol* 2015; 7:411–9. <https://doi.org/10.2147/CLEP.S82389> PMID: 26508888
85. Kline SE, Hedemark LL, Davies SF. Outbreak of Tuberculosis among Regular Patrons of a Neighborhood Bar. *N Engl J Med* 1995; 333:222–7. <https://doi.org/10.1056/NEJM199507273330404> PMID: 7791838

86. Sepkowitz KA. How contagious is tuberculosis? *Clin Infect Dis* 1996; 23:954–62. <https://doi.org/10.1093/clinids/23.5.954> PMID: 8922785
87. Cook VJ, Shah L, Gardy J. Modern contact investigation methods for enhancing tuberculosis control in aboriginal communities. *Int J Circumpolar Health* 2012; 71:18643. <https://doi.org/10.3402/ijch.v71i0.18643> PMID: 22663943
88. Ypma RJF, Altes HK, Van Soolingen D, Wallinga J, Van Ballegooijen WM. A sign of superspreading in tuberculosis: Highly skewed distribution of genotypic cluster sizes. *Epidemiology* 2013; 24:395–400. <https://doi.org/10.1097/EDE.0b013e3182878e19> PMID: 23446314
89. Wells WA, Ge CF, Patel N, Oh T, Gardiner E, Kimerling ME. Size and usage patterns of private TB drug markets in the high burden countries. *PLoS One* 2011; 6. <https://doi.org/10.1371/journal.pone.0018964> PMID: 21573227
90. Wells WA. Onions and prevalence surveys: how to analyze and quantify tuberculosis case-finding gaps 2017; 21:1101–13. <https://doi.org/10.5588/ijtld.17.0271> PMID: 29037290
91. Patterson B, Morrow CD, Kohls D, Deignan C, Ginsburg S, Wood R. Mapping sites of high TB transmission risk: Integrating the shared air and social behaviour of TB cases and adolescents in a South African township. *Sci Total Environ* 2017; 583:97–103. <https://doi.org/10.1016/j.scitotenv.2017.01.026> PMID: 28109661
92. Alene KA, Viney K, Mcbryde ES, Clements ACA. Spatiotemporal transmission and socio-climatic factors related to paediatric tuberculosis in north-western Ethiopia. *Geospat Health* 2018; 12:342–50. <https://doi.org/10.4081/gh.2017.575> PMID: 29239568