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Spatial analysis of tuberculosis in an Urban West African setting: is there evidence of clustering?

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Summary

OBJECTIVES To describe the pattern of tuberculosis (TB) occurrence in Greater Banjul, The Gambia with Geographical Information Systems (GIS) and Spatial Scan Statistics (SaTScan) and to determine whether there is significant TB case clustering.

METHODS In Greater Banjul, where 80% of all Gambian TB cases arise, all patients with TB registered at chest clinics between March 2007 and February 2008 were asked to participate. Demographic, clinical characteristics and GPS co-ordinates for the residence of each consenting TB case were recorded. A spatial scan statistic was used to identify purely spatial and space–time clusters of tuberculosis among permanent residents.

RESULTS Of 1145 recruited patients with TB, 84% were permanent residents with 88% living in 37 settlements that had complete maps available down to settlement level. Significant high- and low-rate spatial and space–time clusters were identified in two districts. The most likely cluster of high rate from both the purely spatial analysis and the retrospective space–time analysis were from the same geographical area. A significant secondary cluster was also identified in one of the densely populated areas of the study region.

CONCLUSIONS There is evidence of significant clustering of TB cases in Greater Banjul, The Gambia. Systematic use of cluster detection techniques for regular TB surveillance in The Gambia may aid effective deployment of resources. However, passive case detection dictates that community-based active case detection and risk factor surveys would help confirm the presence of true clusters and their causes.

keywords tuberculosis, clustering, spatial analysis, Geographic Information Systems, The Gambia

Introduction

An estimated two billion people are infected with *Mycobacterium tuberculosis* (CDC 2006) and approximately two million die from tuberculosis (TB) disease annually (Maher & Raviglione 2005). TB kills more people in the African continent than anywhere else, claiming more than 1500 lives a day (WHO 2005). While the human immunodeficiency virus (HIV) has contributed to the resurgence of TB in Africa (Espinal *et al.* 2001), the disease is far from under control in countries where HIV is relatively uncommon, such as The Gambia (Schim Van Der Loeff *et al.* 2003), where the TB case notification rate for all cases rose from 82/100 000 in 1994 to 119/100 000 in 2007 (KNCV 2008). The annual burden of all forms of TB in The Gambia is estimated to be 4415 (TB incidence of 257 per 100 000 population), including 1893 (113 per 100 000 population) smear positive TB cases (WHO 2009). The disease mostly affects the productive age groups (15–45 years) with a male to female ratio of 2:1 and the case notification rate is 69%.

Despite the increase in the geographical coverage of WHO's Directly Observed Treatment Short course (DOTs)-based strategy, case detection globally for all forms of TB was estimated at 61% in 2008, which is still less than the 70% target (WHO 2009). New approaches, such as mapping and spatial analysis, may be of value in contributing to basic elements of TB control. Public health professionals are now using such tools for visualisation and exploration of disease patterns (Morrison *et al.* 1998;

Frank *et al.* 2002; Munch *et al.* 2003; Tiwari *et al.* 2006) to guide disease control strategies. Several studies have shown these tools to be useful in the detection of clusters of a variety of different diseases in a range of settings (Hjalmars *et al.* 1996; Walsh & Fenster 1997; Kistemann *et al.* 2002; Kulldorff *et al.* 2005; Tiwari *et al.* 2006). The detection of clusters may be useful in the regular surveillance of TB while it may assist in identifying factors behind the spread of the disease. These approaches could further enhance the development of suitable policies and allocation of resources for TB control. In this study, we used GIS and Spatial Scan Statistics to describe the spatial distribution of TB and to identify settlements in Greater Banjul with significant TB clustering.

Methods

Study area and population

This prospective study was conducted in the Greater Banjul Area (GBA) of The Gambia, a mainly urban area comprising settlements with a total approximate population of 600 000 people. This study area is in the western most populated part of the country and accounts for almost 80% of TB cases. The GBA is served by six government TB diagnostic centres and eight treatment centres. Patients with all forms of TB normally residing in GBA were eligible for inclusion in this study. Informed consent was obtained from all study participants, and the study was approved by the joint MRC – Gambia Government Ethics committee.

Data collection

Data were collected on all consenting TB cases registered at the TB diagnostic centres between March 1, 2007 and February 29, 2008. A TB case was included if the TB control programme had commenced the patient on a full course of anti-TB treatment and was identified as smear-positive pulmonary TB, smear-negative pulmonary TB or extrapulmonary TB. At recruitment, all study participants answered a structured questionnaire administered in their own language. Data obtained comprised demographic data (age, sex, ethnicity, occupation, place of residence), clinical information (type of TB, date of diagnosis, date of registration) and past history of TB. The geographical location of diagnostic and treatment facilities and the residential addresses of all study participants in the study area were collected using handheld Global Positioning System (GPS) receivers – Garmin GPS 12 Channel receiver (Garmin Corporation 1998). All study participants were monitored regularly by a team of field workers and their treatment outcomes were categorised according to standard WHO recommended definitions (WHO 2003): defaulted, completed treatment, cured, failed treatment, died and transferred out. The residential status of each patient with TB was also determined and they were categorised as permanent or temporary residents: a permanent resident at a given address was defined as a case normally resident there and not likely to move out on completion of treatment.

Data management and spatial mapping

All data were electronically transferred and double entered into an Access database and checked for errors. Information on the population of the settlements in the GBA by broad age groups and gender was obtained from the 1993 and 2003 census. A settlement in this context refers to aggregations of between 4000 and 68 000 thousand people officially recognised by the government. Data on TB distribution in the study area was aggregated to the level of these settlements as with the census data for spatial analysis. Population growth rates for each settlement were estimated for ≤14 and ≥15-year-old male and female populations. The 2003 gender-and-age-specific population sizes were then extrapolated to mid-2008 for each settlement, assuming the post-2003 rate was the same as that observed between the two latest census years. Geographical analysis was performed using Geographical Information Systems (GIS) techniques. ArcGIS 9.2 version (ESRI, Redlands, CA) was used for mapping all cases and health facilities in the study area. The geographical co-ordinates were obtained using the latitude and longitude of the centre of each settlement (centroid). The output maps were produced using a projected co-ordinate system, UTM Zone 28 North.

Statistical analysis

Spatial scan statistical analyses were conducted using SaTScan™ to test for the presence of statistically significant spatial clusters of TB. The analysis was performed using area-based data aggregated to settlement level. For the purely spatial analysis, case, population and co-ordinate data were used as inputs to SaTScan. A Poisson-based model was used, where the number of events in an area is Poisson distributed according to a known underlying population at risk (Kulldorff *et al.* 2005). The spatial scan statistics works by imposing a circular window on the map and lets the centre of the circle move over the area. At different positions, the window contains different sets of neighbouring areas. The radius of the circular window varies continuously in size from zero up to a maximum

such that the window does not include more than 50% of the total population at risk. For this analysis, the maximum spatial cluster size was first set to include up to 50% of the population at risk, which included all cases of TB diagnosed and permanently resident in the study area between 1 March 2007 and 29 February 2008. The spatial cluster size was then set at 25% to test for high excesses and to discover the possibility of smaller clusters in the study area. The test of significance of the identified clusters was based on comparing the likelihood ratio test statistics against a null distribution obtained from Monte Carlo simulation (Kulldorff *et al.* 1997).

Results

Over the 1 year of the study, 1430 patients were diagnosed with TB and started treatment in the clinics involved in the study, 676 at Serekunda clinic, 323 at Brikama, 261 at Fajikunda clinic, 71 at Banjul Poly clinic, 53 at Jammeh Foundation and the remaining 46 from Banjulnding, Gunjur and Tujereng clinics respectively. Of these, 1152 (81%) agreed to participate in the study and 1145 (99%) had complete information including mapping of their place of residence. The proportion of patients that consented did not vary significantly across the study area. The characteristics of these patients are shown in Table 1. The majority were men and had smear-positive pulmonary disease; less than a third were over 40 years of age. Of the total, 185 (16.2%) were non-permanent residents, leaving 960 patients as permanent residents in the six districts in

Table 1 Characteristics of TB cases by residence

Characteristic	TB cases *n* (%)	
	Permanent residents	Non-permanent residents
Sex		
Male	646 (67.3)	102 (55.1)
Female	314 (32.7)	83 (44.9)
Age, years		
Median (range, years)	31	33
0–14	95 (9.9)	11 (5.9)
15–25	229 (23.8)	37 (20.0)
26–40	351 (36.6)	71 (38.4)
>40	285 (29.7)	66 (35.7)
Type of TB		
Smear Positive	623 (64.9)	108 (58.4)
Smear Negative	288 (30.0)	70 (37.8)
Extra-pulmonary	49 (5.1)	7 (3.8)
Ethnicity		
Mandinka	372 (38.8)	66 (35.7)
Wolof	152 (15.8)	23 (12.4)
Fula	130 (13.5)	38 (20.5)
Jola	163 (17.0)	33 (17.8)
Other	143 (14.9)	25 (13.5)
Total	960 (83.8)	185 (16.2)

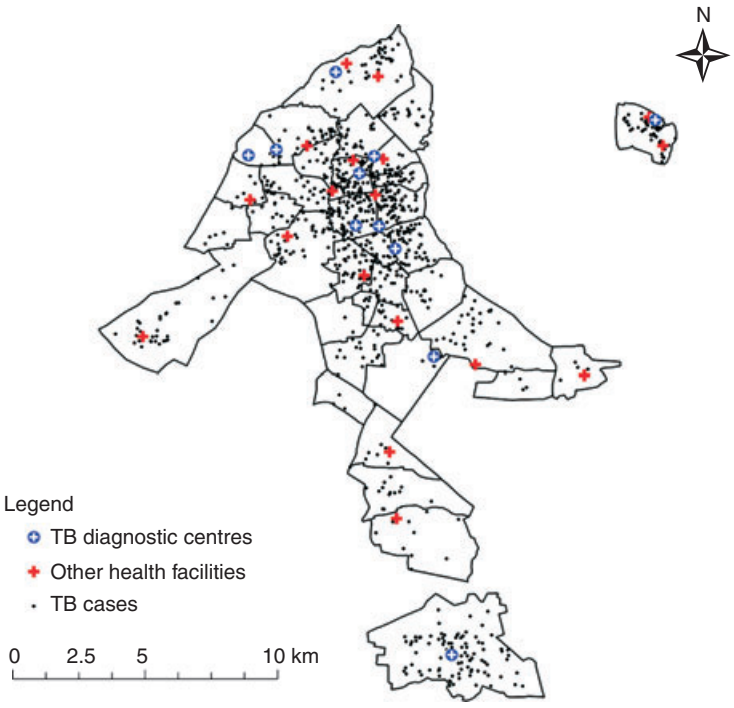

Figure 1 Spatial distribution of TB cases in Greater Banjul, The Gambia in relation to the distribution of TB diagnostic centres and other health facilities.

Table 2 Incidence rate of TB disease by settlement in the Greater Banjul area 2007/8

Settlement	Geocode	Area (sq km)	Cases (*n*)	Population (*n*)	Cases/100 000 (95% CI)
Abuko	20001	4.3	13	12 908	101 (54–172)
Bakau	20003	9.1	41	35 142	117 (84–158)
Bakoteh	20004	3.0	23	27 730	83 (53–124)
Banjul	11001	3.5	49	31 915	154 (114–203)
Banjulnding	30001	5.7	8	5681	141 (61–277)
Bijilo	30003	3.2	6	4149	145 (53–314)
Brikama	32007	16.6	75	67 579	111 (87–139)
Brufut	30004	13.7	34	14 234	239 (165–334)
Bundung	20005	2.7	62	58 099	107 (82–137)
Busumbala	30005	5.5	9	10 877	83 (38–157)
Dippa Kunda	20006	0.9	26	14 910	174 (114–254)
Ebo Town	20007	1.3	27	43 224	62 (41–91)
Fajikunda	20008	3.3	43	32 874	131 (95–176)
Farato	31018	8.0	8	9921	81 (35–159)
Kerewan	30010	2.8	5	5047	99 (32–231)
Kerr Serigne Njaga	30011	2.4	8	14 947	54 (23–105)
Kololi	20009	1.9	5	6136	81 (26–190)
Kotu	20010	4.3	28	18 889	148 (99–214)
Kunkujang Keita	30013	1.5	11	18 305	60 (30–108)
Lamin	30016	9.0	27	23 700	114 (75–166)
Latrikunda German	20011	2.9	22	24 642	89 (56–135)
Latrikunda sabiji	20012	1.2	24	17 192	140 (89–208)
Mandinary	30020	3.0	4	5556	72 (20–184)
Manjai Kunda	20013	1.9	16	24 986	64 (37–104)
Nema Kunkku	30022	2.7	37	31 046	119 (84–164)
New Jeshwang	20014	1.7	16	15 169	105 (60–171)
New Yundum	30023	3.8	4	7163	56 (15–143)
Old Jeshwang	20015	3.6	17	16 742	102 (59–163)
Old Yundum	30024	2.3	4	4784	84 (23–214)
Serekunda	20016	1.2	35	19 497	180 (125–250)
Sinchu Alagie	30025	3.7	15	10 744	140 (78–230)
Sinchu Baliya	30026	0.7	7	6571	107 (43–219)
Sinchu Sorry	30027	3.0	2	4186	48 (6–172)
Sukuta	30029	7.5	44	27 920	158 (115–212)
Sukuta Sanchaba	30030	2.3	15	9463	159 (89–261)
Tallinding	20017	2.6	58	44 994	129 (98–167)
Wellingara	30034	1.9	16	26 830	60 (34–97)
Overall		148.7	844	753 752	112 (104–120)

the study area. Of these, 844 (88%) were living in 37 settlements of which a complete map was created and made available to settlement level for analysis.

Figure 1 shows a map of the 844 patients with TB who were permanent residents, in relation to the diagnostic and treatment facilities. While this figure does not take into account the different sizes of the background population, it appears that cases tended to concentrate around diagnostic or treatment facilities. The overall incidence rate of disease across the study population was 112/100 000 for the year of the study. Table 2 shows the variation in incidence rate across the settlements of Greater Banjul with 95% confidence intervals: it varied five-fold: from 48/100 000 to 239/100 000. This is also highlighted in the choropleth map in Figure 2, a thematic map in which areas are distinctly coloured or shaded to represent TB cases per 100 000 people.

Purely spatial analysis

Using the maximum spatial cluster size of ≤50% of the total population, the purely spatial cluster analysis of high rates identified the most likely significant cluster of TB in Brufut, Sukuta, Sukuta Sanchaba and Bijilo areas (Table 3). Furthermore, a statistically significant secondary cluster was detected in the settlements of Dippa Kunda and Serekunda.

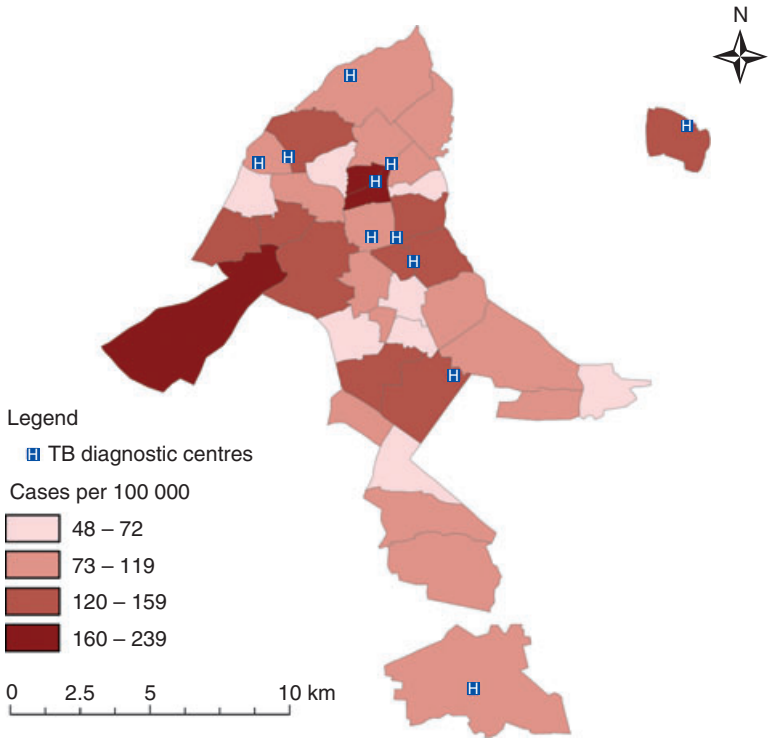

Figure 2 Choropleth map showing incidence of TB cases per 100 000 People in Greater Banjul.

Table 3 Significant high-rate tuberculosis clusters and significant low rates of TB in Greater Banjul, The Gambia detected by retrospective purely spatial analysis

Cluster ID	No. cases	Expected cases	Relative risk	Log likelihood ratio	*P*-value
High-rate cluster					
Most likely cluster					
Brufut, Bijilo, Sukuta & Sukuta Sanchaba	99	62.44	6.33	9.937352	0.001
Secondary cluster					
Dippa Kunda and Serekunda	61	38.53	3.20	5.874088	0.038
Low rate					
Most likely cluster					
Wellingara, Sinchu Baliya, Sinchu Sorry, Kunkujang	36	62.58	2.43	7.123509	0.025

In order to discover the possibility of smaller clusters in the study area, the same analysis was performed with a spatial cluster size of ≤25% of the total population. This analysis identified the most likely significant cluster and secondary cluster in the same locations. Furthermore, using a cluster size of ≤50% to scan for areas with low rates of TB showed the presence of one statistically significant low rate of TB in the settlements of Wellingara, Sinchu Baliya, Sinchu Sorry and Kunkujang. The low–rate clusters and high-rate clusters are shown in Table 3 and highlighted in Figure 3 in relation to the TB diagnostic and treatment centres and other health facilities in the study area. A separate analysis including only smear-positive TB cases showed the same clustering pattern but lost statistical significance with the decrease in numbers (data not shown).

Space–time analysis

The areas of high occurrence of TB from the purely spatial analysis were also statistically significant in the space–time

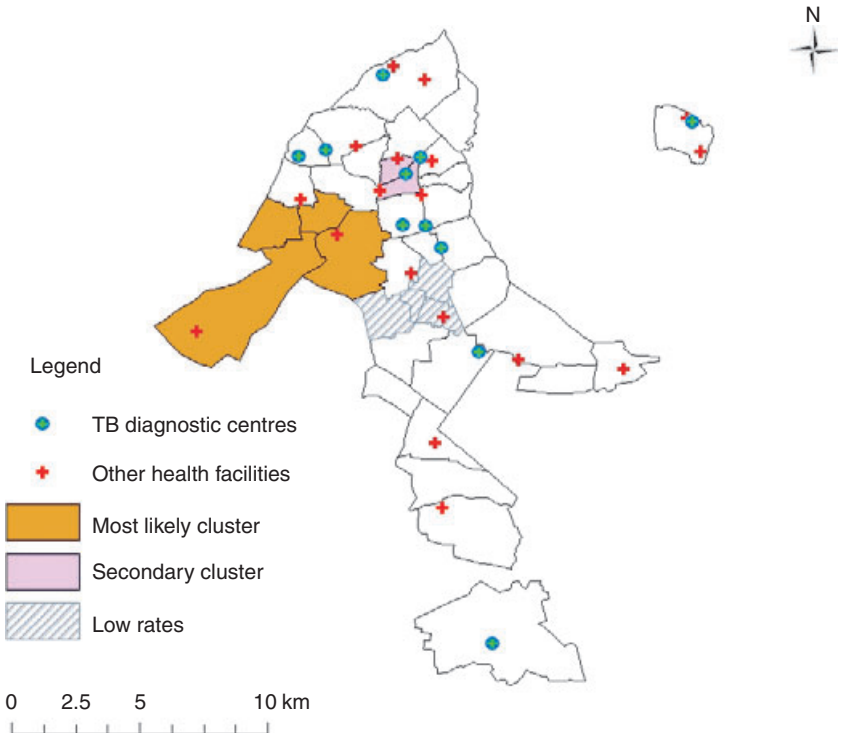

Figure 3 Spatial distribution of high-rate tuberculosis clusters with significant low rates in Greater Banjul, The Gambia. Presented are the most likely statistically significant cluster and secondary cluster detected by the purely spatial analysis with a maximum cluster size of ≤50% of the total population.

analysis. Using a spatial window that could include up to 50% of the population at risk and a maximum temporal window of 50% without including purely spatial clusters, the most likely statistically significant cluster for high rates of TB was again found to exist in Brufut, Sukuta and Bijilo between April and September 2007 (Table 4). The results from this analysis are presented and highlighted in Figure 4.

Discussion

In this study, we have identified settlements in Greater Banjul with significant TB clusters of high rates of TB, and one area with significantly low rates, from the purely spatial and retrospective space–time analysis. Purely spatial analysis showed hotspots of the disease in four settlements, while the retrospective space–time analysis found three of the four settlements had significant TB clusters. For the same analysis, one statistically significant secondary cluster was detected. The results showed that the most likely cluster from both the purely spatial analysis and the retrospective space–time analysis are from the same geographical area. The time frame for the space–time cluster was between April and September 2007. Furthermore, the secondary cluster for the purely spatial analysis was detected in one of the most densely populated areas of the study region, an area with a concentration of government and private TB diagnostic centres. This study has demonstrated the usefulness of spatial analysis in describing the geographical distribution of TB in the Greater Banjul area of The Gambia.

Table 4 Significant high-rate spatial tuberculosis clusters in Greater Banjul, The Gambia, detected by retrospective space–time analysis between April and September 2007

Cluster ID	No. cases	Expected cases	Relative risk	Log likelihood ratio	*P*-value
Most likely cluster					
Brufut, Bijilo, Sukuta	54	23.90	4.91	14.475978	0.002

While several studies have used GIS and spatial analysis to describe the pattern of various infectious diseases in Africa (Rogers & Williams 1993; Beyers *et al.* 1996; Schellenberg *et al.* 1998; Porter 1999; Wilkinson & Tanser 1999; Tanser & Le Sueur 2002; Munch *et al.* 2003; Gaudart *et al.* 2005, 2006; Polack *et al.* 2005; Sasaki *et al.* 2008; Uthman 2008; Randremanana *et al.* 2009), only a handful have focused on TB. In South Africa, GIS was used to show major variation in the

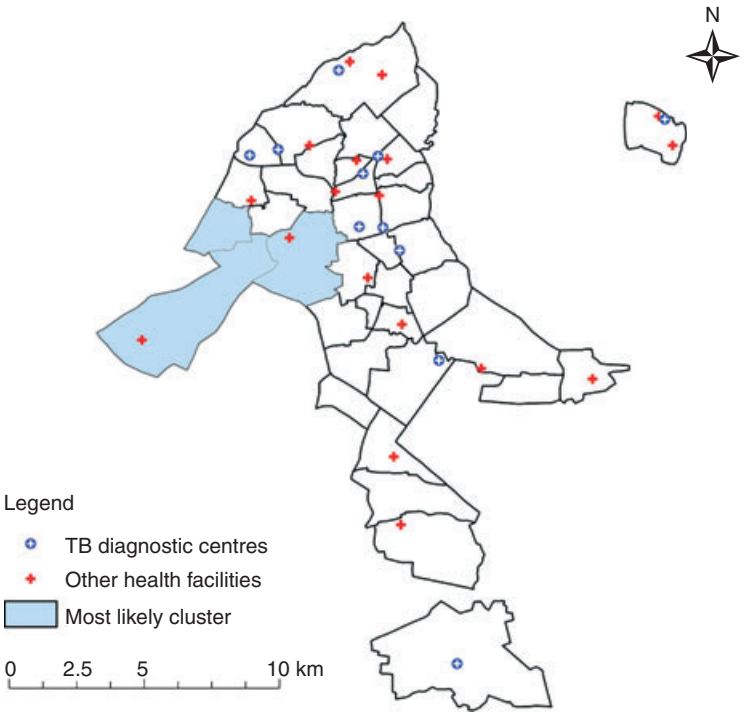

Figure 4 Spatio-temporal and spatial distribution of high-rate tuberculosis clusters in Greater Banjul, the Gambia. This map shows the results of the most likely statistically significant cluster detected by retrospective space–time analysis using a maximum cluster size of 50% of the total population at risk and a maximum temporal window of 50% without including purely spatial clusters.

incidence of TB across an urban community in Cape town (Van Rie *et al.* 1999). In another study, GIS was used to map over 1000 cases of TB in the same city (Beyers *et al.* 1996), and the investigators found that significant clustering of TB was associated with socio-economic factors. Spatial clustering of pulmonary TB was also associated with socio-economic and patient care factors in Madagascar (Randremanana *et al.* 2009). In other South African studies, GIS and spatial analysis were used to study TB transmission patterns in a high-incidence area (Munch *et al.* 2003), while molecular and spatial tools were combined to understand the transmission of specific *M. tuberculosis* strains (Richardson *et al.* 2002). GIS/GPS was also used to document improved access to TB treatment through a community-based programme in rural areas (Tanser & Wilkinson 1999). A multi-country comparison of geographical and temporal distribution of TB (Uthman 2008) suggested that 25 countries in the African continent were at increased risk of TB and ten countries could be grouped as 'hot spots'.

Geographical Information Systems/spatial analysis has also been used for TB research outside Africa. In India, purely spatial and retrospective space–time analysis were used to find significant hotspots of TB in three areas of the Almora district (Tiwari *et al.* 2006). Another study in Mexico examined the geographical distribution of TB cases before and after the introduction of DOTs (Jacobson *et al.* 2005). There was a reduction of incidence of multi-drug resistance, but foci were identified in poorer and more remote areas. With respect to spatiotemporal clustering (Nunes 2007), three high incidence rate space–time clusters were identified in Portugal between 2000 and 2004 and a purely temporal cluster covering the whole country during 2002. In Japan, space–time scan statistics identified TB clusters in Fukuoka (Onozuka & Hagihara 2007). A study in Hong Kong on 2332 TB cases in combination with molecular tools found that low educational attainment, old age and poverty were significant determinants of the rate of TB in different geographical areas (Chan-Yeung *et al.* 2005). GIS and spatial analysis was also used in Beijing to determine the role of migration in the transmission of tuberculosis (Jia *et al.* 2008). TB cases were distributed randomly among 15 078 permanent residents but significant clustering was found in the 7948 migrant population. A significant association between tuberculosis incidence and immigration was also found in Germany (Kistemann *et al.* 2002).

While our study has demonstrated the usefulness of GIS and spatial analysis in our setting, it has some limitations. Firstly, data for cluster analysis was aggregated to the settlement level. Although this is useful in meeting ethical

data protection and anonymity requirements and helping to construct occurrence rates based on known populations within the areal unit, it is subjected to the modifiable areal unit problem (MAUP). For example, a significant cluster in the study area surrounded by sparse events may be divided and diluted to appear insignificant. Secondly, we did not assess possible risk factors that could be associated with clustering, although our previous studies have shown that there is an increased risk of TB with household crowding and history of exposure to a known TB case (Lienhardt *et al.* 2003; Hill *et al.* 2006). Future studies could focus on the effects of various socio-economic and environmental risk factors for the high occurrence of the disease in the clustered areas and analyses of case isolates will enable anti-microbial and strain-specific factors to be considered. Thirdly, data collection over several years would identify spatial and temporal changes in the pattern of TB. This is currently part of a proposal recently approved in principle for funding by the Global Fund to fight AIDS, TB and Malaria. Finally, extrapolation of census data from 2003 to provide up to date denominator population numbers could be affected by uneven population growth across the settlements.

Disease cluster investigation in space and/or time may have a role in informing public health policy. Systematic use of cluster detection techniques for regular surveillance of TB incidence in the Gambia may help the TB program in disease control activities. Of course, in the presence of a policy of passive case detection there are two key polarised possibilities for the presence of clustering- either there is indeed a truly high rate of disease in a clustered area, or there are falsely low measured rates in other areas. The latter possibility may arise where there is a problem with health seeking behaviour or access to health care in those with TB. This first study has highlighted the likelihood of significant geographical variation in TB in the study area. This will form the background to a series of studies that will address whether this holds true in the presence of active case detection and explore whether particular host, organism and environmental differences may be explanatory. In this respect, identifying areas of significantly high rates of disease as well as those with significantly low rates is important. This new information will help guide the provision and optimisation of TB control strategies in The Gambia.

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