

A NEW APPLICATION OF SPATIOTEMPORAL ANALYSIS FOR DETECTING DEMOGRAPHIC VARIATIONS IN AIDS MORTALITY: AN EXAMPLE FROM FLORIDA

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The purpose of the present study was to characterize, geographically and temporally, the patterns of acquired immune deficiency syndrome (AIDS) death disparity in 67 Florida jurisdictions, and to determine if the detected trends varied according to age, race, and sex. The space-time scan statistic proposed by Kulldorff et al was used to examine the excess AIDS deaths that occurred between 1987 and 2004. Results were geographically referenced in maps using EpiInfo and EpiMap made available by the Centers for Disease Control. Miami-Dade and the nearby counties including Broward, Martin, and Palm Beach are the most likely clusters (observed/expected: 1505.16) with temporal dimension (also called cluster's age) persisting from 1996 to the present. Union county had the longest cluster for the cluster period 1987–1998, but not for 1999–2004. African-Americans contributed to more clusters compared with whites. Time trends indicated that AIDS mortality peaked in 1995 and then sharply dropped until 1998, when the decrease stopped. By accounting for the temporal dimension of disease clustering, the present study revealed the persistence of geographic clusters, which is not often provided by other geographic detection methods. These findings may be informative for medical resource allocation and better focus public health intervention strategies for AIDS care.

Key Words: acquired immunodeficiency syndrome, cluster, mortality, spatiotemporal analysis
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In the United States (US), the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) epidemic continues to increase, with more than 250,000 cases of AIDS already diagnosed and more than 35,000 new HIV infections reported yearly [1]. The disease affects certain geographic regions in the US disproportionately. For example,

Florida accounted for 11% of the total number of AIDS cases in the US in 2004, ranking third behind New York and California [2]. Furthermore, the literature suggests that HIV/AIDS disproportionately affects population subgroups according to demographic characteristics, such as age and racial groups (including minority communities) in the US [3–7]. However, there is relatively little research on the geographic and temporal variations among demographic subpopulations in the Eastern US, particularly the state of Florida.

Incidence of HIV/AIDS in Florida is generally reported by the Centers for Disease Control (CDC) [2]. Currently, however, information on AIDS mortality for Florida is poor, particularly from geographic



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and temporal viewpoints. An understanding of the geographic variation of the disease distribution may provide explanations regarding the possible contributors to disease morbidity and mortality. For this reason, knowledge of the geographic distribution of AIDS mortality can inform and improve public health practices.

Many methods for examining clusters (e.g. case assembling or hot spots) have been described in the literature. They can be broadly divided into “global clustering tests” and “cluster detection tests”. References in applications, experiences, and comparisons when using different geostatistical methods in the earlier studies have been provided [8–11]. The “cluster detection method” can provide estimates of the geographic location and extent of the clusters [8,9], and which is most appropriate to the purpose of the present study.

Epidemiology is concerned with the distribution of a disease by either the affected communities (such as by race or ethnicity), by geographic locations, or by time frame, which is the temporal dimension of the cluster (we subsequently refer to it as the cluster’s “age”). The time frame includes information concerning when the cluster starts and ends, how long the cluster exists, the extent of the excess risk, and whether the cluster persists into the present time. Space-time analysis has been used to identify periodic clusters of reported *Escherichia coli* cases in Canada [12], to prioritize shigellosis case investigations in urban Chicago [13], to detect excess cases of brain cancer across time periods in Los Alamos [14], and to conduct simulated syndromic surveillance of daily emergency department visits in New York City [15]. However, very few studies have applied this method to AIDS mortality. This underscores the importance of the current study, which aimed to clarify the spatiotemporal variation in AIDS mortality in different race, sex and age groups.

The purpose of this research was: (1) to describe the characteristics of HIV/AIDS mortality in terms of age categories, race, sex, and study periods in Florida; (2) to adopt a statistical approach to characterize the spatiotemporal clusters of AIDS mortality to quantify the burden of HIV/AIDS mortality in Florida by race across space and time; and (3) to demonstrate the applicability of this analysis in studying AIDS mortality by applying different window (or parameter) settings in space-time scan statistics in order. Overall, the goal

of the present study was to understand the spatial and temporal variation of HIV/AIDS distribution in Florida.

METHODS

Data sources

Information on age, sex, race/ethnicity, and county of residence for the AIDS mortality data of 67 jurisdictions of Florida was collected from the CDC Compressed Mortality website (available online at <http://wonder.cdc.gov/mortICD9J.html> for the years 1987–1998 and <http://wonder.cdc.gov/mortICD10J.html> for the years 1999–2004) [16,17]. Population estimates during the study period were also obtained from the same website [16,17]. African-Americans, whites, and other categories of race were chosen. Data were collected between 1987 and 2004, for an 18-year study period. For the deaths between 1987 and 1998, the *International Classification of Diseases, Ninth Revision* (ICD-9) codes (042) were used, and for the deaths after 1998, the ICD-10 (B20–B24) codes were used.

Data analysis

To account for geographic and temporal clustering simultaneously, the optimal statistical tool proposed by Kulldorff et al is space-time scan statistics [15,17,18]. When compared with other statistical methods for cluster detection, this statistic was found to have good power to detect localized hot-spots of excess events [18,19]. By meeting the assumptions of a set of statistical models, an unusual rise in mortality in a specific spatial and temporal window (with adjustments for covariates such as age, sex, or other substantial risk factors) can be identified. The step-by-step progression of the method has been thoroughly described by Kulldorff et al [15,20]. The Poisson model was chosen in the present study to analyze the data for AIDS deaths. The null hypothesis was that the expected death counts in each county would be proportional to the population size in that area; whereas the alternative hypothesis was that deaths were not randomly distributed and occurred in some areas in a manner disproportionate to the size of the population at risk. Once the null hypothesis was rejected, clusters were formed, which meant that the detected cases/deaths in this region were significantly different from those in the other study areas.

In our study, a point corresponding to the centroids of a county and different maximum spatial window sizes were set. Information on county centroids, which represent the geometric center of each polygonal-shaped country, and latitude and longitude were downloaded from the 2000 US Gazetteer portion of the US Census Bureau (available online at <http://www.census.gov/geo/www/gazetteer/places2k.html>). Geographic coordinates for each county were used as a proxy for the location of the Florida counties under study. If the result of the cluster revealed that the time frame ends at the end of the study period (in the current study, 2004), it was defined as an “active” cluster. This means that the cluster requires further attention. In this study, the temporal window was set as 90% of the study period to detect the longest persistent clusters. Our results were all adjusted by sex and by race, which is permitted in space-time scan statistics. The statistical significance of the detected clusters was evaluated by comparing the test statistic from the real data set with those computed from simulated data sets. We used 999 replications for simulation and hence the smallest possible *p* value is 0.001. Clusters with a *p* value ≤ 0.01 were reported with cluster information such as the observed and expected number of cases, time frame (i.e. duration of the cluster occurrence), and the geographic location.

Two computer software programs were used for the study: the space-time scan statistic was implemented in SaTScan™ version 7.0.3 software [20], which was

used to conduct the cluster detection analyses; and the geographic information system EpiInfo version 3.4.1 (CDC, USA) was used to visualize the scan statistical analysis results by presenting cluster information in map form.

RESULTS

Characteristics of study subjects

Our study included 40,106 HIV/AIDS death cases among the 67 counties of Florida across the 18-year study period (1987–2004) (Table). The ages presented in this study refer to the “mortality age”. The proportion of AIDS deaths occurring among the youngest age category (<25 years old) was 3.5% (1,395 out of 40,106). Among the 1,395 AIDS deaths under age 25, 72.3% of the cases were African-American and 27.7% were whites. With regard to sex, 22.4% (8,973/31,133) of the total deaths were women. Considering the proportion of subjects in each race, deaths among African-American women accounted for a greater proportion (35.0%) compared with white women (10.5%). Thus, according to sex (proportion B), African-Americans contributed a greater proportion (75.9%) of AIDS deaths among women than whites (24.1%). Concerning the study periods, there were differential trends in race by study period. We found from proportion B that the proportion of African-Americans of the total AIDS deaths increased from 44.3% before 1998 to 60.8% after 1998.

Table. Characteristics of AIDS deaths in Florida, 1987–2004

	All (N=40,106)	African-Americans (n=19,456)		Whites (n=20,588)		Others* (n=62)	
	n (%)	n (%)	B% [†]	n (%)	B% [†]	n (%)	B% [†]
Age (yr)							
<25	1,395 (3.5)	1,009 (5.2)	72.3	386 (1.9)	27.7	0 (0)	0
25–34.9	10,769 (26.9)	5,189 (26.7)	48.2	5,565 (27.0)	51.7	15 (24.2)	0.13
35–44.9	14,957 (37.3)	7,018 (36.0)	46.9	7,921 (38.5)	53.0	18 (29.0)	0.13
45–53.9	8,547 (21.3)	3,891 (20.0)	45.5	4,633 (22.5)	54.2	23 (37.1)	0.26
≥54	4,438 (11.0)	2,349 (12.1)	52.9	2,083 (10.1)	47.0	6 (9.7)	0.1
Gender							
Female	8,973 (22.4)	6,809 (35.0)	75.9	2,159 (10.5)	24.1	5 (8.1)	0.05
Male	31,133 (77.6)	12,647 (65.0)	40.6	18,429 (89.5)	59.2	57 (91.9)	0.2
Study period							
1987–1998 (12 yr)	29,803 (74.3)	13,197 (67.8)	44.3	16,566 (80.5)	55.6	40 (64.5)	0.1
1999–2004 (6 yr)	10,303 (25.7)	6,259 (32.2)	60.8	4,022 (19.5)	39.0	22 (35.5)	0.2

*Subjects who were not African-American or white; [†]proportion B = percentage of the row.

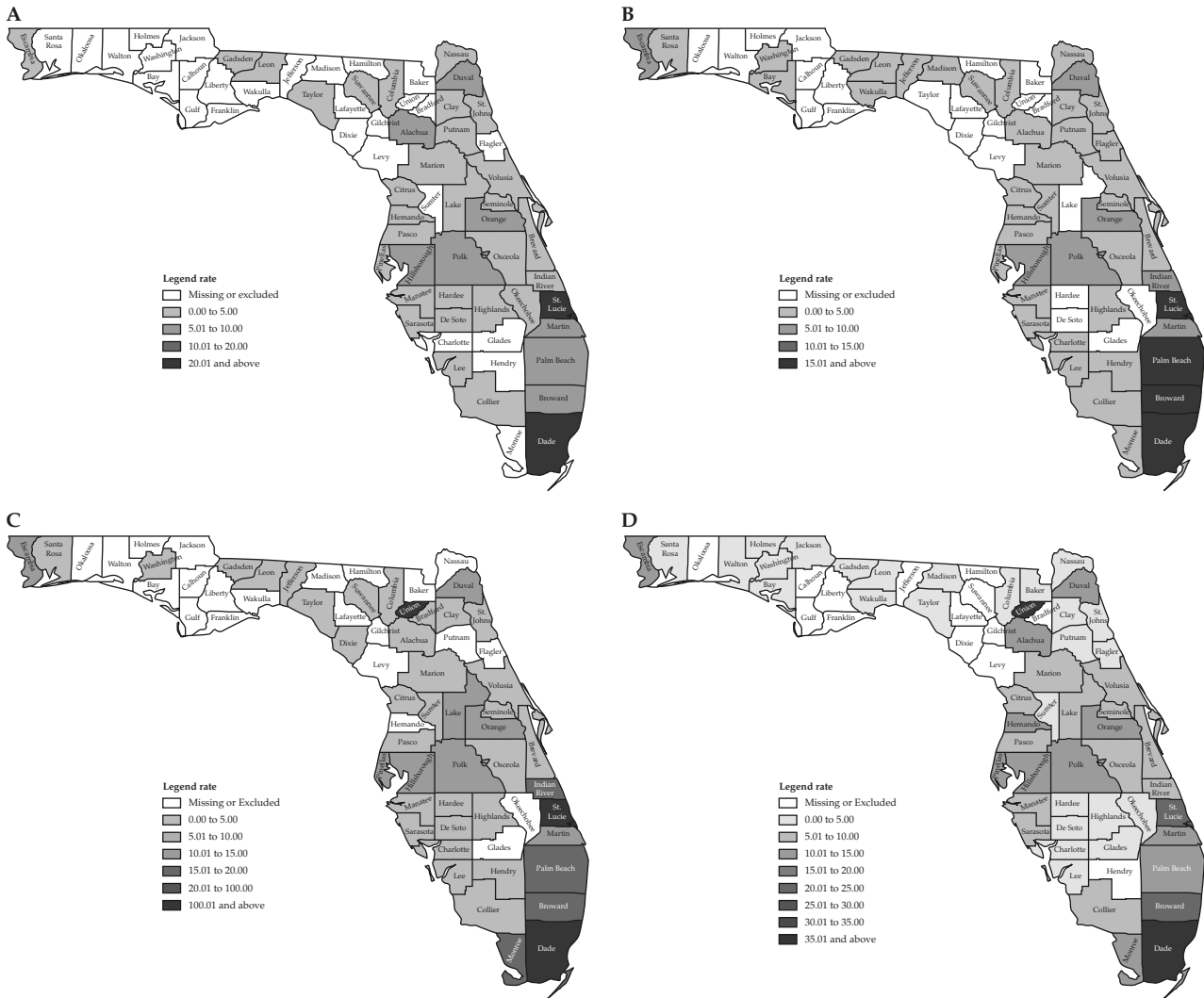


Figure 1. Spatial information of age-adjusted AIDS mortality rate (per 100,000) in Florida, 1998 and 2004, according to sex. (A) Female AIDS deaths in 1998; (B) Female AIDS deaths in 2004; (C) Male AIDS deaths in 1998; (D) Male AIDS deaths in 2004.

Spatial information

The county-level spatial distribution of age-adjusted AIDS mortality rate (per 100,000) among the 67 counties of Florida in 1998 and 2004 is shown in Figure 1 according to sex. Darker shading shows a higher age-adjusted AIDS mortality rate. The counties with the most female AIDS deaths were St. Lucie (22.4/100,000) and Miami-Dade (12.1/100,000) in 1998; in 2004, the counties included St. Lucie (15.5/100,000), Miami-Dade (12.4/100,000), Broward (11.1/100,000), and Palm Beach (10.1/100,000). The counties with the most male AIDS deaths included Union and Miami-Dade in both 1998 and 2004. However, the rate decreased from 162.8/100,000 in 1998 to 55.5/100,000 in 2004 for Union; and from 27.1/100,000 in 1998 to 25.3/100,000 in 2004 for Miami-Dade.

Temporal trends

Figure 2 shows the time trend of the age-adjusted AIDS mortality rate per 100,000 by sex and by racial group. The ranks from high to low of the four groups represent African-American males, African-American females, white males and white females. The peak in age-adjusted mortality rates for the four groups was in 1995; then there is a sharp drop between 1995 and 1997. However, the decrease stops in 1998 and then stabilizes or fluctuates mildly until 2004.

Space-time scan statistics

Figure 3 shows the clusters of all AIDS deaths (including for whites, African-Americans, and others) identified by cluster rank, time frame (the start and end of clusters), and observed/expected (O/E) ratio of the

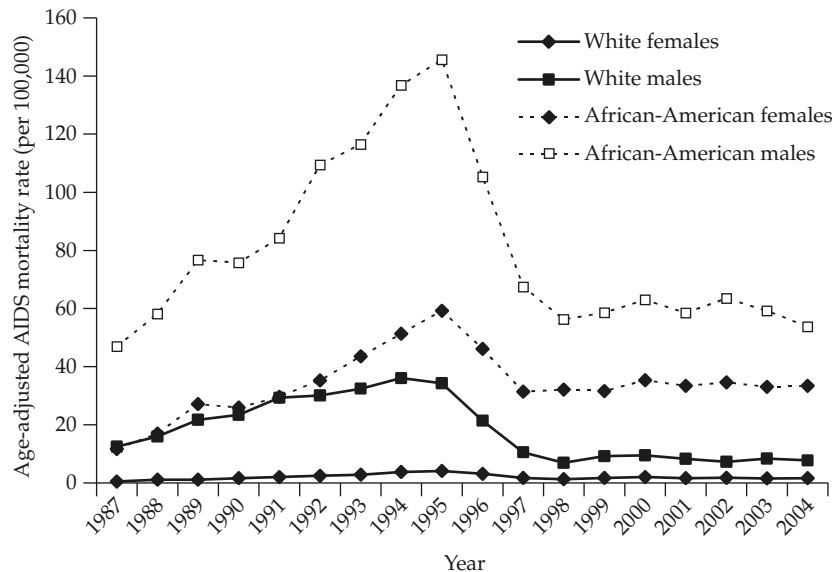


Figure 2. Time trend of age-adjusted AIDS mortality rate per 100,000 by sex and by race (African-Americans and whites) in Florida, 1987–2004.

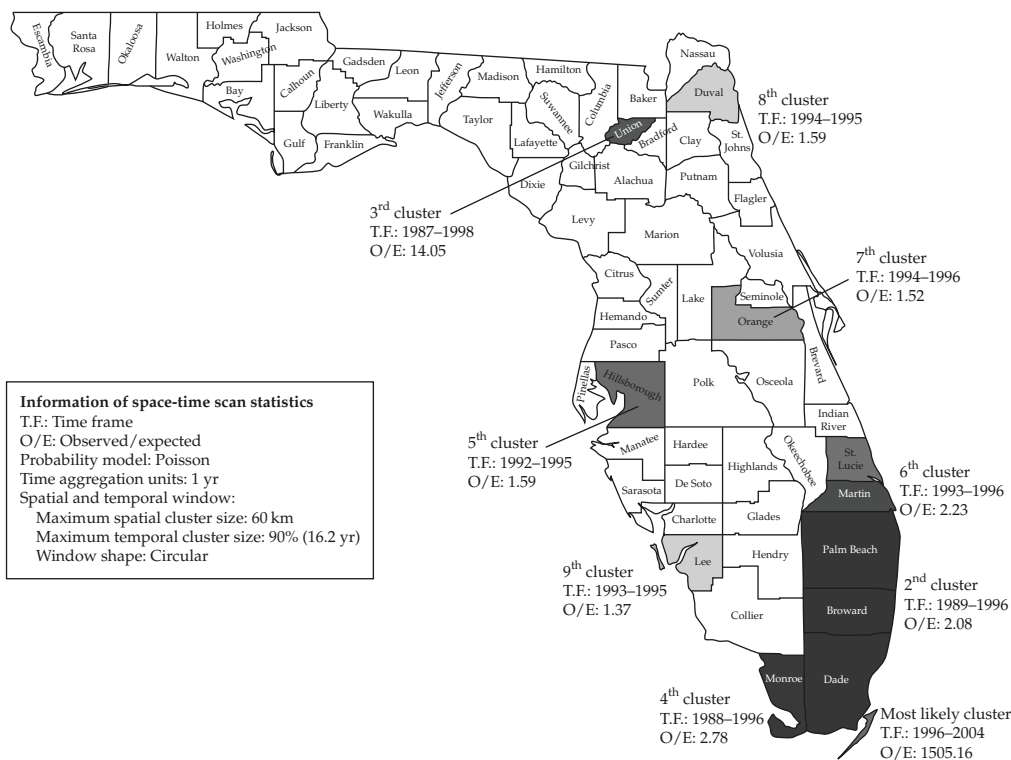


Figure 3. Clusters of AIDS deaths in Florida based on SaTScan space-time scan statistics, 1987–2004.

cluster. Only the cluster in Miami-Dade (which was also the most likely cluster with O/E 1505.16) persisted to the present period (the year 2004 in our study). With regard to the time frame of the clusters, Union county was the longest cluster (1987–1998, 11 years), followed by

Miami-Dade (8 years) and Monroe (8 years). However, the time frame of the cluster in Union county did not persist to the end of the study period, and ended in 1998.

The growth and decline of the clusters of African-American AIDS deaths are shown in Figure 4.

With regard to the temporal trends, as shown in Figure 2, the year 1995 represented a peak in mortality among both sexes and among whites and African-Americans. In following years, the mortality rates decreased. Of interest, highly active antiretroviral therapy (HAART) was introduced in 1995. The effect of HAART appears to be remarkable in all races and in both sexes [24]. However, there was no continuous decrease in AIDS mortality after 1998. The reason for why the decrease stopped warrants further evaluation and assessment for drug resistance or drug adherence [25,26].

Our study demonstrates a marked increase in AIDS mortality amongst the African-American population in Florida. The age-adjusted AIDS mortality rate of African-American males after 1998 was around 60/100,000, which was more than six times the rate for white males (less than 10/100,000). Space-time scan statistics also demonstrated that the clusters of African-Americans were far greater in number than the clusters of other ethnicities. A number of studies have reported disparities in care provided to minority patients who are less likely to receive medication or start HAART later in the disease course [27–29]. Therefore, public health care providers should consider strategies to optimize the health care delivery and medications available for minority patients such as African-Americans. This may help reduce disparities in AIDS mortality.

From our experience, the use of space-time scan statistics on disease is applicable in cases of infectious diseases or cancers. The method simultaneously describes the geographic and temporal disease distributions, which is not provided by other statistics such as disease mapping or spatial-only analysis. Space-time scan statistics can be of benefit in the surveillance of disease control and prevention. Our current experience demonstrates that, for the detection of cluster distributions with hot-spot-like or irregular shapes, the smallest maximum spatial cluster size possible, such as 10, 20 or 30 km, is optimal. Alternatively, to detect the clusters with a larger geographic scope, setting the spatial window with a larger population at risk (such as 50% population at risk) is more advantageous. Of course, the parameters of spatial windows should be adjusted according to the available information level in the study, such as state level, county level, and ZIP code level.

With regard to the temporal window, we suggest that the parameter of temporal windows (maximum

temporal cluster size) should be set as long as possible, such as the largest 90%, particularly in the space-time scan statistics. This would ensure that we do not miss clusters with longer time frames. Clusters with longer time frames may represent longer epidemics of morbidity or mortality.

The strength of our study is that we used space-time scan statistics, which can examine temporal effects unlike other spatial-only clustering methods. A limitation of the present study was that we could not distinguish deaths directly related to AIDS from non-HIV related deaths in our dataset. This is particularly noteworthy because non-HIV related causes of death may account for as many as one-quarter of all deaths of AIDS patients [30]. Furthermore, the growing numbers of illegal immigrants into Florida might constitute another limitation. They do not have legal status and are therefore not adequately documented by death registries. This might result in an underestimate of the AIDS deaths and mortality rates of the “other” race category in our study. Another limitation was that in 1987, a new category for HIV infection was added to the ICD-9. In 1999, the ICD-10 was introduced, which may have resulted in additional deaths being classified into the HIV/AIDS category. Therefore, the death rates for 1987–1998 may not be directly comparable with those computed after 1998 [3]. However, we found only small changes between the two systems.

In conclusion, this study provides a first attempt to visually and quantitatively describe the geographic and temporal characteristics of AIDS mortality in Florida; thus demonstrating the utility of space-time scan statistics in characterizing public health problems. These findings can serve to inform medical care allocation and focus public health intervention strategies for AIDS care.

REFERENCES

1. Centers for Disease Control. Commentary. Cases of HIV infection and AIDS in the United States, 1981–2006. *MMWR Morb Mortal Wkly Rep* 2006;55:585–9.
2. Centers for Disease Control. HIV/AIDS diagnoses among Blacks—Florida, 1999–2004. *MMWR Morb Mortal Wkly Rep* 2007;56:69–73.
3. Centers for Disease Control. The global HIV/AIDS pandemic, 2006. *MMWR Morb Mortal Wkly Rep* 2006;55: 841–4.

4. Centers for Disease Control. HIV/AIDS among women (available at <http://www.cdc.gov/hiv/topics/women/resources/factsheets/pdf/women.pdf>). *CDC HIV/AIDS Fact Sheet* 2007.
5. Dean HD, Steele CB, Satcher AJ, et al. HIV/AIDS among minority races and ethnicities in the United States, 1999–2003. *J Natl Med Assoc* 2005;97:5S–12S.
6. 2006 Report on the Global AIDS epidemic. Geneva: UNAIDS, 2006. Available at <http://www.unaids.org/en/> [Date accessed: May 18, 2006]
7. Merson MH. The HIV-AIDS pandemic at 25—the global response. *N Engl J Med* 2006;354:2414–7.
8. Kulldorff M, Song C, Gregorio D, et al. Cancer map patterns: are they random or not? *Am J Prev Med* 2006;30: S37–49.
9. Ozdenerol E, Williams BL, Kang SY, et al. Comparison of spatial scan statistic and spatial filtering in estimating low birth weight clusters. *Int J Health Geogr* 2005;4:19.
10. Costa MA, Assunção RM. A fair comparison between the spatial scan and Besag-Newell disease clustering tests. *Environ Ecol Stat* 2005;12:301–19.
11. Aamodt G, Samuelsen SO, Skrondal A. A simulation study of three methods for detecting disease clusters. *Int J Health Geogr* 2006;5:15.
12. Pearl DL, Louie M, Chui L, et al. The use of outbreak information in the interpretation of clustering of reported cases of *Escherichia coli* O157 in space and time in Alberta, Canada, 2000–2002. *Epidemiol Infect* 2006;134:699–711.
13. Jones RC, Liberatore M, Fernandez JR, et al. Use of a prospective space-time scan statistic to prioritize shigellosis case investigations in an urban jurisdiction. *Public Health Rep* 2006;121:133–9.
14. Kulldorff M, Athas WF, Feurer EJ, et al. Evaluating cluster alarms: a space-time scan statistic and brain cancer in Los Alamos, New Mexico. *Am J Public Health* 1998;88:1377–80.
15. Kulldorff M, Heffernan R, Hartman J, et al. A space-time permutation scan statistic for disease outbreak detection. *PLoS Med* 2005;2:e59.
16. Gething PW, Noor AM, Gikandi PW, et al. Improving imperfect data from health management information systems in Africa using space-time geostatistics. *PLoS Med* 2006;3:e271.
17. Kulldorff M, Nagarwalla N. Spatial disease clusters: detection and inference. *Stat Med* 1995;14:799–810.
18. Song C, Kulldorff M. Power evaluation of disease clustering tests. *Int J Health Geogr* 2003;2:9.
19. Kulldorff M, Zhang Z, Hartman J, et al. Benchmark data and power calculations for evaluating disease outbreak detection methods. *MMWR Morb Mortal Wkly Rep* 2004;53:144–51.
20. Kulldorff M. Information Management Services, Inc. *SaTScan™ User Guide. SaTScan v. 7.0: Software for the Spatial and Space-time Scan Statistics*, 2006.
21. Akin M, Fernandez MI, Bowen GS, et al. HIV risk behaviors of Latin American and Caribbean men who have sex with men in Miami, Florida, USA. *Rev Panam Salud Publica* 2008;23:341–8.
22. Marcelin LH, McCoy HV, Diclemente RJ. HIV/AIDS knowledge and beliefs among Haitian adolescents in Miami-Dade County, Florida. *J HIV AIDS Prev Child Youth* 2006;7:121–38.
23. Lieb S, Rosenberg R, Arons P, et al. Age shift in patterns of injection drug use among the HIV/AIDS population in Miami-Dade County, Florida. *Subst Use Misuse* 2006; 41:1623–35.
24. Yeni P. Update on HAART in HIV. *J Hepatol* 2006;44: S100–3.
25. Sukasem C, Churdboonchart V, Sukeepaisarncharoen W, et al. Genotypic resistance profiles in antiretroviral-naive HIV-1 infections before and after initiation of first-line HAART: impact of polymorphism on resistance to therapy. *Int J Antimicrob Agents* 2008;31:277–81.
26. Maggiolo F, Airoidi M, Kleinloog HD, et al. Effect of adherence to HAART on virologic outcome and on the selection of resistance-conferring mutations in NNRTI- or PI-treated patients. *HIV Clin Trials* 2007;8:282–92.
27. Moore RD, Stanton D, Gopalan R, et al. Racial differences in the use of drug therapy for HIV disease in an urban community. *N Engl J Med* 1994;330:763–8.
28. Stone VE. Optimizing the care of minority patients with HIV/AIDS. *Clin Infect Dis* 2004;38:400–4.
29. Turner BJ, Cunningham WE, Duan N, et al. Delayed medical care after diagnosis in a US national probability sample of persons infected with human immunodeficiency virus. *Arch Intern Med* 2000;160:2614–22.
30. Sackoff JE, Hanna DB, Pfeiffer MR, et al. Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. *Ann Intern Med* 2006;145:397–406.

將時間空間分析方法新應用在偵測 AIDS 死亡的人口學變異上 — 以 Florida 州為例

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本研究的主要目的是以時間和空間分析的角度去研究佛羅里達州後天免疫缺乏症候群死亡情形的特異性，並且了解這些被檢測出的特異性是否受人口學特質所影響。**Kulldorff** 等學者所提出的“時間空間統計方法”被用來測量 1987 年至 2004 年間，美國佛羅里達州 67 個行政區不同年齡、種族、及性別在哪些時間點或空間上被計算出有特別多的（或群聚的）後天免疫缺乏症候群死亡個案。研究結果以美國疾病管制局（CDC）所研發的 **EpiInfo** 和 **EpiMap** 軟體來呈現地圖上的特異性。時間空間統計方法偵測出不同年齡、種族、及性別在特定時間或空間所呈現的後天免疫缺乏症候群死亡個案群聚現象（clusters）的消長情形。**Miami-Dade** 以及附近的郡包括 **Broward**、**Martin**、**Palm Beach** 是後天免疫缺乏症候群的死亡群聚（clusters）最嚴重的地區（觀察值 / 預期值：1505.16），而且其群聚時間從 1996 到研究結束（2004 年）仍持續。**Union** 郡曾經是發生群聚時間最長的一個郡（1987–1998），但是此群聚現象並未延伸至今。不同種族而言，黑人比起白人有較多的死亡群聚被偵測出。以時間分布而言，後天免疫缺乏症候群死亡群聚發生在 1995 年，之後死亡率逐漸往下降，直到 1998 年下降的情形停止。藉由將時間構面考慮計算進去，我們能偵測出地理上疾病或死亡的群聚現象的延續情形，而這一點也是其他地理統計分析方法所無法提供的。這些研究發現能提供在後天免疫缺乏症候群照顧上，公共衛生政策及醫療資源分布的參考。

關鍵詞：後天免疫缺乏症候群，群聚，死亡率，時間空間分析

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