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Heterogeneity in the Spatial Distribution of Bacterial STIs

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ABSTRACT

Objectives: Detailed knowledge of the spatial distribution of disease is required to inform service delivery and plan effective interventions. In order to further elucidate the spatial epidemiology of three common sexually transmitted infections (STIs), our aim was to detect and describe any significant spatiotemporal clustering of gonorrhea, chlamydia or syphilis cases in New South Wales.

Methods: Eleven years of notified STI case data were analyzed. Calculation of age- and sex-stratified incidence rates was followed by spatiotemporal cluster analyses to investigate differences in the epidemiology of gonorrhea, chlamydia and syphilis.

Results: More than one-third of all gonorrhea, chlamydia and syphilis cases in New South Wales were detected within cluster areas. Gonorrhea cases were the most highly clustered, followed by syphilis, then chlamydia. Clusters were highly significant, and relative risk estimates ranged from 1.6 to 22.9.

Conclusion: Our findings establish the high degree of geographic heterogeneity in STI incidence in New South Wales and indicate that postal area of residence is an important predictor of STI incidence. Geographical surveillance could be incorporated into routine STI surveillance to identify populations in need of intervention. The evidence presented in this report indicates a need to implement geography-specific and phase-appropriate STI prevention and control strategies.

INTRODUCTION

Despite readily available treatments to cure gonorrhea, chlamydia and syphilis, these bacterial sexually transmitted infections (STIs) remain prevalent globally (1). Bacterial STIs are a significant cause of morbidity and mortality, with physical and psychological consequences for infected persons (1, 2). Over the past decade in Australia, notification of chlamydia has increased fourfold, notification of gonorrhea has doubled, and notification of infectious syphilis has shown major increases in some states, including New South Wales (3). Substantially higher STI rates have been documented from different subpopulations in the country; for example, men who have sex with men and Indigenous Australians living in remote settings (3).

Investigation of the spatial distribution of STI cases is a relatively new research focus (4-8) that has contributed to the knowledge of the epidemiology of these infections, and findings have implications for control (9, 10). Traditional STI control strategies focus on sociocultural and behavioural risk factors for exposure or infection (11). Recently observed increases in STI rates in Australia (12) may indicate shortcomings in this approach. Furthermore, it has been proposed that STI prevention and control strategies should correspond to the phase of the epidemic (9, 10). Wasserheit and Aral (13) illustrated the progression of disease incidence over time in terms of epidemic phases: the growth phase, the hyperendemic phase, the decline phase, and the endemic phase. Epidemic phase, in conjunction with the density of the sexual network required to facilitate transmission, is thought to be associated with the differing geographical distributions of STIs (14).

Australia's National Notifiable Diseases Surveillance System (15) contains postcode data, yet, these data are not regularly used to report geographic trends in STI diagnosis beyond the level of state or territory. The aim of this study is to detect and describe any spatiotemporal case clustering of gonorrhea, chlamydia or syphilis in New South Wales and to relate cluster results to trends in incidence over the 11-year study period. Here, the use of a spatial scan statistic allowed for the detection of areas experiencing disproportionately high STI incidence not geographically restricted by conventional classification boundaries.

METHODS

Rate calculations and spatio-temporal cluster detection analyses were performed using nationally notified case reports from New South Wales (NSW) with disease onset between January 1, 1993 and December 31, 2003 for gonorrhea and syphilis, and disease onset between January 1, 1998 and December 31, 2003 for chlamydia, as chlamydia has only been notifiable in NSW since 1998. According to the Public Health Act 1991 gonorrhea, and chlamydia are notifiable to local public health units by laboratories, and syphilis is notifiable by clinicians, hospitals and laboratories. Public health unit staff record case details on the NSW Notifiable Diseases Database, which are then reported to the National Notifiable Diseases Surveillance System (NNDSS). Data collected for bacterial STI cases by the NNDSS are limited, unfortunately, and do not include detailed epidemiological information such as reason for testing or route of infection. While indigenous status is a field reported to the NNDSS, details of Aboriginality are not notified by laboratories. The overall low proportion of notifications with coded information for indigenous status (<19%) limited the use of this variable for analysis. The data indicate that cases were notified from all regions of the state during the study period. State midyear population estimates (16) were used to calculate age- and sex-specific incidence rates for five-year age groups ranging in age from 15 to 34 years. Population data by postal area of residence were used for cluster detection analyses (17).

Geocoding

Cases were disaggregated geographically by the 593 New South Wales postal areas described by the Australian Bureau of Statistics, which approximate and provide estimated population data for postcodes based on the 2001 census (14). While most reported postcodes (99%) corresponded to defined postal areas, some required reallocation for inclusion in the analysis including post office box postcodes and those for which population data or spatial data were lacking. For post office box postcodes located in suburbs that also had an assigned 'delivery area' postcode, as listed by a postcode locality database (http://www1.auspost.com.au), the 'delivery area' was reassigned. For the remaining unmatched postcodes, a mapping application (http://www.travelmate.com.au/MapMaker/mapmaker.asp) was consulted, and cases were reallocated to the geographically nearest postal area. For a small proportion of cases (0.2%), postcode data did not correspond to an Australian Post postcode and the postal area assigned was that which was closest in numerical value on the assumption of error in recording. Repeat analyses excluding reassigned cases did not alter the significance or location of clusters detected.

Cluster Analysis

Space-time analyses were performed using SatScan (18) to detect statistically significant spatial and spatio-temporal case clusters. The software was used to test areas of varying size for higher numbers of observed cases than expected using a Poisson probability model. Postal area centroid data were entered as latitude/longitude coordinates. Space-time cluster analyses specified a maximum circular spatial cluster size of 50 per cent of the population, and a maximum temporal period of 90 per cent of the study period. Purely spatial clusters were included for detection. Purely temporal analysis of the data was not conducted. The statistical significance of a cluster was determined by a likelihood ratio test statistic and corresponding p-value obtained from 999 Monte Carlo replications. Relative risk estimates calculated by SatScan are based on the adjusted incidence rate within the cluster window compared to that outside of the cluster window. SatScan adjusts for any underlying spatial heterogeneity in the background population. Analyses were conducted with adjustment for age, using five-year age groups as a covariate. Spatial data for significant clusters ($p<0.05$) were imported to MapInfo for mapping. Ethic approval for this study was obtained from the Curtin University Human Research Ethics Committee.

RESULTS

Of the 41,772 cases studied, the majority were diagnoses of chlamydia, followed by gonorrhea, then syphilis (Table 1). Gonorrhea cases were the most highly concentrated within the population, followed by syphilis, and finally by chlamydia (Table 1). Gonorrhea rates in New South Wales display an increasing trend in males aged 20-24, 25-29, and 30-34 years from 1995 to 1999 (Figure 1). After 1999, notification rates in these groups plateau and remain higher than rates in other strata. The data show an increasing trend in chlamydia notification rates in all strata over the study period. From 1997 to 2003, syphilis rates in most strata remained relatively stable while those in men aged 25-29 years and 30-34 years displayed increasing trends.

Table 1. Notified cases and case clusters of gonorrhea, chlamydia, and syphilis in New South Wales between 1993 and 2003.

	Total Cases	**% Male**	**% Cases within Cluster areas**	**% Population within Cluster areas**
Chlamydia	24352	44.2	59.5	49.7
Gonorrhea	9625	88.1	44.3	3.6
Syphilis	7364	60.3	34.8	22.7
Total	41341	64.2	46.2	25.3

Table 2. Description of spatial clusters of notified gonorrhea, chlaymdia, and syphilis cases detected between 1993 and 2003 in New South Wales.

STI	**Cluster**	**Relative Risk**	**p-value**	**Cases**	**Population within Cluster area**	**Median age**	**% Male**	**Period**
Chlamydia	1	5.19	0.001	14481	3116297	25	47.0	Feb 1999 – Dec 2003
Gonorrhea	1	15.06	0.001	4115	207417	32	94.9	Jan 1993 – Dec 2003
	2	5.67	0.001	145	19729	20	62.1	July 1993 – April 2003
	3	22.93	0.001	35	1244	24	54.3	Aug 1994 – June 2003
Syphilis	1	5.73	0.001	1778	280177	40	75.8	Jan 1993 – Dec 2003
	2	14.76	0.001	274	43730	22	30.3	Jan 1993 – March 1997
	3	8.17	0.001	70	22293	28	50.0	Jan 1993 – Nov 1996
	4	4.08	0.001	100	45328	22	26.0	Aug 1993 – Dec 1998
	5	1.61	0.001	320	1019729	46	63.8	Jan 2002 – Nov 2003
	6	5.61	0.002	22	13470	23	50.0	Jan 1993 – Nov 1995

The primary gonorrhea cluster in the Sydney area had an estimated relative risk over 15, cases were largely male (94.9%), and the median age of the cases was 32 years (Table 2). The two secondary gonorrhea clusters displayed lower proportions of male cases and had lower median ages than the primary cluster. A significant clustering of chlamydia cases comprised a grouping of 270 postal areas along the eastern coast of the state from the

Sydney area to the state's northern border. In contrast to the majority of the syphilis clusters detected, the median ages calculated for the syphilis Clusters 1 and 5 were 40 years or older, and the cases comprising these two clusters were predominantly male (Table 2).

Postal areas occupied by 2.6% of the population were common to clusters of all three STIs in the Sydney area (Figure 1). Gonorrhea and syphilis clusters shared common postal areas outside the Sydney area, in the northern region of the state, occupied by 0.2% of the population. Syphilis and chlamydia clusters shared common postal areas outside of the Sydney area, in the northeast region of the state, occupied by 0.6% of the population.

DISCUSSION

Geography is becoming recognized as an important factor contributing to STI risk, and spatial scan statistics have been used to investigate STI case clusters in North America (5, 19) and now Australia. Our findings establish the high degree of geographic heterogeneity in STI incidence in New South Wales and indicate that postal area of residence is an important predictor of STI incidence. Bacterial STIs differed greatly in the concentration of cases. We found that 44% of gonorrhea cases were concentrated in areas occupied by 3.6% of the population; 35% of syphilis cases were concentrated in areas occupied by 23% of the population; and 60% of chlamydia cases were concentrated in areas occupied by 50% of the population. This type of geographical surveillance could be easily incorporated into routine STI surveillance to identify populations in need of intervention.

Our findings confirm that trends observed in state gonorrhea and syphilis data can be largely attributed to disproportionately high incidence of infection, or outbreaks, in relatively small geographical areas. The increasing incidence of gonorrhea observed in men aged 20-34 years is a reflection of the epidemic largely affecting men who have sex with men (20, 21). This trend can be attributed, at least in part, to the 95% male gonorrhea case cluster in the Sydney area. Similarly, a 76% male syphilis case cluster in the Sydney area is consistent with evidence of a syphilis epidemic in Sydney largely among homosexually active men who are HIV-positive (22). The agreement between our findings and current epidemiological analyses provides support for the validity of cluster detection analyses of routinely collected STI surveillance data.

The geographic distribution and concentration of cases provide indications of the phase of an epidemic. Gonorrhea cases were the most highly concentrated, followed by syphilis. Chlamydia case distribution was diffuse in comparison. Reflecting the statewide findings, clustering of STIs in the metropolitan Sydney area also displayed the same hierarchy of case concentration. Our findings are in agreement with North American studies which have shown much greater geographical clustering of gonorrhea and syphilis cases compared to chlamydia (4, 6, 23). According to epidemic phase classification (13), gonorrhea and syphilis in New South Wales could be classified as Phase IV epidemics, when endemicity persists, and chlamydia could be classified within epidemic phase II′, a hyperendemic phase in which control efforts have been introduced. In New South Wales, a population-based intervention may be warranted for chlamydia control whereas targeted interventions may be required to effectively control the concentrated phase IV gonorrhea and syphilis epidemics (21), during which core groups are thought to carry most of the burden of infection. Clusters of long duration indicate transmission persists in these areas despite existing control strategies.

Factors potentially contributing to the increasing trend in chlamydia reporting in Australia are currently the subject of much discussion (3, 24, 25). With the proportion of infections that are asymptomatic estimated at up to 80% (26), it is clear that testing practices will greatly influence chlamydia case detection. Test positivity rates have risen with the increasing use of nucleic acid amplification techniques over the study period (24). A bias introduced by higher chlamydia testing rates in the cluster area may have affected the cluster analysis findings, as the single cluster detected comprises the most populous region of the state. Unfortunately, Australia lacks national data on the number of chlamydia tests performed, reasons for testing, behavioural risk factors, and the type of facility where the diagnosis was made (27). Further evaluation of chlamydia testing and reporting practices is required to distinguish the effects of differential testing practices on the detection of case clustering.

Limitations of the study include the availability of accurate postcode and population data. While reported postcodes should correspond to the place of residence of a case, some postcodes represented non-residential locations and required reallocation. All population data were the best available approximations based on available census data (17). Discrepancies between postcode and postal area data are considered to have had little affect on the results given the high statistical significance of the clusters detected. Recent changes to the units used to spatially reference population data by the Australian Bureau of Statistics will facilitate more accurate spatial analyses in the future. Other spatial analysis methods, such as Bayesian disease mapping, may also be of value in the routine analysis of notifiable STI data; however, SatScan readily identifies space-time clusters and is highly sensitive (28).

Contact tracing is mandatory in New South Wales for all diagnosed gonorrhea, chlamydia, and syphilis cases. While case-finding strategies will contribute to clustering, some clusters may go undetected with such a control strategy and this analysis has revealed areas that have experienced significantly elevated rates of STIs over an 11-year period. This information could be valuable for resource allocation. Reporting bias could also affect the findings of cluster detection analyses. Cluster locations may indicate a higher density of practitioners who are more likely to report notifiable STIs. If practitioners who report the diagnosis of one type of bacterial STI are also more likely to report the diagnosis of another, similar spatial cluster distributions would be expected for each STI. Our findings indicate that this was not the case, suggesting that detected clusters represent true case clustering.

As the data analyzed represent only the 'notifiable fraction' of true cases (29), it is important to consider how the inclusion of unreported STI cases could affect the findings. Due to the considerable heterogeneity in STI incidence observed, at least for gonorrhea and syphilis, and probable heterogeneity in reporting practices, it is unlikely that the unreported cases are homogeneously distributed across New South Wales. It is more conceivable that unreported cases are concentrated, either within the clusters identified in this analysis or elsewhere. Testing practices are also unlikely to be uniform across the state and any screening programs targeting risk groups may lead to overrepresentation of these groups in surveillance data. For example, implementation of sensitive nucleic acid amplification tests for gonorrhea diagnosis is greater in remote areas of Australia (30). For the routine application of cluster detection analyses to enable the optimal identification and control of areas with increased incidence of infection, consistency in STI testing and notification practices is required.

The idea of geographically targeting STI control strategies is not novel (6, 8, 23, 31). The data presented here provide evidence of the great concentration of gonorrhea cases, and to a lesser extent syphilis cases, in Australia's most populous state through analysis of a large routinely collected population-based dataset. Traditional epidemiological studies of STIs often produce relative risk estimates for individual or group level factors below two (32). We found relative risk estimates in excess of 15 based on postal area of residence. While information on risk behaviours is not available from routinely collected notifiable disease datasets, geographic information is available and appears underutilized. Disease prevention and control strategies should be planned according to the known spatial epidemiology of each sexually transmitted infection.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

CONTRIBUTIONS

Study concept and design: E Schleihauf, RE Watkins, AJ Plant

Acquisition of data: RE Watkins, AJ Plant

Analysis and interpretation of data: E Schleihauf, RE Watkins

Drafting of the manuscript: E Schleihauf

Critical revision of the manuscript: RE Watkins

KEY MESSAGES

- There is a high degree of geographic heterogeneity in STI incidence in New South Wales, Australia.
- Postcode of residence is an important risk factor for bacterial STI.

- STI prevention and control strategies should be planned according to the known spatial epidemiology of each sexually transmitted infection.
- Geographical surveillance could be incorporated into routine STI surveillance to identify populations in need of intervention.

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Figure 1. Age-specific incidence and spatial clustering of bacterial STI cases in New South Wales (inset of Sydney area) from 1993 to 2003: chlamydia *A*, gonorrhea *B*, syphilis *C*. (Map boundaries represent postal areas of residence. Numbered clusters correspond to numbered clusters described in Table 2.)

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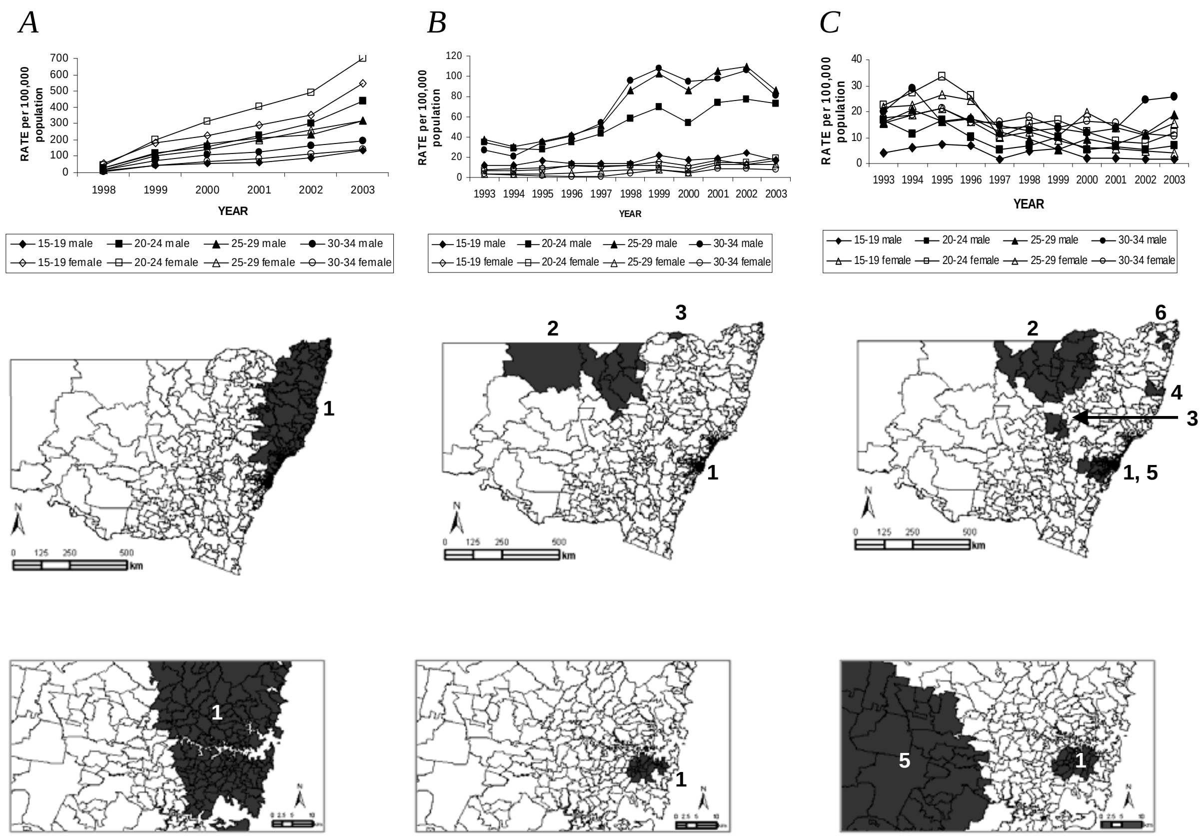
Figure 1. Age-specific incidence and spatial clustering of bacterial STI cases in New South Wales (inset of Sydney area) from 1993 to 2003: chlamydia *A*, gonorrhea *B*, syphilis *C*. (Map boundaries represent postal areas of residence. Numbered clusters correspond to numbered clusters described in Table 2.)



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