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RESEARCH ARTICLE

Multi-drug-resistant tuberculosis clusters in Mpumalanga province, South Africa, 2013–2016: A spatial analysis

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Abstract

Objective: To identify spatial clusters with unusually high levels of MDR-TB, which are highly unlikely to have arisen by chance in Mpumalanga Province, South Africa.

Methods: Home addresses of all MDR-TB patients were collected from four MDR-TB facilities from 2013 to 2016. We mapped all addresses, linking them to the nearest ward with population estimates. A spatial analysis was conducted using kernel density in ArcGIS to estimate and map the distribution of the disease and used Gertis-Ord Gi to test for significant clustering.

Results: A total of 4065 MDR-TB patients were mapped. Ten significant clusters (p-value <0.05) were found across the province in six sub-districts: Mbombela, Nkomazi, Emalahleni, Govan Mbeki, Lekwa and Mkhondo. Mbombela has the highest number of significant clusters. The central region did not have any MDR-TB clusters.

Conclusion: There is clear evidence of MDR-TB clustering in Mpumalanga. This calls for concentrated TB prevention efforts and proper allocation of resources. Further investigations are needed to identify MDR-TB predictors.

KEYWORDS
clustering, geographic information systems, hotspot, MDR-TB

INTRODUCTION

TB is currently a global emergency, especially in developing countires [1]. It is recognised by the World Health Organization (WHO) as one of the major public health threats [2,3]. It was identified as the seventh most common disease in the world [4]. It still remains one of the biggest threats to public health due to low cure rates as well as co-infection with other diseases [5]. In 2015 alone, there were 10.4 million estimated new infections globally [6]. In 2013, it was estimated that 1.5 million people died from TB [7]. Between 1998 and 2030, 225 million new TB cases and 79 million cases of deaths related to TB are expected [8]. In September 2017, TB was declared a priority pathogen for the development of new antibiotics by WHO [9]. This means that TB remains one of the most important infectious diseases that is affecting human beings today [10]. Currently, South Africa has the highest TB incidence in the world and this is mainly resulting from a very high population prevalence of HIV [11,12]. In 2015, nearly 454,000 new TB cases [6] were reported with an incidence rate of about 860 cases per 100,000 population [13].

TB gets more critical and hazardous when it becomes multi-drug-resistant tuberculosis (MDR-TB). Globally, it is estimated that 3.3% of new TB cases plus 20% of TB cases that were treated previously are MDR-TB [14]. The emergence of MDR-TB has undermined the TB control efforts that have been achieved in the past decades [1,15]. This is due to increased MDR-TB cases in the last few years [7]. Four lakhs and fifty thousand estimated cases were reported [16]

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in 2012 and 481,000 in 2015 [17]. Currently, it is estimated that there are about 580,000 new MDR-TB cases each year [18] with South Africa rated as one of the ten countries with the highest drug-resistant TB burden globally [16].

In Mpumalanga province, MDR-TB cases have increased from 190 in 2009 to 385 in 2011 [19]. In 2016, Mpumalanga was identified as a province with the highest rate of TB that is resistant to rifampin (RIF) [20]. Timely identification of new cases of MDR-TB in the province and the continuous monitoring is very important in efforts to control and prevent further infections.

TB, like many other infectious diseases, is prone to clustering or spatial aggregation [4]. It is therefore important to understand the spatial distribution of the disease when implementing strategies to prevent new infections. For this reason, geographic information system (GIS) has become a valuable tool in public health. GIS has been used to identify geographical areas that have ongoing disease transmission using spatio-temporal techniques. These techniques aid in the identification of greater density of occurrences of a disease in certain places at certain times [21]. This method of evaluating disease clusters leads to effective prevention and control of TB [22]. Specifically for TB, GIS has been used more frequently in recent years to identify hotspots [17,22–28]. Although similar studies have been conducted in South Africa, they only focused in one province, which is KwaZulu-Natal.

This study therefore aimed to use GIS and spatial statistics to identify spatial clusters of MDR-TB in Mpumalanga province from 2013 to 2016 and to determine if the clusters are statistically significant.

STUDY POPULATION AND METHODS

Study area

Mpumalanga is one of the nine provinces in South Africa. It has three districts, Gert Sibande, Nkangala and Ehlanzeni, and 17 sub-districts. The total population according to the Statistics South Africa 2017 mid-year estimates is 4,444,073. Ehlanzeni has the highest population of 1,770,748, followed by Nkangala with 1,501,278 people, then Gert Sibande with 1,172,047. At 7.8%, Mpumalanga has the highest rate of MDR-TB of all provinces in South Africa, much higher than the national average of 6.2% [20].

Data collection

Data were retrospectively collected from four MDR-TB facilities in Mpumalanga, that is Bongani, Standerton, Witbank and Barberton TB hospitals. These facilities cover all MDR-TB cases in the three districts. The required data were obtained from the sputum/admission books in these facilities rather than the EDRWeb electronic database (the MDR-TB database). The electronic database did not have the patient addresses that were needed for geocoding their locations. The data collected included the following attributes for each patient: age, sex, year of diagnosis, district, sub-district, town and village.

All patients confirmed with MDR-TB over a 4 years period from 2013 to 2016 were included. The geographical location of the patients was manually geocoded using their residential addresses. The patients' addresses were geocoded to the village in which they fall under instead of their actual homes. This is because Mpumalanga province is mostly rural and the majority of the addresses provided could not be found, which meant that they could not be geocoded to the exact location. However, most of the villages had a radius of less than 5 km, with a few going up to 10 km. Therefore, the accuracy of the geocoded locations is still within the acceptable range for the purpose of this study. Previous studies have also indicated that results are similar when the analysis is done with precise point locations compared to the use of local areas [29]. Manual geocoding was done in Google maps by searching for a village (provided in the address). A random location within the selected village was then chosen and assigned to a patient. The coordinates were captured in MS Excel with all the other patient attributes and exported to ArcGIS 10.5 for analysis.

Ethical approval to conduct this study was obtained from the Research Ethics Committee, Faculty of Health Sciences, University of Pretoria (ref 295/2017) and the Health Research Committee of the Mpumalanga Health Department (ref MP_MP_201708_010). The requirement to obtain informed consent from patients was waived by both committees.

Spatial analysis

Spatial analysis was done using ArcGIS 10.5. Patient's addresses were geocoded and displayed as point data. The geocoded patient addresses were aggregated to the ward level using a spatial join to the ward dataset from Statistics South Africa. The ward is the smallest administrative unit in South Africa. The spatial join combined the MDR-TB data with the ward population data. Population data were used as a denominator (with MDR-TB cases as numerator) when performing the spatial analysis. Analysis was performed at ward level using MDR-TB incidence.

Kernel density was analysed using the Spatial Analyst extension in ArcGIS 10.5 to produce a smoothed map of TB incidence across the study area. This analysis describes how the density at one area can influence its neighbouring areas [30]. The neighbouring radius was determined automatically and set to 14 km. Kernel density analysis was done for all the years combined as well as for each individual year, from 2013 to 2016. The population was adjusted for each year by applying a growth rate of 1.7%. This rate was calculated from the Mpumalanga province mid-year population estimates (Statistics South Africa) for the period between 2012 and 2016. The provincial growth rate was 1.7% across the four years. The same rate was applied to the 2011 Census ward population data to estimate the population between 2013 and 2016. For the combined analysis, the average population of the four years was used as the denominator.

The Getis-Ords Gi extension in ArcGIS 10.5 determined whether the hotspots/clusters identified from the kernel density analysis were statistically significant. This extension uses a calculated z-score, and it is based first on the intensity of the feature and then on the intensity of neighbouring features. Wards with clusters of p-values <0.05 were identified. These were classified as statistically significant. This analysis was done for all the years combined and for each year in order to identify trends of MDR-TB clusters in the province.

RESULTS

A total of 4204 MDR-TB patients were captured from the four TB facilities in Mpumalanga between 2013 and 2016. About 139 patients were excluded from the analysis because they came from other provinces or had incomplete addresses. Patients were distributed across all 3 districts and 17 sub-districts.

Over half of the patients were male (n = 2231, 54.9%). The age group with the most cases is 25–34 years (n = 1225, 30.1%). Only 10 patients (0.2%) were younger than 5 years. Demographic characteristics of the patients are shown in Table 1.

The total number of MDR-TB patients increased between 2013 and 2015 (884–1,139). Barberton hospital had the highest number, with 1,252 patients. However, a reduction of 6% was observed between 2015 and 2016.

The MDR-TB combined incidence for the entire province was calculated to be 93.1 cases per 100,000 persons for the 4-year period. The incidence was calculated using the 2016 population estimates from Statistics South Africa [31]. Of the 3 districts, Ehlanzeni had the highest incidence of 110.5 cases per 100,000 persons, followed by Gert Sibande with 104.9 cases. Nkangala district had the lowest incidence of 58.5 cases per 100,000 persons. Annual incidence was also calculated using the population estimates for that specific year (2013, 21.3; 2014, 27.1; 2015, 26.5; and 2016, 20.6). In terms of the actual number of MDR-TB cases, Ehlanzeni also had the highest with 1,956 patients (48.1%), which is almost half of the total MDR-TB cases across the province. Figure 1 shows combined MDR-TB incidence per 100,000 persons for the 4-year period. Figure 2 shows the MDR-TB incidence for each year per 100,000 persons.

TABLE 1 Characteristics of MDR-TB patients, Mpumalanga province, 2013–2016

Characteristic	*N*	(%)
Total	4065	
Sex		
Male	2231	(54.9)
Female	1745	(42.9)
Unknown	89	(2.2)
Age group, years		
0–4	10	(0.2)
5–14	110	(2.7)
15–24	495	(12.2)
25–34	1225	(30.1)
35–44	1131	(27.8)
45–54	675	(16.6)
55–64	283	(7)
>=65	100	(2.5)
Unknown	36	(0.9)
Year of diagnosis		
2013	884	(21.7)
2014	1143	(28.1)
2015	1139	(28)
2016	899	(22.2)
District		
Nkangala	879	(21.6)
Gert Sibande	1230	(30.3)
Ehlanzeni	1956	(48.1)
Hospital		
Standerton	988	(24.3)
Bongani	617	(15.2)
Barberton	1252	(30.8)
Witbank	1208	(29.7)

Spatial analysis for all years combined

Spatial cluster analysis detected ten significant clusters (p-value <0.05) across the province. Ehlanzeni and Gert Sibande districts had the highest numbers of clusters. These two districts had four statistically significant clusters each, which means that they account for 80% of MDR-TB clusters in the province. The clusters in Ehlanzeni district are concentrated in one sub-district, which is Mbombela. This is the most burdened sub-district in the province with 1040 cases of MDR-TB patients across the four years. The most burdened sub-district in Gert Sibande is Govan Mbeki with two significant clusters. Nkangala has the least number of significant clusters. No clustering was observed is in the central region of the province. Figure 3 shows the results of the combined spatial analysis.

Spatial analysis for each year

Spatial analysis by year produced similar results. Hotspots/clusters were consistently identified in similar places across the years. The most clusters were observed in 2015 with eight identified. However, in 2016, the total number of significant clusters went down to six. The reduction was mostly in Ehlanzeni and Gert Sibande districts. Figure 4 shows the results of spatial analysis by year.

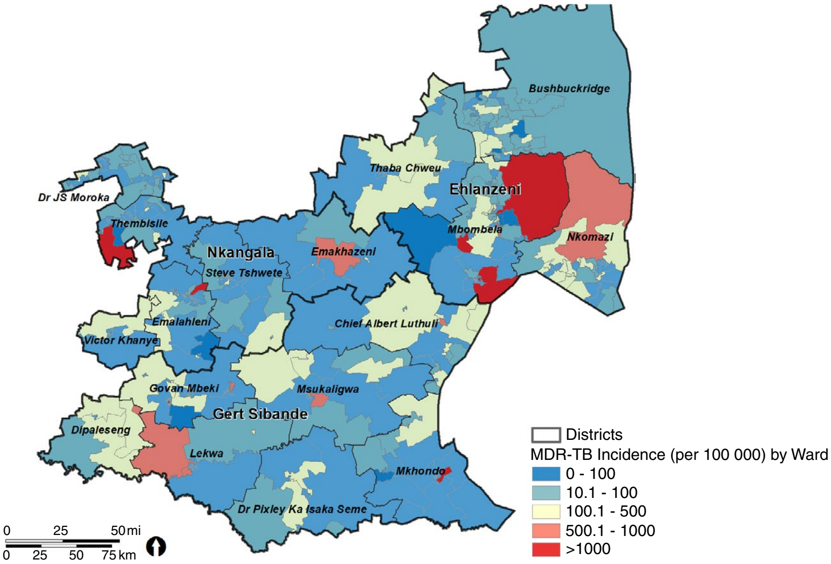


FIGURE 1 Combined MDR-TB incidence (per 100,000 persons) in Mpumalanga province, South Africa between 2013 and 2016

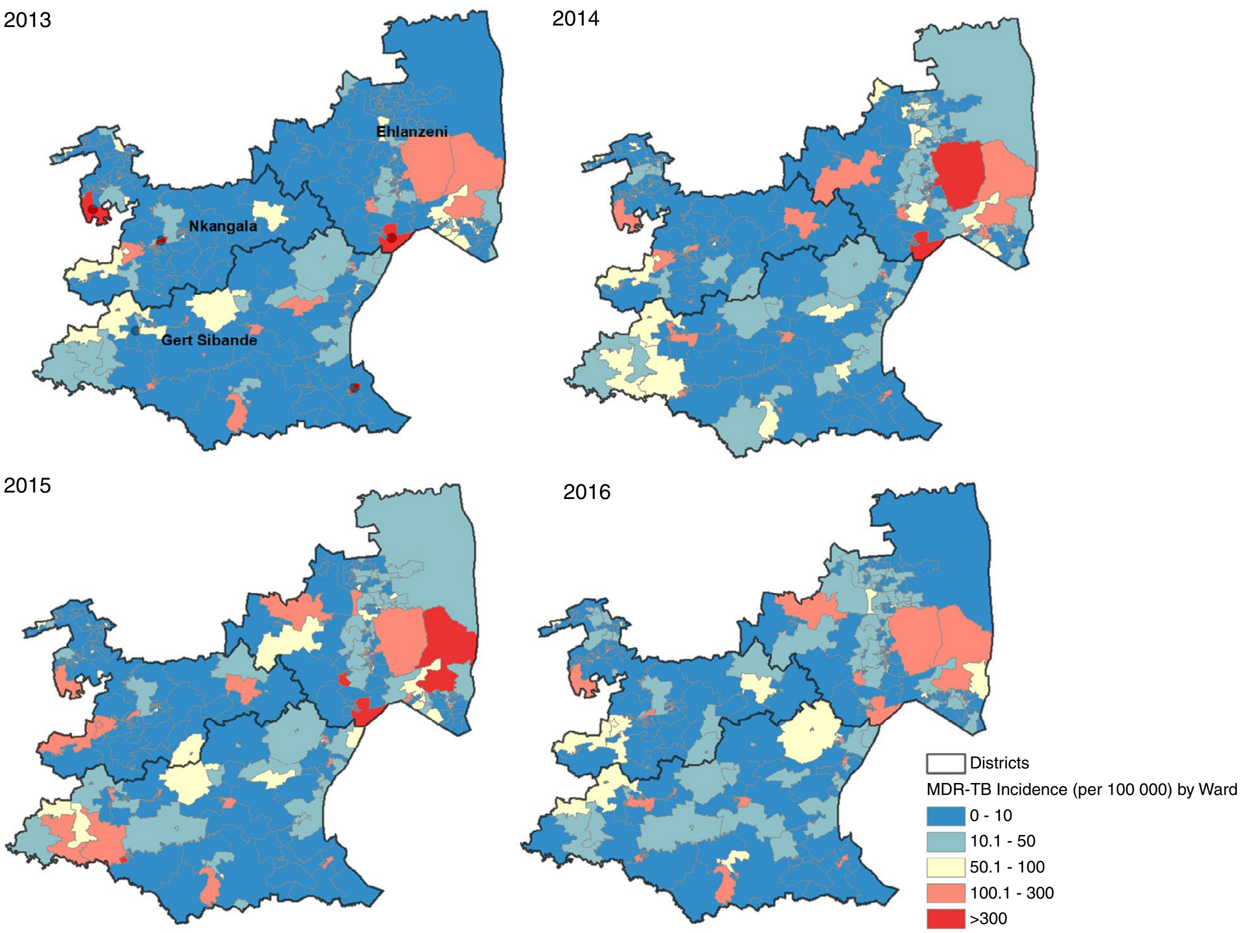
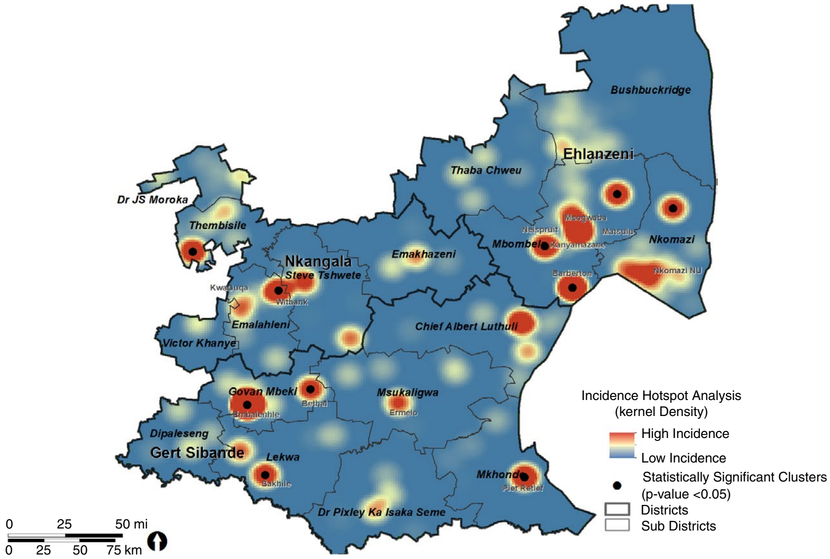


FIGURE 2 MDR-TB incidence in Mpumalanga province, South Africa between 2013 and 2016

DISCUSSION

MDR-TB is still a major infectious disease in Mpumalanga province with over 800 cases identified each year from 2013 to 2016. This study has described the spatial distribution of MDR-TB in the three districts of Mpumalanga province between 2013 and 2016. The study has also compared spatial clustering between the four years. To our knowledge, this is the first spatial analysis of MDR-TB looking at all the three districts and 17 sub-districts

FIGURE 3 Distribution and spatial clustering of MDR-TB incidence in Mpumalanga province, South Africa between 2013 and 2016



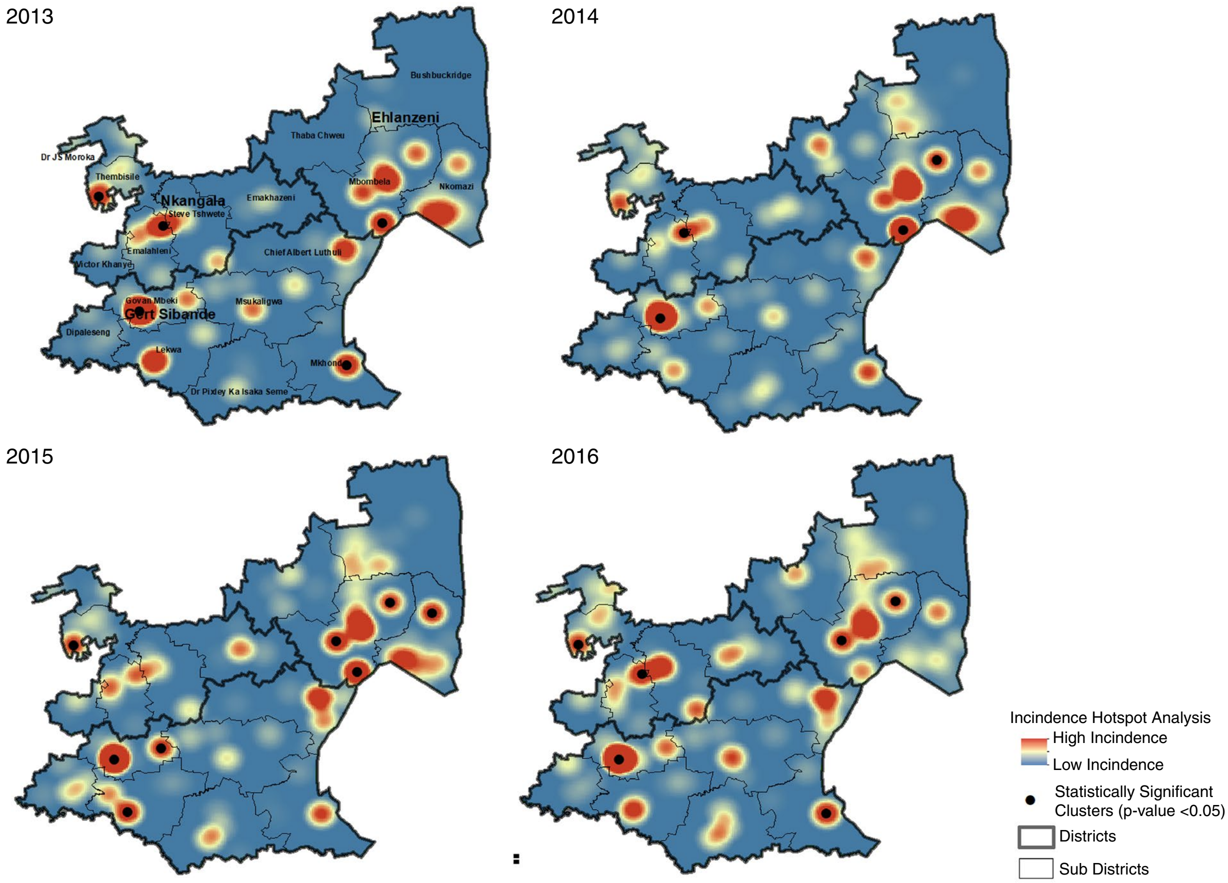


FIGURE 4 Distribution and spatial clustering of MDR-TB incidence in Mpumalanga province, South Africa; 2013–2016

in the Mpumalanga province. The results of the study have shown evidence of significant spatial clustering of MDRR-TB. There is also evidence of a high incidence of the disease in the province.

Ehlanzeni district carries the highest burden of MDR-TB. This finding is in line with previous studies that assessed MDR-TB in the province [19,20]. Ehlanzeni district is also characterized by a high prevalence of HIV (17.5%), followed by Gert Sibande with an HIV prevalence of 17.3% and Nkangala at 11.1% [20]. Ehlanzeni has the highest population of the three districts, and it carries the most burden. Regarding high HIV prevalence and spatial aggregation of MDR-TB (TB-HIV co-infection), the results of this study are consistent with those of other similar studies conducted in high-burden rural areas [29].

The number of significant clusters increased between 2013 and 2015. However, there was a reduction between 2015 and 2016. This could be due to the improved efforts to control the transmission of MDR-TB in the province, for example screening all HIV positive patients for TB. The reduction could also have been due to successful TB treatment outcomes in the province. According to the 2017 District Health Barometer, Mpumalanga has a TB treatment success rate of 81.4%, which is higher than the country's average of 81% [20].

This study had some limitations. First, the patients' home addresses could not be geocoded to the precise location. This is because the Mpumalanga province is mostly rural and does not have street addresses. Patients were geocoded to the village under which the address falls. Second, not all patients captured had a complete address. This led to the exclusion of some of the patients in the analysis. However, the number of patients excluded was minimal and does not influence the outcome of the cluster analysis. Third, some patients may be captured twice. In 2013, some MDR-TB cases were initially treated in Witbank hospital in the Nkangala district. After they became stable, patients were transferred back to one of the other three TB hospitals, which means that they were recorded twice, from both hospitals. The proportion of these patients is unknown. Fourth, the combined incidence (between 2013 and 2016) may not be accurate. Some patients may have been re-infected with MDR-TB and diagnosed a second time after they were cured. These patients would be counted twice when calculating incidence, and their proportion is unknown. Fifth, the population data at ward level are from Census 2011. No other official statistics were available. In order to account for an increase in population, a growth rate was applied.

Sixth, at the time of the study, data were available up to 2016. More timely data for analysis and use are recommended. This would provide TB programme managers and policymakers more relevant data to identify trends and new clusters as they happen. Timely data allow for prompt interventions where needed. Lastly, the study only identified where spatial MDR-TB clustering occurred, but does highlight what the risk factors are. Further research is required to identify the social determinants/risk factors of these clusters.

CONCLUSION

MDR-TB is concentrated in certain areas in the province of Mpumalanga. The risk of contracting MDr-TB is not uniform across the province. In order to be more effective in controlling transmission and eradicating MDR-TB, strategies targeted at high burden sub-districts should be implemented rather than applying the same treatment strategies across the province. Targeted strategies should include improved contact investigations or active case finding, early TB and MDR-TB detection and treatment. We also recommend the inclusion and electronic capturing of patients' geographic data, for example home address, town or village. This kind of analysis can be easily conducted when data are available electronically without requiring manual data extraction from patient paper records. Manual capturing can be timely, costly and prone to more errors. A readily available electronic database can help in making this analysis more routine.

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