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## Geographic predictors of primary multidrug-resistant tuberculosis cases in an endemic area of Lima, Peru

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### SUMMARY

**SETTING:** Peru reports among the highest multidrug-resistant tuberculosis (MDR-TB) rates in the Americas, with a growing proportion in previously untreated tuberculosis (TB) cases. The identification of clusters of primary MDR-TB compared with drug-susceptible TB (DS-TB) could help prioritize interventions.

**OBJECTIVE:** To examine the clustering of primary MDR-TB case residences and their proximity to high-risk locations in San Juan de Lurigancho District, Lima, Peru.

**DESIGN:** Enrolled primary MDR-TB and primary DS-TB cases were interviewed and their primary residence was recorded using handheld Global Positioning System devices. Kuldorff's spatial scan statistic was used for cluster detection (SaTScan<sup>TM</sup>, v. 9.1.1). Identified clusters were visualized in Quantum Geographic Information Systems software (v1.8.0). The following cluster

centers were tested: a health centre with the highest TB and MDR-TB rates (Clinic X), a hospital and two prisons. Using regression analyses, we examined predictors of primary MDR-TB cases.

**RESULTS:** A statistically significant cluster of primary MDR-TB cases was identified within a 2.29 km radius around Clinic X. Proximity to Clinic X remained a significant predictor of primary MDR-TB in adjusted regression analyses.

**CONCLUSION:** We identified a hotspot of primary MDR-TB cases around Clinic X in a TB-endemic area. Causes of this clustering require investigation; targeted interventions for this high-risk area should be considered.

**KEY WORDS:** spatial; clusters; urban; high risk; hotspot

THE EMERGENCE of multidrug-resistant tuberculosis (MDR-TB) strains, i.e., resistant to first-line drugs isoniazid (INH) and rifampicin (RMP), is a major threat to tuberculosis (TB) control worldwide. The World Health Organization (WHO) standardized DOTS strategy aims to prevent the development of MDR-TB strains in drug-susceptible TB (DS-TB) patients entering treatment.<sup>1–3</sup> Once acquired, the propagation of MDR-TB in the community is not easily managed by national TB programs (NTPs). As a result, primary MDR-TB, or resistant strains in new untreated TB cases, now represents an increasing majority of all MDR-TB cases globally, in both human immunodeficiency virus (HIV) positive and HIV-negative TB-endemic populations.<sup>4</sup> The focused

investigation of primary MDR-TB cases examines the community transmission of drug-resistant strains.

Although Peru consistently meets WHO performance indicators for treatment completion with standardized first-line regimens, it is still a global hotspot of MDR-TB transmission.<sup>4,5</sup> In 2012, 5% of all reported TB cases in Peru were MDR-TB, of which approximately 40% were primary MDR-TB.<sup>4</sup> Furthermore, household and workplace exposure to TB or MDR-TB cases were found to predict primary MDR-TB even compared to DS-TB, suggesting that the transmission of primary MDR-TB is occurring in the community and is no longer restricted to high-risk populations such as prisoners, drug users or the homeless.<sup>6</sup>

Within TB-endemic districts of Lima, identifying local clustering or MDR-TB hotspots could help focus intervention efforts. Spatiotemporal analysis from four districts of Eastern Lima between 2005 and 2007 found an aggregation of MDR-TB cases specifically due to increased clustering of primary MDR-TB disease.<sup>7</sup> We examined geographic clustering and predictors of primary MDR-TB in the district of San Juan de Lurigancho (SJL), Lima.

## MATERIALS AND METHODS

SJL District is one of the poorest and most densely populated urban areas of Lima (population density: 8 400/km<sup>2</sup>), with among the highest TB and MDR-TB burdens in Peru (2012 TB incidence: 187 per 100 000 population, 7% of new cases MDR-TB).<sup>8-10</sup> DS-TB and MDR-TB case data were assembled from two mutually exclusive research studies recruited from all existing Ministry of Health NTP designated areas in 33 primary health centers and one hospital in SJL District.

### Enrollment

Eligible NTP patients were recruited by study personnel; informed written consent was provided by all study participants. Demographic and socio-economic data were collected using structured questionnaires. Study personnel used handheld Global Positioning System (GPS) devices to record the latitude, longitude and altitude at the front entrance of each case residence located.

A total of 1245 TB cases were included from a population-based cohort study conducted in the district clinics between May 2004 and March 2006 (Study A).<sup>11,12</sup> An additional 140 TB cases were included from a case-control study conducted from April to August 2008 in the same district clinics (Study B).<sup>6</sup> MDR-TB and DS-TB patients were acid-fast bacilli (AFB) smear-positive pulmonary TB patients, aged  $\geq 18$  years, and enrolled in treatment with the NTP of a SJL health center. At the time of the original studies, the NTP did not routinely perform sputum culture and drug susceptibility testing (DST); DS-TB was therefore defined as TB patients who became AFB smear-negative within 2 months of a standard first-line anti-tuberculosis treatment regimen and no report of relapse or failure at the time of interview. In Study A, all consecutive NTP registered DS-TB cases were eligible for enrollment in the study, and DS-TB cases were further confirmed with research study DST results against INH, RMP, ethambutol and streptomycin (SM). In Study B, a random sample of all NTP-registered DS-TB cases was selected from a database representative of all cases across SJL District and their medical records reviewed for eligibility.

MDR-TB cases were defined as AFB smear-

positive patients with laboratory-proven resistance to first-line drugs INH and RMP. All consecutive MDR-TB patients were considered eligible for participation in the study. Primary cases were defined as newly diagnosed cases without a history of previous anti-tuberculosis treatment. In Study A, primary MDR-TB cases were additionally considered if treatment history was  $>5$  years before the current episode. Mono-resistant (resistant to only one of the tested first-line drugs and not meeting the criteria for MDR-TB), pan-resistant (resistant to all tested first-line drugs) and extensively drug-resistant TB (XDR-TB, defined as MDR-TB plus resistance to any fluoroquinolones and one of the three injectables) cases were excluded from baseline analyses. In sensitivity analyses, patients with mono-resistant TB were added to the DS-TB group, while pan-resistant and XDR-TB patients were combined with MDR-TB cases.

### Spatial analysis

Kulldorff's spatial scan statistic (SaTScan<sup>TM</sup>, v. 9.1.1, Boston, MA, USA) was used to detect clusters of primary MDR-TB cases compared with DS-TB cases using a Bernoulli model and a standard circular scanning window.<sup>13,14</sup> An unfocused scan tested each case as a centerpoint, while a focused scan used a selected location as the centerpoint around which it scanned for potential clusters. A focused spatial scan around the following SJL locations reporting the highest TB rates in the area was tested: a large central hospital (Hospital A), a health center with the highest TB rate (Clinic X), and two large prisons (Prisons A and B). SaTScan increases the likelihood ratio required for reaching  $P < 0.05$  as multiple scans are conducted. SaTScan cluster detection results were visualized in Quantum Geographic Information Systems (QGIS) software (v1.8.0).

Logistic regression analysis was used to examine geographic and demographic predictors (Tables 1 and 2) of primary MDR-TB compared with DS-TB (Table 3). The Euclidean distance (in km) between patient residences and high TB rate locations of interest were included in the analysis, as was the main district roadway and elevation of case homes (in meters from sea level) and all individual level variables (Table 1). The adjusted regression model included variables significant at  $P = 0.20$  in bivariate analyses, and forward selection was used to build the final model. Statistical analyses were performed using R statistical software.<sup>15</sup>

### Ethics approval

Ethics approval was granted by the Human Ethics Research Boards of the McGill University Health Centre (Montreal, QC, Canada), the University of Alabama at Birmingham (Birmingham, AL, USA), the

**Table 1** Demographic characteristics of the study population

Characteristic	(n = 854) n (%)
Age	
Mean age ( $\pm$ SD)	30.6 ( $\pm$ 11)
Median age [range]	27.5 [18–73]
Sex	
Female	355 (41.6)
Male	499 (58.4)
Civil status	
Single	427 (50.0)
Cohabiting	248 (29.0)
Married	107 (12.5)
Divorced	63 (7.4)
Widowed	9 (10.0)
Housing status	
Rented	126 (14.8)
Family home	351 (41.1)
Owns	367 (43.0)
Squatting*	9 (1.0)
Missing	1 (0.1)
Number of rooms in dwelling	
0–2	233 (27.3)
3–4	279 (32.4)
$\geq$ 5	341 (40.0)
Missing	1 (0.3)
Number of persons sharing living space	
0–2	96 (15.1)
3–4	209 (26.0)
$\geq$ 5	549 (58.9)
History of incarceration	
No	806 (94.4)
Yes	47 (5.5)
Missing	1 (0.1)
Employment status at the time of diagnosis	
Employed	352 (41.1)
Unemployed	424 (49.6)
Student	73 (8.5)
Retired	4 (0.5)
Missing	1 (0.1)
Monthly income, USD	
0–50	525 (61.5)
51–100	128 (15.0)
101–300	166 (19.5)
$\geq$ 301	32 (3.7)
Missing	3 (0.3)

\* Taking over abandoned housing or self-constructed housing built without the landowner's permission.

SD = standard deviation; USD = US dollar.

Universidad Peruana Cayetano Heredia (Lima, Peru) and the Direcccion de Salud Lima IV Este (Lima, Peru).

## RESULTS

Of 1385 patients, the following were excluded from analysis: 210 cases with missing DST results, 206 cases with mono-resistance to one first-line drug (non-MDR-TB), 4 XDR-TB cases, 37 non-primary MDR-TB cases and 12 DS-TB cases reporting anti-tuberculosis treatment within the past 5 years, and 62 cases with missing GPS data (Figure 1). The final study data set contained 104 primary MDR-TB cases and 750 DS-TB cases. The mean age of the cases included was 30.6 years; 58.4% were male, 50% were unmarried, and 58.9% were cohabiting with more than five persons. Nearly half of the participants reported no formal employment at the time of diagnosis, 60% of all participants earned less than US\$50 per month and less than 5% reported ever having been to prison (Table 1).

Case residences were distributed across the district, with a third each of participants living within 2 km, 2–4 km away and >4 km away from the high-incidence area, comprising Clinic X, with the highest TB rate in the district, and the nearby hospital (Hospital A). The majority of the participants (94.4%) lived within 2 km of the major roadway that crosses the entire length of the district, and less than 20% of participants lived within 2 km of one of the large prisons located in the district (Table 2).

In SaTScan analysis of clustering around Hospital A, Clinic X and Prisons A and B, a significant cluster of primary MDR-TB cases compared with DS-TB cases was detected around Clinic X (radius = 2.29 km,  $P = 0.037$ , Figure 2). In the unfocused SaTScan analysis, the largest cluster identified, comprising 56 primary MDR-TB cases, was nearest to the location of Clinic X, although due to adjustments for multiple testing this did not reach statistical significance ( $P = 0.183$ ).

**Table 2** Proximities of study patients' primary residence to a priori selected points of interest

	Hospital A*	Clinic X <sup>†</sup>	Prison A <sup>‡</sup>	Prison B <sup>‡</sup>	Main thoroughfare roadway <sup>§</sup>	Elevation of patients' home (m) <sup>¶</sup>
Distance from TB patients' place of residence at the time of diagnosis, km						
Mean ( $\pm$ SD)	3.10 ( $\pm$ 1.93)	3.40 ( $\pm$ 2.40)	3.48 ( $\pm$ 1.50)	3.36 ( $\pm$ 1.34)	0.95 ( $\pm$ 0.68)	294 (176)
Median	2.82	2.80	3.45	3.22	0.84	280.8
Range	0.06–8.51	4.9–9.7	1.94–8.954	0.10–8.21	0.01–4.76	1–616
Participants' residences, n (%)						
<2 km	293 (34.3)	302 (35.4)	147 (17.2)	128 (15.0)	806 (94.4)	854 (100.0)
2–4 km	315 (36.9)	251 (29.4)	414 (48.5)	477 (55.8)	43 (0.05)	0 (0.0)
>4 km	246 (28.8)	301 (35.2)	293 (34.3)	249 (29.1)	5 (0.05)	0 (0.0)

\* Single large Ministry of Health tertiary care hospital serving SJL District.

<sup>†</sup> Health center with the highest TB rate in the district (incidence >350/100 000).

<sup>‡</sup> Two prisons located in SJL with TB rates estimated at >5000/100 000.

<sup>§</sup> Main route for the use of mass transit, a previously identified predictor of TB transmission in SJL District.

<sup>¶</sup> Hilly areas where case clusters could exist.

TB = tuberculosis; SD = standard deviation; SJL = San Juan de Lurigancho.

**Table 3** Bivariate logistic regression models for the prediction of MDR-TB\*

	OR (95%CI)	P value
Age, years		
≥ 35	Reference	
<35	1.68 (1.02–2.91)	0.051
Sex		
Female	Reference	
Male	0.81 (0.54–1.22)	0.312
Civil status		
Single	Reference	
Cohabiting	0.78 (0.48–1.24)	0.305
Married	0.50 (0.21–1.01)	0.073
Divorced	0.77 (0.31–1.65)	0.527
Widowed	0.76 (0.04–4.27)	0.802
Housing status		
Rented	Reference	
Family home	1.21 (0.65–2.35)	0.563
Owens	1.10 (0.60–2.13)	0.792
Squatting	NA <sup>†</sup>	NA <sup>†</sup>
Number of rooms in dwelling		
≥ 5	Reference	
3–4	1.52 (0.93–2.50)	0.098
0–2	1.49 (0.88–2.50)	0.134
Number of persons sharing living space		
≥ 5	Reference	
3–4	0.846 (0.50–1.38)	0.513
0–2	0.886 (0.43–1.68)	0.725
Employment status at the time of diagnosis		
Employed	Reference	
Unemployed	0.83 (0.54–1.28)	0.397
Student	1.06 (0.48–2.13)	0.885
Incarceration prior to diagnosis		
No	Reference	
Yes	0.15 (0.004–0.891)	0.035 <sup>‡</sup>
Monthly income, USD		
0–50	Reference	
51–100	0.43 (0.19–0.86)	0.028
101–300	0.83 (0.47–1.39)	0.489
≥ 301	1.18 (0.39–2.93)	0.737
Elevation, m		
<250	Reference	
250–350	1.61 (0.99–2.68)	0.059
>350	1.48 (0.81–2.69)	0.194
Prison 1, km		
>4	Reference	
2–4	0.87 (0.56–1.38)	0.558
<2	0.79 (0.42–1.45)	0.468
Prison 2, km		
>4	Reference	
2–4	1.44 (0.89–2.38)	0.144
<2	1.01 (0.49–2.02)	0.972
Clinic X, km		
>4	Reference	
2–4	1.17 (0.66–2.07)	0.582
<2	2.06 (1.26–3.43)	0.004
Hospital A, km		
>4	Reference	
2–4	1.08 (0.62–1.90)	0.779
<2	1.77 (1.06–3.03)	0.033
Main thoroughfare roadway, km		
>1	Reference	
≤ 1	1.01 (0.67–1.54)	0.956

\* Total (n = 854); DS-TB (n = 750); MDR-TB (n = 104).

<sup>†</sup> Too few counts per cell to converge.

<sup>‡</sup> Fisher's exact test performed due to low cell counts; only one MDR-TB case had been previously incarcerated.

MDR-TB = multidrug-resistant tuberculosis; OR = odds ratio; CI = confidence interval; USD = US dollar; DS-TB = drug-susceptible TB.

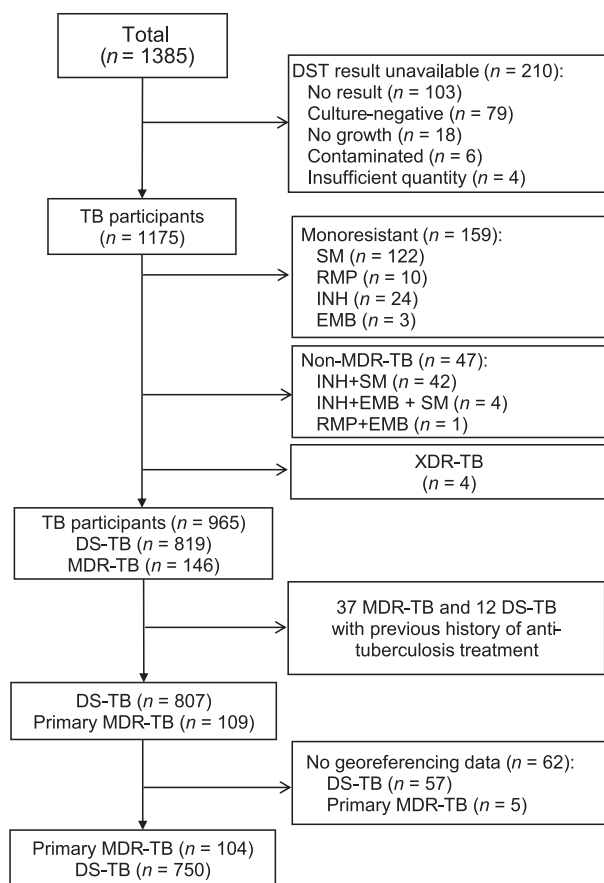
In bivariate analyses, primary MDR-TB cases were significantly more likely than DS-TB cases to be aged <35 years, live within 2 km of both Clinic X and Hospital A and earn US\$51–US\$100 compared with those earning <US\$50 per month (Table 3). Neither elevation nor distance of residence to main roadway or to either prison was significantly associated with primary MDR-TB compared with DS-TB. In the final model adjusted for age and sex (Table 4), patients living within 2 km of Clinic X had twice the odds of primary MDR-TB compared with patients living >4 km from this center (adjusted odds ratio [aOR] 2.10, 95% confidence interval [CI] 1.29–3.51, Table 4). In sensitivity analysis, the strength of the association between living near Clinic X and primary MDR-TB remained when poly-resistant cases were included along with MDR-TB cases and compared with DS-TB patients, including mono-resistance to first-line drugs plus or minus SM.

## DISCUSSION

We detected significant clustering of primary MDR-TB cases in the 2 km area surrounding Clinic X in the northern part of SJL District using focused spatial scan statistics and logistic regression models (cluster radius = 2.29 km,  $P = 0.037$ , Figure 2), (aOR 2.10, 95%CI 1.29–3.51, Table 4). Clinic X was selected a priori for analysis because it had TB and MDR-TB rates nearly four times the national and local SJL District TB incidence.

The observed clustering of primary MDR-TB might be explained by several hypotheses. First, nosocomial exposure of visiting non-infected patients to MDR-TB in Clinic X could explain the clustering of cases. There is no evidence that Clinic X was specifically located due to high TB and MDR-TB rates in the area; rather, primary health facility placements are based on population density. In general, SJL health centers are well-ventilated, including open air waiting rooms (without roof covering or with open doors and windows to facilitate air flow), and NTP consultation rooms are physically separated from the general admission area, which should potentially reduce transmission within the health center.<sup>16</sup> The approximately 2 km radius surrounding Clinic X encompasses a significant portion of the catchment areas of at least eight distinct neighboring health centers (denoted as a shaded zone in Figure 2), and TB patients must attend the health center of their primary residence, suggesting that primary MDR-TB is not limited to contact with Clinic X alone. Nonetheless, infection control practices such as wearing masks and isolation of infectious TB and MDR-TB patients should remain a priority.

In the community, primary MDR-TB cases have been significantly associated with higher self-reported



**Figure 1** Flow diagram of study population. DST = drug susceptibility testing; TB = tuberculosis; SM = streptomycin; RMP = rifampicin; INH = isoniazid; EMB = ethambutol; MDR-TB = multidrug-resistant TB; XDR-TB = extensively drug-resistant TB; DS-TB = drug-susceptible TB.

exposure to TB cases in the household and the workplace than even DS-TB cases.<sup>6</sup> In Lima, a large proportion of secondary cases in households of MDR-TB also had MDR-TB and a DST that matched the index case.<sup>17</sup> Housing and neighborhood characteristics, such as poverty and crowding, have long been associated with clustering of TB cases, and in our data this result appears consistent for DS-TB patients. However, we found that primary MDR-TB cases were significantly more likely to be living with fewer than two persons at the time of diagnosis.<sup>18–20</sup> Further investigation is needed to understand the role played by population density and household crowding in the spread of primary MDR-TB in SJL.

Social mixing outside of households, such as in bars, cafes, schools and workplaces, has an important role in TB transmission.<sup>21,22</sup> Community socializing could contribute to the high rates of primary MDR-TB around Clinic X, which treats mobile patients. As prisoners do not have the same mobility, this could potentially explain the lack of clustering of cases near the prisons. Of note, in these data, primary MDR-TB cases were significantly younger than DS-TB cases,

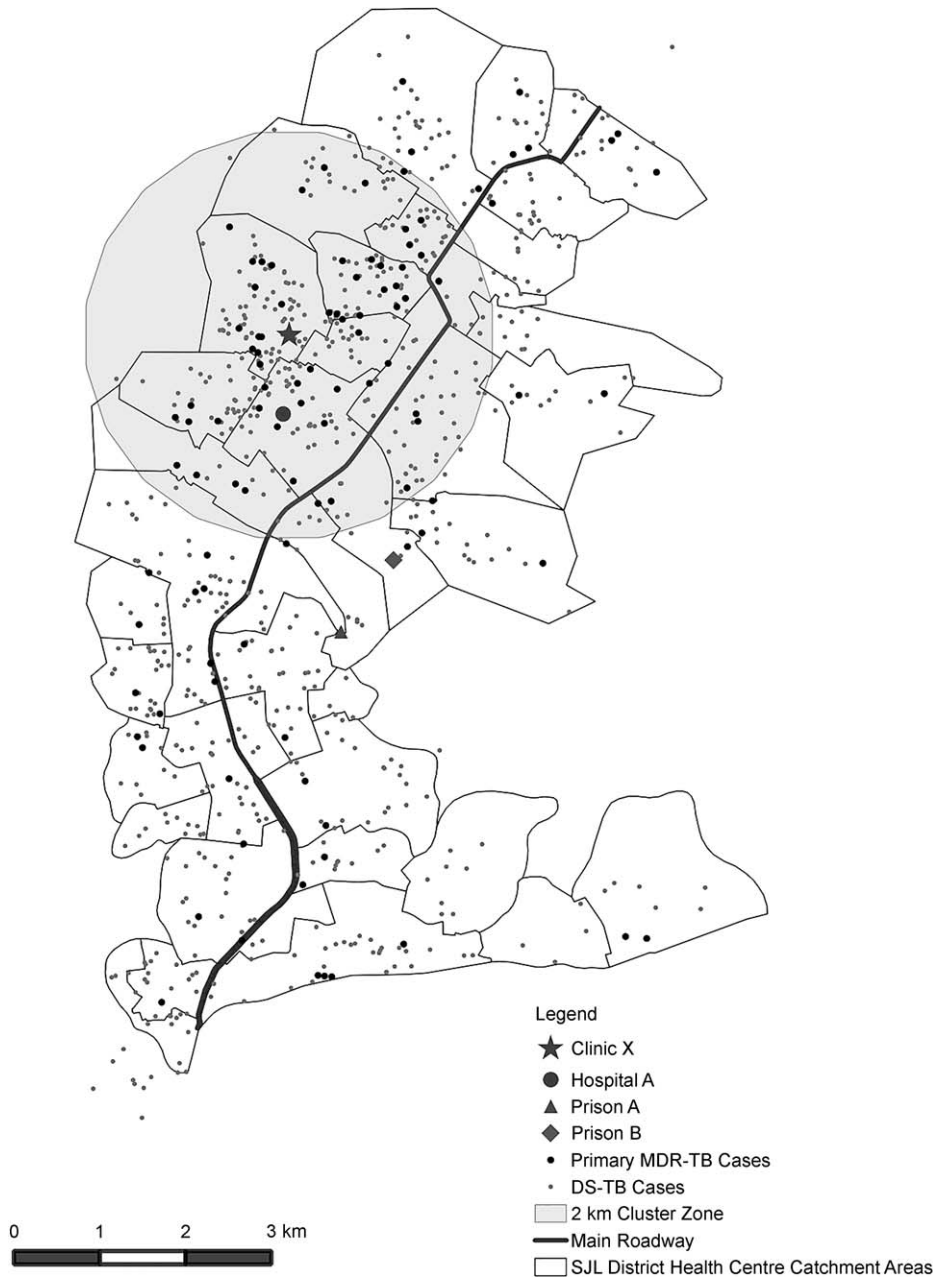
which could indicate social networks of younger primary MDR-TB cases or venues frequented by younger persons in the community.<sup>23,24</sup>

In addition, biological, social and environmental factors could also explain the clustering of primary MDR-TB around Clinic X, although further data confirming these hypotheses are needed.<sup>25,26</sup> While detailed strain typing was unavailable, the strain virulence could be a consideration, as could host characteristics of the population in the area.<sup>27</sup> HIV co-infection rates in SJL are relatively low (1.3%, personal communication, L Otero) and are not considered the primary driver of MDR-TB in this area. On the other hand, human T-lymphotropic virus type 1 (HTLV-1) patients in this population have high rates of TB co-infection and are associated with higher grade AFB on sputum smear, suggesting higher infectiousness.<sup>28</sup> Although HTLV-1 rates among SJL's primary MDR-TB cases remain unknown, the district receives migration from known HTLV-1-endemic Andean regions.<sup>28,29</sup> Finally, environmental factors such as humidity, population density and crowding all favor TB transmission and, along with air quality studies, require further investigation among primary MDR-TB cases in SJL.<sup>20,30</sup>

No clustering of primary MDR-TB cases was detected around district prisons, where TB is epidemic, suggesting that living near the prison is not a risk for primary MDR-TB. Nor was any clustering detected along the main roadway, which was a proxy measure for the use of mass public transport, such as buses and collective mini buses, previously associated with risk of TB transmission in Lima.<sup>31</sup> However, in our study population, >90% of patients lived within 2 km of the roadway, and only 5% of patients lived near the prison, limiting these analyses.

Our findings are subject to limitations. Selection of primary MDR-TB cases from certain areas of the district would have biased recruitment to the original studies; however, all MDR-TB cases across the district were sought for study inclusion and were not different from DS-TB cases in the length of time living in the district or in their current household.<sup>6</sup> We limited analyses to purely spatial cluster analysis using Kuldorff's spatial scan statistic, a common approach to identifying disease clusters (or hot spots). While the statistic considered geography, it did not account for variation in times of infection or patients' dates of symptom onset; it is therefore possible that TB cases that cluster geographically are epidemiologically unrelated.

SaTScan adjusts the likelihood ratio for *P* values for the multiple scans it conducts to avoid falsely detecting clusters (false-positives). A drawback of this conservative approach is that the likelihood required to be statistically significant increases as more data are included, resulting in a loss of power. Therefore, if



**Figure 2** Location map of primary MDR- and DS-TB cases, with high TB rate locations of interest and significant cluster zone in San Juan de Lurigancho District. The 2 km grey shaded area represents the approximate location around Clinic X with clustering of MDR-TB cases and the area within which a higher expected number of primary MDR-TB cases was found compared to drug-susceptible TB cases. Source: Kuldorff's space-time scan statistic (SaTScan™, v 9.1.1) for space-only cluster, 50% maximum window using a Bernoulli model ( $n = 348$  in this cluster; 58 MDR-TB cases;  $P = 0.037$ ). Case data presented have a small random error to protect patient confidentiality. Map plotted using QGIS software (v.1.8.0.). (Total MDR-TB cases  $n = 104$ , DS-TB cases  $n = 750$ .) MDR-TB = multidrug-resistant tuberculosis; DS-TB = drug-susceptible TB; SJL = San Juan de Lurigancho; QGIS = Quantum Geographic Information Systems.

many scans are conducted, there is a chance that even a sizeable cluster could be missed (Type II error or false-negative).<sup>32</sup> This adjustment may explain the large cluster, which in an unfocused scan including 105 primary MDR-TB cases (therefore 105 tests), did not reach statistical significance, although it was significant during specific a priori defined focused

scans. Finally, genotyping data were unavailable to determine if cases represent a single primary MDR-TB strain from a single common source or widespread community transmission of various strains. Strain type data would provide additional valuable information; however, even in the absence of genotyping information it is possible to undertake important

**Table 4** Adjusted final logistic regression model\*

	aOR (95%CI)	P value
Age, years		
≥35	Reference	
<35	1.74 (1.05–3.02)	0.040
Clinic X, km		
>4	Reference	
2–4	1.21 (0.69–2.15)	0.501
<2	2.10 (1.29–3.51)	0.004
Sex		
Female	Reference	
Male	0.85 (0.56–1.29)	0.440

\* Full model included age, sex, civil status, income, elevation and Hospital A, number of rooms in dwelling and number of persons sharing living space. Backward selection was used to select the final model. aOR = adjusted odds ratio; CI = confidence interval.

public health actions based on these epidemiologic and geographic data.

We identified a hotspot or cluster of primary MDR-TB, which could help target interventions, such as preventing nosocomial spread of MDR-TB, evaluation and monitoring of close contacts of patients with MDR-TB and active case detection using both intramural and extramural strategies.<sup>33–35</sup> While further investigation could identify causes for the clustering of primary MDR-TB cases, prioritizing and ensuring active prevention efforts in the 2 km surrounding Clinic X could be a first step towards controlling MDR-TB in the district.

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Conflicts of interest: none declared.

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## RESUME

**CONTEXTE :** Le Pérou connaît un des taux les plus élevés de tuberculose multirésistante (TB-MDR) dans les Amériques, avec une proportion croissante chez des patients encore jamais traités.

**OBJECTIF :** Identifier des grappes de cas de TB-MDR primaires, comparés à des cas pharmacosensibles (DS-TB), contribuerait à prioriser les interventions. Nous avons étudié le regroupement des lieux d'habitation des cas de TB-MDR primaire et leur proximité avec des zones à haut risque du district de San Juan de Lurigancho, Lima, Pérou.

**SCHEMA :** Les cas de TB-MDR et de DS-TB primaires participant à l'étude ont fait l'objet d'un entretien au cours duquel leur lieu de résidence a été enregistré grâce à un système de positionnement global. Les statistiques d'exploration spatiale de Kuldorff ont permis de détecter des grappes de cas (SaTScan<sup>TM</sup> v 9.1.1). Celles-ci ont été visualisées en Quantum Geographic Information

Systems (v1.8.0). Les centres des grappes suivantes ont été testés : un centre de santé présentant les taux les plus élevés TB et de TB-MDR (Centre X), un hôpital et deux prisons. Une analyse de régression a examiné les facteurs prédictifs de TB-MDR primaire.

**RÉSULTATS :** Un regroupement statistiquement significatif de cas de TB-MDR primaire a été identifié dans un rayon de 2,29 km autour du Centre de santé X. La proximité du Centre de santé X est restée un facteur prédictif significatif de TB-MDR primaire en analyse de régression ajustée.

**CONCLUSION :** Nous avons identifié un «point chaud» de cas de TB-MDR primaire autour du Centre de santé X dans une zone d'endémie tuberculeuse. Les raisons de ce regroupement nécessitent une investigation. On doit cependant envisager des interventions ciblées sur cette zone à haut risque.

## RESUMEN

**MARCO DE REFERENCIA:** La tasa de tuberculosis multidrogorresistente (TB-MDR) que notifica el Perú es una de las más altas de las Américas y comporta una proporción creciente de casos de TB sin antecedente de tratamiento previo.

**OBJETIVO:** La detección de conglomerados de TB-MDR primaria y su comparación con los casos de TB farmacosensible (DS-TB) contribuiría a definir las intervenciones prioritarias. Se analizó la proximidad del domicilio de los casos en los conglomerados de TB-MDR con las localidades de alto riesgo de enfermedad en el distrito de San Juan de Lurigancho de Lima, Perú.

**MÉTODO:** Se entrevistó a los pacientes con TB-MDR primaria y DS-TB incluidos en el estudio y se registró la localización de su residencia primaria mediante dispositivos portátiles con sistema posicionamiento global. Se aplicó la estadística espacial de Kuldorff con el fin de detectar los conglomerados (SaTScan<sup>TM</sup> v9.1.1). Los conglomerados detectados se visualizaron en el programa Quantum Geographic Information Systems

(v1.8.0). Se analizaron los siguientes centros de conglomerados: un centro de salud con las tasas más altas de TB-MDR (consultorio X), un hospital y dos prisiones. Mediante un análisis de regresión se evaluaron los factores pronósticos de aparición de TB-MDR primaria.

**RESULTADOS:** Se detectó un conglomerado de casos de TB-MDR primaria estadísticamente significativo en un radio de 2,29 km alrededor del consultorio X. Los análisis de regresión revelaron que la proximidad a este consultorio representaba un factor pronóstico significativo de aparición de TB-MDR primaria.

**CONCLUSIÓN:** En el presente estudio se localizó un 'punto caliente' de casos de TB-MDR primaria alrededor del consultorio X en una zona endémica de TB. Es preciso investigar las causas de esta aglomeración, pero se debe considerar la posibilidad de realizar intervenciones dirigidas a esta zona de alto riesgo.