## ORIGINAL ARTICLE

# GEOGRAPHICAL INFORMATION SYSTEM (GIS) APPLICATION IN TUBERCULOSIS SPATIAL CLUSTERING STUDIES: A SYSTEMATIC REVIEW

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## ABSTRACT

*Tuberculosis (TB) is known as a disease that prone to spatial clustering. Recent development has seen a sharp rise in the number of epidemiologic studies employing Geographical Information System (GIS), particularly in identifying TB clusters and evidences of etiologic factors. The aim of this systematic review is to determine evidence of TB clustering, type of spatial analysis commonly used and the application of GIS in TB surveillance and control. A literature search of articles published in English language between 2000 and November 2015 was performed using MEDLINE and Science Direct using relevant search terms related to spatial analysis in studies of TB cluster. The search strategy was adapted and developed for each database using appropriate subject headings and keywords. The literature reviewed showed strong evidence of TB clustering occurred in high risk areas in both developed and developing countries. Spatial scan statistics were the most commonly used analysis and proved useful in TB surveillance through detection of outbreak, early warning and identifying area of increased TB transmission. Among others are targeted screening and assessment of TB program using GIS technology. However there were limitations on suitability of utilizing aggregated data such as national cencus that were pre-collected in explaining the present spatial distribution among population at risk. Spatial boundaries determined by zip code may be too large for metropolitan area or too small for country. Nevertheless, GIS is a powerful tool in aiding TB control and prevention in developing countries and should be used for real-time surveillance and decision making.*

*Keywords: Tuberculosis cluster, geographical information system, spatial analysis*

## INTRODUCTION

Geographical Information Systems (GIS) and spatial analyses have been used to describe the spatial distribution and clustering of various infectious diseases including Tuberculosis (TB)[1]. GIS aids better and faster TB mapping and analysis than the conventional methods. It enables its users quick and easy access to large volumes of data[2]. There are numerous types of spatial analysis tools and mapping techniques that provide different approach of monitoring and management of epidemics[3]. Many countries have used GIS and spatial analysis to study TB disease distribution and have shown a distinct geographical clustering of TB cases, suggesting the likelihood of on-going transmission in that areas[4-9]. These clusters identify populations at increased risk of disease due to geographic proximity, which may correspond to recent transmission from one or more individuals to their contacts, reactivation of latent TB infection in an aggregate of individuals infected elsewhere, or both[10].

In epidemiology, cluster analysis is vital to detect aggregation of disease, to test the occurrence of any statistically significant clusters and ultimately to find evidences of etiologic factors. Cluster analysis identifies whether geographically grouped cases of disease can be explained by chance or are statistically significant[2]. It detects true clusters of disease from cases grouped around population centers[11]. Spatial cluster analysis plays an important role in quantifying geographic variation patterns. Researchers can detect patterns and relationships in the data based on geography through spatial analysis. Because these clusters carry a disproportional burden of excess TB cases, the results are helpful for TB control activities that direct public health action and guide interventions[9]. Interventions may include targeted intensified case finding, contact investigations and provision of ionized preventive therapy.

While control efforts are best designed when areas of high incidence are known, it is also important to determine why rates are abnormally high given the underlying risk factors. In recent years more research have surfaced particularly to evaluate the spatial distribution of TB and to identify high risk areas especially in developing countries. Many studies have demonstrated that the distribution of endemic diseases is also determined by social processes that are intrinsically related to the

space where they occur[4, 7, 10, 12-13]. Better knowledge of transmission risk factors may help to develop more effective prevention strategies to target high-risk populations. We therefore conducted a systematic review of spatial studies to determine evidence of TB clustering, its risk factors and the application of GIS in TB surveillance and control.

## METHOD

The electronic databases MEDLINE and Science Direct were searched from January 2000 to November 2015. The following terms were used in combination in keyword searches: spatial OR spatial analysis OR spatial analyses OR spatio-temporal analysis OR geographical information system OR geographic information system (All fields) AND tuberculosis (Title, abstract, keywords). Apart from English language, no search constraints were used. A hand search of all relevant articles was conducted up to November 2015 inclusive. References cited by review articles were screened. Included studies had to be published from year2000 in English and in peer-reviewed journals. Data must be sampled from human adult population with cases of tuberculosis. Articles will be excluded if they were animal studies, review paper, report or community trials. Studies that did not explicitly report spatial analysis or spatial mapping were also excluded in this review. Titles and abstracts were screened to assess its eligibility according to inclusion and exclusion criteria as the beginning process of systematic review. Subsequently, the full texts were assessed and exclusion of studies done based on the specific references to the exclusion criteria. At least two authors were involved in conducting the extraction and assessment of the articles. For doubt or hesitation that emerged about an article, the third opinion among the authors involved will be gathered to resolve those issues. Among variables extracted were types of study design, year and duration of data collection, sociodemographics of both individual tuberculosis cases and population background at study site, types of spatial analysis and software used, and main spatial findings.

## RESULTS

The database searches provided a total of 2842 citations and no additional citations were identified through the manual reference search. After duplicates were removed, 2456 citations remained. Among these, 2250 citations were excluded because they did not meet the criteria following our review of the titles and abstracts. The full texts of the remaining 197 citations were examined and 124 articles were excluded for

different reasons (Figure 1). In total, 71 studies were included in the systematic review. More than two third of these studies originated from developing world. Majority of the articles here were recent as 75% published in 2010 and beyond whereas 20% were produced in 2015. Initial period of data collection for a quarter of these studies dated back before 2005 whereas 15 more stemmed back as far as 1992. The duration of retrospective data range between 2 to 12 years, with most collected for 3 and 5 years.

For type of spatial analysis (see Table 1), a third of these studies applied spatial scan statistic that makes it the most used technique[6, 8-11, 14-32]. The next popular method was Moran I[4, 7,9, 28, 32-43] followed by both kernel density[13, 36, 44-48], Getis-ord Gi[7, 13, 32-33, 38, 40, 43] and local indicators of spatial association (LISA)[7, 39]. Some of the researchers utilized GIS basic application such as simple cloropeth mapping to describe TB distribution, layered on socioeconomic index for instance to represent neighbourhood deprivation[5, 49-63]. These visualizations were followed by distance measurement between cases using inverse distance weighting[3, 37, 64]and cluster analysis such as point cluster[65] or Average Nearest Neighbourhood[13, 44,66]. Some of the methods require advanced user such as novel technique in dynamic analysis[67], Geographical Weight Regression (GWR)[13, 68-69], Kriging and cokriging interpolation[70]and Bayesian method[7, 32, 41, 43, 71-73]. Many of these studies utilized more than 1 type of analysis such as combination of spatial scan statistics or Moran I with Getis-ordGi or GWR or others[7, 9, 13, 32-33, 38, 40, 43]. Summary of each study are presented in supplementary table 2.
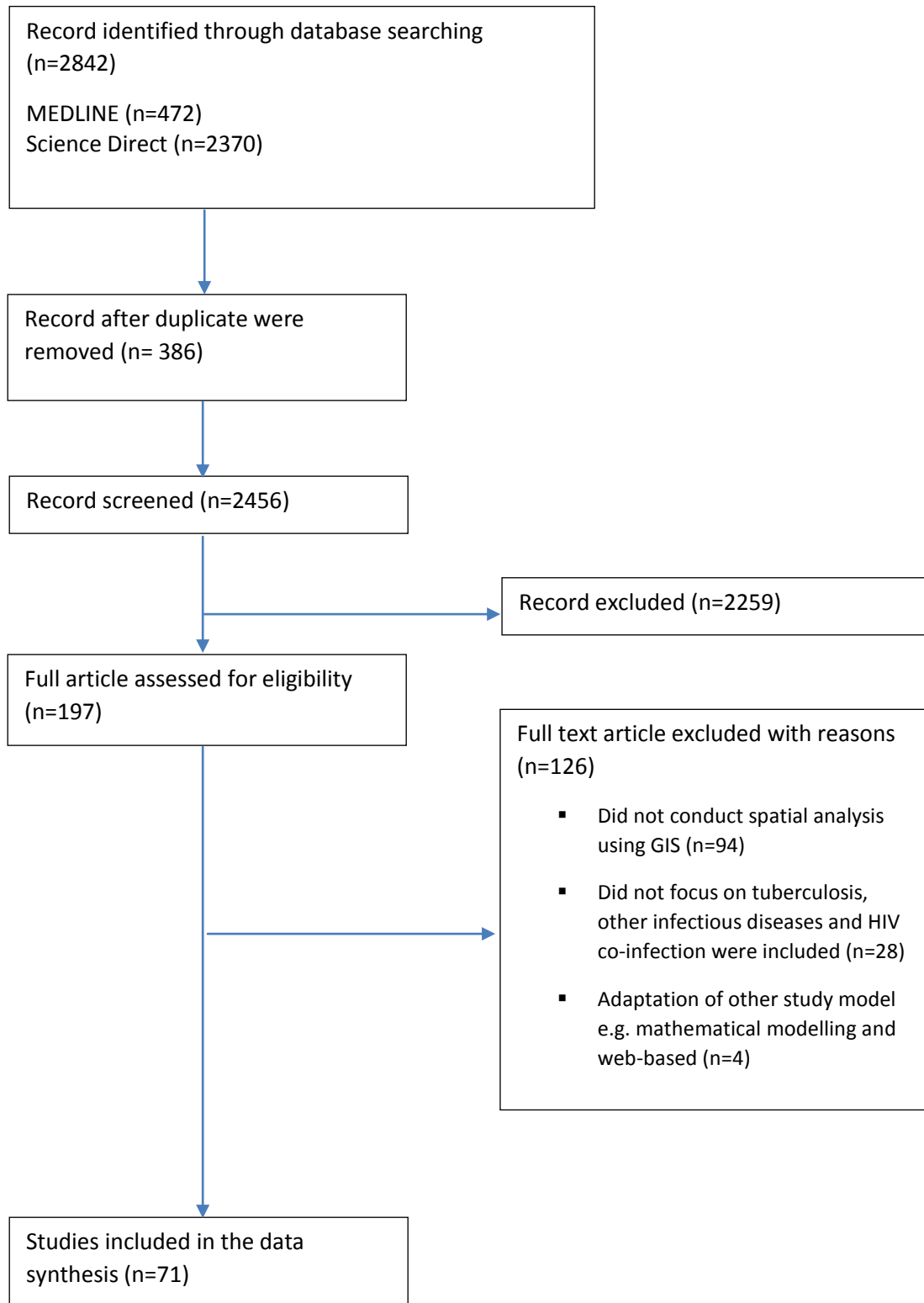
### Clustering of TB cases

Evidence of clustering were abundance as most of the studies reported detection of this type of TB distribution in the study population. In United States, statistically significant spatial clusters were detected in Baltimore City and Montgomery & Prince George County in Maryland[10], 3 zip code areas in Tarrant county[3], census tracts in Houston[13], 2 defined neighbourhoods in Smith county[53] and in several outbreak spots in San Francisco[26]. Study in Canada centred on Montreal whereby 5 out of 539 census tracts had higher TB incidence with relative risk (RR) range from 1.3 to 4.1[24]. There were 3 studies analysing TB spatial pattern in India with 1 involved a substantially large area of the country. Pure and retrospective spatial analysis carried out in Almora district of Uttaranchal and Dehradun, shown presence of 3 and 5 TB clusters at the same geographical areas respectively[11, 21]. Another study found that high proportions of patients were clustered in the densely populated north eastern part of Chennai[55].

There was strong heterogeneity of TB distribution across Urmia, one of the largest cities in north- west Iran whereby 3 spatial clusters were spotted[67].

**Figure 1: Flow of paper through selection process for identification of relevant articles.**

Record identified through database searching (n=2842)

MEDLINE (n=472)
Science Direct (n=2370)

Record after duplicate were removed (n= 386)

Record screened (n=2456)

Record excluded (n=2259)

Full article assessed for eligibility (n=197)

Full text article excluded with reasons (n=126)

- Did not conduct spatial analysis using GIS (n=94)

- Did not focus on tuberculosis, other infectious diseases and HIV co-infection were included (n=28)

- Adaptation of other study model e.g. mathematical modelling and web-based (n=4)

Studies included in the data synthesis (n=71)

In different parts of Asia, townships with higher TB incidence had substantial spatial spill over effects to neighbouring area that mainly located in northern, western and eastern parts of Taiwan[42]. Similar high TB incidence was spotted by simple GIS mapping in Kathmandu where higher TB rates occurring in the Terai region and relatively moderate and low rates in the Hill and Mountain regions, respectively[5]. Spatial analysis of TB clusters in Bandar Lampung, Indonesia showed that the incidence of smear-positive TB was not equally distributed throughout 13 sub municipalities being studied as cases tended to be concentrated in areas of high population[18]. Spatial clusters also were identified in prefecture of Fukuoka, Japan; city of Karachi, Pakistan and in Cambodia[16, 64, 56].

There were many studies from South America continental with majority based in Brazil. Global Moran's I test indicated clear patterning of municipal TB notification notably high in urban areas on the eastern seaboard and in the west of the country[4]. Distribution of TB incidence rate was high in the neighbourhoods of Olinda City around the central and east region[71]. Spatial clustering was also evidence in Porto Alegreas rate of TB incidence in a neighbourhood tends to be more similar to the surrounding neighbourhoods than to the more distant ones since Moran's I was significantly positive[36]. All these sites demonstrated clustering of TB cases. In European continental, 8% of the municipalities in Portugal had aggregated TB cases with 2 major clusters located at Metropolitan Area of Porto and Lisbon[6, 23]. In Spain, 28 most likely TB clusters were detected by spatial analysis comprised of 7 municipalities in Greater Barcelona Area. TB distribution was also shown to be concentrated in the north of the country and along Mediterranean coast[8].

Study in Moldova looked at spatial variation in MDR-TB burden and the finding was striking; the estimated MDR-TB incidence rate in some rayons (health administration) was 20 times that of others. It was concluded that there were several areas with statistically significant clustering of high MDR-TB risk and localities that had substantially higher MDR-TB risk than those around them[37]. However, a few of the literature found limited or no aggregation of TB cases. A study on foreign-born patients in US revealed that 84% of the cases were due to reactivation TB and was not spatially clustered[27]. Upon combining GIS with spoligotyping, another study showed that less than a quarter of cases can be classified as both genotypically and spatially clustered[12].

**GIS application in TB surveillance and control**

GIS has been applied in quantifying improved access to community-based TB treatment points that consists of clinics, hospitals and homes of both community health workers (CHW) and volunteers which also function as place for DOTS in South Africa[62]. Prior to setup of community-based TB treatment points, the average mean distance from homestead to nearest hospital was 29.6km. Through establishment of more clinics and then CHWs as treatment points, it led to reduction of the mean distance to 4.2 km and to 1.9 km respectively whereas inclusion of volunteers further decreased the distance to 800m. Thus it can be concluded that access to treatment supervision point based on distance factor have been proven satisfactorily using GIS application[62]. In terms of monitoring for health facilities adequacy for TB treatment, study in Pakistan found that many TB registering centres were located near unplanned or encroached and slum areas of within the city. This is justifiable since most of TB patients were poor and did resided in those slums. However through GIS mapping, health centres were mostly located in cluster forms under 1 kilometre square radius, which considered not optimum to provide TB service to population in general due to close proximity of one centre to another[64]. Access to health care can be assessed using spatial analysis too whereby in Cambodia, areas with high TB incidence were associated with lowest vaccination coverage and the worst physical barrier of distance to health care facilities[56].

GIS do play a role in the outcome assessment of a TB programme from spatial aspect. When compared to data before and after reinforcing several elements in DOTS, improvement could be seen especially for MDR-TB whereby cases were located 78% further away from city centres (1.92 km) than non - MDR-TB (1.08 km), representing a 55% increase (1.24km) in median distance over time. This geographical analysis revealed an intended shift in the distribution of MDR-TB after DOTS was strengthened[63]. A different TB programme was formulated to screen and treat home residents with latent TB infection (LTBI) in Smith County, US. The researcher delineated 2 largest and densest clusters, subsequently identified 2 highest incidence neighbourhoods in the county. Prophylactic treatments were started for those with positive Tuberculin Skin Test (TST) and LTBI. After 10 years of follow up, the study found that there was no TB case in those neighbourhoods unlike the rest of the county. This indicates that GIS application in targeting high-incidence neighbourhoods for active, community-based screening proved useful[53].

Using county-based log-likelihood ratio and spatial scan statistics on retrospective data, researchers in US were successful in detecting TB outbreaks months before they were known by health authorities. 8 out of 9 TB outbreaks were detected, with 6 of these are known 1 to 52 months (median 10 months) before identified by health authorities[14]. In contrast, applying spatial analysis in space-time surveillance had low accuracy in low transmission and non-endemic TB setting in Montreal as it detected too many false alarms. Simulation over 11.5 years found that 89 out of 101 transmission chains managed to be detected but with higher false alarms of 1.3 monthly. Upon different setting, false alarm was lowered to 0.05 monthly but only 5 out of 101 transmission chains detected[15].

**Table 1: Total studies reviewed classified according to type of spatial analysis used**

| Type of spatial analysis | No. of articles N (%) | Author/year |
|---|---|---|
| Spatial scan statistics | 25 (35.2) | Couceiro L., et al. (2011), Gómez-Barroso D., et al. (2013) Zhao F., et al. (2013), Prussing C., et al. (2013) Tiwari N., et al. (2006), Kammerer JS., et al. (2013) Verma A., et al. (2014), Onozuka&Hagihara (2007) Randremanana RV., et al. (2009), Wardani DW., et al. (2014), Nana Yakam A., et al. (2014), Tadesse T., et al. (2013), Tiwari N., et al. (2010), Touray K., et al. (2010) Nunes C. (2007), Haase I., et al. (2007), Zaragoza Bastida A., et al. (2012), Higgs BW., et al. (2007) Ricks PM., et al. (2011), Moonan PK., et al. (2012) Shea KM., et al. (2013), Gurjav U., et al. (2014) Gurjav U., et al. (2015), Dangisso MH., et al. (2015) Hassarangsee S., et al. (2015) |
| Global/Local Moran I | 16 (22.5) | Harling & Castro (2014), Maciel EL., et al. (2010) Zhao F., et al. (2013), Dangisso MH., et al. (2015) Jia ZW., et al. (2008), Yazdani-Charati J., et al. (2014) Queiroga RP., et al. (2012), Acosta &Bassanesi (2014) Jenkins HE., et al. (2013), Liu Y., et al. (2012) Alvarez-Hernandez G., et al. (2010), Izumi K., et al. (2015) Pereira AGL., et al. (2015), Ng IC., et al. (2012) Wang T., et al. (2012), Hassarangsee S., et al. (2015) |
| Kernel density | 7 (9.8) | Feske ML., et al. (2011), Acosta &Bassanesi (2014) Munch Z., et al. (2003), Yamamura M., et al. (2015) Manjourides J., et al. (2012), Pinto ML., et al. (2015) Santos-Neto M., et al. (2014) |
| Getis-ordGi | 7 (9.8) | Maciel EL., et al. (2010), Feske ML., et al. (2011), Dangisso MH., et al. (2015), Jia ZW., et al. (2008) Liu Y., et al. (2012), Izumi K., et al. (2015) Wang T., et al. (2012) |
| Bayesian Spatial Modelling | 7 (9.8) | Maciel EL., et al. (2010), Dangisso MH., et al. (2015) Pereira AGL., et al. (2015), Wang T., et al. (2012) Souza WV., et al. (2007), Randremanana RV., et al. (2010) Roza DLD., et al. (2012) |
| Geographical Weight Regression | 3 (4.2) | Feske ML., et al. (2011), Li XX., et al. (2014) Sun W., et al. (2015) |
| Average Nearest Neighbourhood | 3 (4.2) | Munch Z., et al. (2003), Feske ML., et al. (2011) Kolifarhood G., et al. (2015) |
| Local indicators of spatial association (LISA) | 2 (2.8) | Alvarez-Hernandez G., et al. (2010) Maciel EL., et al. (2010) |
| Kriging interpolation | 1 (1.4) | Li XX., et al. (2010) |
| Point cluster analysis | 1 (1.4) | Nava-Aguilera E., et al. (2010) |
| Dynamic analysis | 1 (1.4) | Dos Santos RM., et al. (2010) |

## DISCUSSION

GIS when combined with spatial analyses can be used to identify disease clusters and determine the potential risk factors involved with clustering. It allows visual assessment of TB risk factors distribution and notification rate, as well as revealing trends and inter-relationships that would be more difficult to discover in tabular format. In additiontocharacterizing epidemic durations and locations, GIS provide a valuable early warning mechanism through rapid identification of increasing case counts and high-risk areas by utilizing routine on-going surveillance data. Recognizing areas of high TB burden should help prioritize resources and allow for targeted studies aimed at understanding the local drivers of emergence and spread of TB. Overall, GIS and spatial analysis can be a valuable addition to traditional means of assessing TB control programmes as showed by this study.

However, as each spatial statistical technique has its own advantages and disadvantages, more than one method is sometimes needed to validate results. For instance, the use of Kernel Density which is calculated from points of cases can map areas of greater disease density[13, 44]. Methods such as local indicator of spatial association (LISA) and spatial scan statistics on the other hand can be used to measure relative risk of disease by area[6, 8, 11, 16-17, 19-22, 25]. The latter is extremely capable in identifying clusters of both high and low risk and also assess its significance by testing the null hypothesis; that the relative risk of the disease is homogeneous throughout the study area. Moran's I, a global index of spatial autocorrelation meanwhile can help to determine relationship among variables in space[33-36].

Among challenges faced when working with GIS are with respect to data utilization and type of data available[74]. Most spatial studies on TB required pre-collected population or health information for GIS database application but they must be used with caution. Although these types of data are relatively cheap and updatable, it may be overly optimistic to expect that they can be manipulated by the technology to such an extent that they provide great new insight. Disease mapping and spatial modelling studies have become increasingly detailed and sophisticated, with rigorous handling of uncertainties built in, but are limited when it comes to estimating populations at risk. Detailed spatial datasets on population distributions now exist, but maps of other demographic and socioeconomic characteristics to identify vulnerable subgroups remain lacking[74-75]. Even where census data are valid for the spatial scale of the problem, it must often be assumed quite unrealistically, that the population is evenly distributed over the area of the spatial unit in which the data are presented. Sociodemographic data such as national census are collected at discrete intervals, normally every 5 to 10 years which dictate the use of estimates of inter-censual population[76].

The spatial boundaries imposed by the pre-collected data, such as zip code area are rarely those desired by the researcher, nor are all the ideal data items presented[76]. This issue is of particular challenge since appropriate geographical boundary should be utilized to examine TB transmission in the study area. For example, using zip codes as the spatial unit may be too large in very populated metropolitan areas. Some towns with insignificant clustering on the other hand might be covered by the clusters based on these zip codes. The proper use of small area data means that a project's objective should not require high levels of spatial precision and accuracy. Census block groups may provide greater resolution in determining localized transmission[3]. These boundaries may also change over time, thus not suitable for future comparison. It is nevertheless possible to use pre-collected ecological data as long as the level of spatial accuracy is acknowledged and researchers do not assume that the full capabilities of GIS are being utilised[76].

Spatial TB clusters cases are not always due to recent ongoing transmission. Unlike some other infectious diseases, a person can be infected with latent TB. A latent infection can be reactivated decades after the original infection. Since some risk factors for latent infections cluster in space and time, reactivated cases can also form space-time clusters[24]. Fortunately it is possible to distinguish between reactivation and recent transmission by culturing and genotyping the bacteria from TB patients. When cases are involved in a chain of transmission, TB organisms will share a similar genotype[15]. Molecular genotyping will significantly augment GIS findings by further narrowing in on specific recent transmission[10, 77].

Combining GIS with molecular epidemiological surveillance can be an effective solution for identifying tuberculosis transmission not identified during standard contact tracing. This method can enhance targeted screening and control efforts, with the goal of interruption of disease transmission and ultimately incidence reduction. Findings from this review demonstrated that by using existing health data, GIS can identify

previously undetected TB transmission[12-14]. Evaluating changes in the geographical location of cases after the initiation or reinforcement of a TB control programme may be critical to fully understanding its effectiveness. While decreased incidence rates can reflect the overall impact of DOTS, the burden of TB may not be evenly reduced across all communities covered by the programme. Monitoring changes in local case numbers could help in targeting additional health services required in specific areas with greater disease burden. In the present study, we showed that GIS can delineate the impact of local TB control program on the geographical location of TB cases.

There were several limitations in conducting this systematic review. While the search terms were few and broad, we may have missed relevant articles. As we focus on publication in English, we have excluded important findings particularly from developing regions. Assessing methodological quality of each study can be difficult and misleading since we relied on author-supplied information that can concealed flaws of research design. Selective publication for review in this paper especially studies that report dramatic effects of TB clusters may result in bias even though systematic appraisal tend to be more transparent than a conventional or narrative review. Finally, almost all studies included here were observational; they can identify associations between characteristics of population background and TB cluster but not the direction of causation.

## CONCLUSION

GIS is a powerful tool for TB control and prevention in developing countries, and should be used for real-time surveillance and decision making. GIS has a vital role to play in detecting TB cluster, area with increased transmission and determine population at risk. The possibilities that can be explored are limitless, depending on the skill and imaginative use of the researchers and the willingness of health sector management to resource its implementation. Health administrators, professionals and researchers need training and user support in GIS technology, data and epidemiological methods in order to use GIS properly and effectively.

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