GeoDa Center
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Nicholas Malizia and Elizabeth A. Mack

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Nicholas Malizia and Elizabeth A. Mack

GeoDa Center for Geospatial Analysis and Computation
School of Geographical Sciences and Urban Planning
Arizona State University
975 S. Myrtle Ave.
Tempe, AZ 85287-5302, USA

Abstract

The Jacquez k nearest neighbor test, originally developed to improve upon shortcomings of existing tests for space-time interaction, has been shown to be a robust and powerful method of detecting interaction. Despite its flexibility and power however, the test has three main shortcomings: (1) it discards important information regarding the spatial and temporal scale at which detected interaction takes place; (2) the results of the test have not been visualized; (3) recent research demonstrates the test to be susceptible to population shift bias. This study presents enhancements to the Jacquez k nearest neighbors test with the goal of addressing each of these three shortcomings and improving the utility of the test. Data on Burkitt's lymphoma cases in Uganda between 1961-1975 are employed to illustrate the modifications and enhance the visual output of the test. Output from the enhanced test is compared to that provided by alternative tests of space-time interaction. Results show the enhancements presented in this study transform the Jacquez test into a complete, descriptive, and informative metric that can be used as a stand alone measure of global space-time interaction.

Keywords: space-time interaction, Jacquez k nearest neighbor, visualization, space-time cube, population shift bias

1 Introduction

A pattern of events exhibits space-time interaction when pairs of events which are close to each other in space are also close to each other in time. Although events within the same pattern may be closer to each other in space or time than would be expected under the null hypothesis of spatio-temporal randomness, space-time *interaction* occurs only in instances where, generally speaking, there is a positive relationship between the spatial and temporal distances between pairs of events [1, 2]. Given the specific nature of space-time interaction, methods to establish its presence are necessarily distinct from conventional methods for detecting purely spatial or temporal clustering. Tests of interaction are designed to "detect space-time clustering above and beyond any purely spatial or purely temporal clustering;" meaning, the tests determine if event pairs that are close in space are also close in time [1, pg. 58].

Originally developed within the field of spatial epidemiology, tests of space-time interaction remain popular tools to analyze patterns of disease cases [1–6]. In this context, the identification of space-time interaction may indicate an infectious or viral etiology, or the presence of transient, localized hazard exposure [7, 8]. The Knox test for space-time interaction, for example, has been used extensively to provide evidence in support of a viral etiology of leukemia [9–13]. In addition to the field of spatial epidemiology, tests of space-time interaction have also been used increasingly in the field of criminology [14–16] and ecology [17–20].

One of the most commonly used tests of space-time interaction is the Jacquez k nearest neighbor test [8]. The test has a number of positive attributes that contribute to its utility and prevalence in the literature. First, as the name implies, it employs a nearest neighbor approach to establishing proximity in space and time instead of defining explicit distance- or time-based thresholds. This unique approach to detecting space-time interaction ensures the test is robust to non-linear associations in space and time and has been demonstrated to be quite powerful [2, 8]. It also reduces the subjectivity associated with parameter selection common to alternative tests [8, 16]. Second, the test and its significance can be computed quickly relative to some other tests. Independent of its flexibility, speed and power, however, the Jacquez test does have three key shortcomings. First, the k nearest neighbor approach discards important information regarding the spatial and temporal scale at which the detected interaction takes place [21]. Second, the current formulation of the test does not produce any explicitly spatial or temporal output that can be visualized to determine when and where interaction may be taking place. Third, recent research has shown the test to be susceptible to population shift bias [22]. The goal of this paper is to enhance the Jacquez test by addressing each of these shortcomings, thereby increasing the utility of this test for researchers.

The first enhancement to the test offered here provides supplementary information about the spatial and temporal scales at which events are interacting. This information links the abstract concept of nearest neighbor interaction to tangible spatial and temporal information for each of the events of interest. Second, several methods for visualizing the interaction identified by the nearest neighbor test are presented. Finally, an unbiased version of the Jacquez test is formulated and implemented to account for potential bias resulting from a shift in the underlying population over time. Throughout the paper, the utility of the modifications and visualization techniques are illustrated by comparing the results of the enhanced Jacquez test to those produced by the Knox test for space-time interaction. These comparisons are demonstrated using a dataset compiled by Williams et al. [23], which provides location and time of onset for 188 cases of Burkitt's lymphoma in the West Nile District of Uganda during the period 1961-1975.

2 Background on Space-Time Interaction Tests

Before proceeding to a discussion of the enhancements to the Jacquez test developed in this paper, this section will provide a brief overview of the three other popular tests for space-time interaction: the Knox test, Mantel test and space-time K function. For a more complete technical review of these methods, readers are referred to the original citations noted in the text or to the extensive review provided by Tango [2].[1]

The first method formulated to detect global space-time interaction was the Knox test [26]. Developed within the context of epidemiology, the Knox test compares all possible pairs of events within a pattern and evaluates whether or not they fall within critical thresholds for distance in space and in time of each other [26]. The Knox test statistic is a count of the number of event pairs that are within both thresholds simultaneously. While there has been work focused on deriving the exact distribution of the test statistic [e.g. 26, 27], most implementations of the test today determine the significance of the statistic using a permutation approach [28]. Although widely used in the literature, concerns identified surrounding the Knox test include: the impact of edge effects [2, 29], an inability to detect non-linear interaction [8], the subjectivity introduced by the selection of critical distances [8, 16, 30] and a loss of power associated with a high concentration of points across the study area [29]. Numerous alternative formulations have been suggested to deal with one or more of these problems or to adapt the test to different applications [11, 31–33]. For example, Kulldorff and Hjalmars [11] formulated an unbiased version of the Knox test to account for the issue of population shift bias (i.e., the propensity of the test to identify spurious interaction due to shifts in the underlying population over time and not true interaction resulting from the data generating process responsible for producing the events of interest). This phenomenon will be discussed in greater detail below, in the context of the Jacquez test.

A more generalized version of the Knox test was proposed by Mantel [34]. Although

[1] Also, it should be noted that scan-based tests including Kulldorff et al.'s space-time scan statistic [24] and Takahashi et al.'s flexible space-time scan statistic [25] which are concerned with the detection of localized clusters of events in three-dimensional space are not considered here. Tango [2] distinguishes these from tests of space-time interaction in that the latter have a global focus whereas the scan statistics are interested in finding significant local clusters in space and time.

mathematically related to the Knox, this test removes the subjectivity associated with the selection of critical space and time thresholds required by the Knox test, and instead detects interaction by considering the spatial and temporal distances between all pairs of events [2]. There are two versions of the Mantel test statistic, an unstandardized and a standardized version. The unstandardized statistic is calculated by computing spatial and temporal distance matrices for the event pattern, multiplying the two matrices together in an element-wise fashion and then summing the elements of the resulting matrix of products. The standardized test statistic is calculated by measuring the correlation between the elements of the spatial and temporal distance matrices. Mantel advocated the addition of a constant to the raw distance matrices to prevent multiplication by zero. Additionally, he prescribed a reciprocal transformation of the resulting distances to temper the effect of events distant from each other in space and time [34]. Irrespective of the version of the test statistic computed, the resulting statistic is highly dependent upon the selection of these parameters [2, 8].

A third global test for space-time interaction is the space-time K function proposed by Diggle et al. [35]. The test extends the spatial K function, which is used to detect clustering in point patterns [36, 37], to the realm of space-time event patterns. The method operates by calculating K functions in space and time independently and then comparing the product of these functions with a K function which takes both dimensions into account from the outset [35, 38]. In the absence of space-time interaction, the difference between the combined space-time K function and the product of the two individual K functions for both space and time will not be significantly different than zero [35]. One of the major issues associated with this test, however, which has perhaps prevented its more widespread use, is that it is relatively more computationally burdensome.

3 Jacquez Test

As discussed above, each of the aforementioned tests have drawbacks associated with them. In response to these drawbacks, Jacquez [8] proposed a test based on a nearest-neighbors distance calculation. The test offers two distinct improvements over other tests of space-time interaction: (1) it eliminates the need for the user to specify an absolute threshold distance within which interaction will be detected; (2) it inherently accounts for geographic variation in population density by identifying interaction based on nearest neighbor relationships rather than absolute distance.

3.1 Calculation

The test is composed of two statistics: a cumulative measure of interaction, J_k, and a k-specific measure of interaction, ΔJ_k. The cumulative measure locates the k nearest neighbors to a point in both space and time and then tabulates the number of events that are nearest neighbors in *both* dimensions. This is expressed mathematically in

Equation 1, where n = number of cases; a^s = adjacency in space; a^t = adjacency in time.

$$J_k = \sum_{i=1}^{n} \sum_{j=1}^{n} a^s_{ijk} a^t_{ijk} \tag{1}$$

$$a^s_{ijk} = \begin{cases} 1, & \text{if event } j \text{ is a } k \text{ nearest neighbor of event } i \text{ in space} \\ 0, & \text{otherwise} \end{cases}$$

$$a^t_{ijk} = \begin{cases} 1, & \text{if event } j \text{ is a } k \text{ nearest neighbor of event } i \text{ in time} \\ 0, & \text{otherwise} \end{cases}$$

To determine if event j is a k nearest neighbor of event i in a particular dimension (either space or time) a distance matrix, $\mathbf{D}$, for that dimension must be calculated. Entries in the distance matrix, d_{ij}, denote the distance between all pairs of events in the event pattern. The first nearest neighbor of an event is the closest neighboring event. For values of k larger than 1, the kth nearest neighbor is the kth closest neighboring event. The set of k nearest neighbors for an event, however, includes the kth nearest neighbor and the nearest neighbors associated with all lower orders of k [8]. For example, the third nearest neighbor of an event of interest i is the third closest event to i while the set of $k = 3$ nearest neighbors of an event include i's first, second and third nearest neighbors.[2]

The k-specific statistic, ΔJ_k, is a measure of space-time interaction for J_k in excess of that observed for J_{k-1}. This additional metric was formulated because values for the cumulative test statistic (J_k) are not independent of one another. This dependence is due to the fact that pairs of events included in smaller values of k are also included in larger values of k. Therefore, larger values of k will exhibit increased space-time interaction by virtue of the fact that more space-time case pairs are included in the calculation of the test statistic [8]. The ΔJ_k statistic, however, is completely independent of other levels of k. The formulation of this statistic is given in Equation 2.

$$\Delta J_k = J_k - J_{k-1} \tag{2}$$

Jacquez [8] advocated that significance of both statistics be assessed using a Monte Carlo permutation method similar to that originally advocated for the Mantel test [34], where the spatial coordinates are fixed, but the temporal coordinates of the data are permuted and the observed statistics are then compared to the distribution of statistics generated by running the test on the permuted data.

[2]For instances where neighbors are equidistant from the event of interest, ties may either be broken randomly or assigned a weighted average based on the number of tied events.

3.2 Combined Test

As formulated, the Jacquez test statistics resolve several of the issues mentioned associated with other tests for space-time interaction, however, a remaining problem is the subjectivity related to the selection of an appropriate value for k. This shortcoming is overcome by constructing a combined test based on multiple values of k as proposed by Jacquez [8]. The combined test evaluates whether significant interaction between events exists over a range of values for k instead of just at a single value of k. The mechanics of the combined test involve calculating either of the test statistics (J_k or ΔJ_k) at multiple levels of k and then assessing the combined probability of the results.

This assessment of combined probability needs to account for the problem of multiple testing [39]. Jacquez noted however that the popular Bonferroni and Simes adjustments both result in an excessively conservative assessment of combined significance [8]. To resolve this issue, he proposed a centroid distance method for combining probabilities across multiple levels of k. This approach involves converting the results of the test across multiple levels of k to a $1 \times m$ vector $\mathbf{j}$ where the result at each level of k occupies an element in the vector [8]. These vectors are saved for each of the N permutations in the Monte Carlo procedure. The vectors can then be conceptualized as a cloud of points in m-dimensional space. The centroid of this cloud is determined and the distances from the centroid to the points composing the cloud are calculated. Pseudo-significance of the observed $\mathbf{j}$ vector is assessed by tallying the number of points in the cloud that are closer to the centroid than the observed vector. This value, c, is then inserted into Equation 3 to calculate the pseudo-significance of the combined test results.

$$p = \frac{c+1}{N+1} \tag{3}$$

3.3 Issues and Proposed Solutions

Despite the improvements offered by the Jacquez test relative to the other tests of space-time interaction outlined above, the test has problems of its own. First, although the nearest neighbors approach to detecting interaction has been found effective, it does not provide any indication as to the spatial and temporal scales at which the detected interaction occurs. Second, there have been no efforts to visualize the results in a spatio-temporal context. Finally, the test has been shown to be highly susceptible to population shift bias [22]. These points are discussed in greater detail in this section. The enhancements outlined by this work address each of these shortcomings.

While there are issues of subjectivity associated with computing space-time interaction tests based on absolute distance thresholds in space and time [8, 16, 30], completely abandoning real-world linkages in exchange for the relativistic approach offered by nearest neighbors proximity creates different problems. Although the nearest neighbor based Jacquez test effectively detects interaction between events, at what spatial and temporal scales does the interaction occur? As designed, the test does not indicate to the user the real-world spatial and temporal scales at which the interaction is observed. Consider, what does it actually mean in terms of distance to be a third nearest neighbor of an event in time and space? Inherent in the Knox test and the space-time K test are ways to determine the scale of interaction. When a spatial and temporal scale is specified with the Knox test and significant interaction is identified, the results indicate the scale of the interaction in metrics of both space and time that are familiar to the user. With the Jacquez however, translating the detection of significant interaction for a specific value of k to familiar measures of distance and time is less intuitive.

Another question of interest left unanswered by the Jacquez test is, where and when within the study area and period does the identified interaction occur? Although locating and assessing the significance of local event clusters pertains to the realm of space-time scan statistics [i.e. 24, 25], efforts have been made to identify the locations of potential space-time clusters by visualizing the results of the Knox test. This is done by mapping the links between events that are within the specified critical spatial and temporal distances of each other. Although not suggested in Knox's original paper, over time, it has become a conventional method of displaying the results graphically. An early example of this can be found in Williams et al. [23] and a more modern example in Grubesic and Mack [16]. Given the similar structure of the Knox and Jacquez tests with respect to identifying spatial and temporal adjacency, it seems logical to extend a similar visualization approach to the Jacquez test. In the context of this test, the links between events would identify instances where one event is both a spatial and temporal k nearest neighbor of another event. The problem with this approach to visualizing results, as currently implemented for the Knox test, is that it remains essentially atemporal and therefore, it is not possible to assess how close in time the links are relative to one another on the map. The majority of work on space-time visualization has focused on visualizing space-time paths within a cube or aquarium [40–43]. Visualizing individual events in a cube is perhaps more challenging though, as it is difficult to plot discrete points in time and space and contextualize their positions in space and time relative to one another because of their lack of dimensionality. This study demonstrates two examples for visualizing the spatio-temporal results of the Jacquez test employing the space-time cube.

The third and final issue regarding the Jacquez test addressed in this paper is population shift bias. This phenomenon was first identified by Mantel [34] in the results of the Knox test and explored in greater detail by Kulldorff and Hjalmars [11]. It was shown to affect other tests of space-time interaction by Mack and Malizia [22]. Collectively, these studies demonstrate that spatially heterogenous change in the distribution of the underlying population from which space-time events are drawn is capable of significantly biasing the results of these tests. This stems from the fact that traditional methods of assessing the significance of these statistics assume the events are drawn randomly from a probability distribution that is static across time and space. Instead, the significance of the tests must be determined using a probability distribution which accounts for the dynamic nature of the underlying population from which events are drawn. Failing to do so leads the tests to detect interaction due to clustering of the underlying population in space and time, unrelated to interaction stemming from the data generating process of interest. This results in artificially inflated α levels for the tests, yielding an increase in Type I errors. Here, we demonstrate the construction and implementation of a version of the Jacquez test which accounts for this population shift bias. The significance of the statistics calculated by this unbiased test are also determined using a Monte Carlo procedure, however, in this case, the reference distribution does not come from a permutation of the observed data. Instead, the reference distribution is simulated based on knowledge of the underlying population and its dynamics over time. Use of this simulated distribution results in a more accurate estimation of the significance of the test results.

4 Data

The data used in this paper to illustrate the proposed enhancements come from a study conducted by Williams et al. [23], investigating the spatio-temporal patterns of Burkitt's lymphoma in the West Nile district of Uganda during the period 1961 to 1975. A data appendix accompanying their study provides spatial and temporal coordinates for the onset of 188 cases of the disease throughout the region over the 15 year study period. The locations of Burkitt's lymphoma cases are shown in Figure 1 along with the counties in the West Nile district of Uganda. A shapefile of the counties in the West Nile district was created by georeferencing and digitizing the study area map from the original publication [23]. Although the map from the publication is clearly crude, it provides a reasonable basis for approximating the spatial area and extent of the West Nile district and its composite counties as they were demarcated at the time the study was conducted.

[Figure 1 about here.]

This dataset was chosen to illustrate the enhancements presented in this study for two reasons. First, these data are freely available both online and in print so interested readers of this paper may replicate the results and explore the methods proposed in this paper simply by downloading the data and the software used to produce the results. Second, it is a dataset that has been thoroughly explored in the literature, and as a result, there is a solid understanding of both the space-time pattern of Burkitt's lymphoma [23, 44, 45] and the etiological processes that are primarily responsible for this disease [46]. This knowledge will help in the interpretation of the results of the methods proposed in this paper. It will also provide a means of comparing the results generated in this paper to those provided by other studies. For the analyses carried out here, the data were divided into the same time periods used by Williams et al. [23]: three five year periods (1961-65, 1966-70, 1971-75) and one two year period (1972-3).

[Table 1 about here.]

In addition to the locations and times for disease cases, the calculation of the unbiased Jacquez test also requires an estimate of the density of the susceptible population and its change throughout time. Due to a paucity of digital spatial or demographic data for the West Nile district of Uganda for the time the case data were collected, we rely on the maps and demographic statistics published in Williams et al. [23] to generate these estimates. Estimated population data based on the 1968 Ugandan census were published with the original paper along with the estimated change from 1959 to 1969 for each county in the West Nile district. These data were used to estimate the compound annual growth rate during the study period which was then extrapolated to estimate the populations in each year during the study for each county, following the methodology of Kulldorff and Hjalmars [11]. These populations, along with the lymphoma cases observed in each county are shown in Table 1. These data are used in the subsequent sections to illustrate the enhancements offered by our version of the Jacquez test.

5 Methods

In this section, methods are described which address the problems in the Jacquez test outlined above. The methods developed have been implemented in Python and in some cases R. Some of these methods have been packaged as part of the open-source spatio-temporal analysis software, PySAL [47]. Where appropriate, the enhancements to the Jacquez test presented here are compared to results from existing tests of space-time interaction using the Burkitt's Lymphoma data.

5.1 Establishing the Spatial and Temporal Scale for k

As mentioned previously, one drawback associated with the Jacquez test's nearest neighbor approach to testing for space-time interaction is the ambiguity surrounding how values of k relate to real-world metrics of spatial and temporal distance. This section illustrates a simple, yet effective technique for linking each value of k to a spatial and temporal scale. Given that each value of k corresponds to a set of nearest neighbors for each observation in the dataset, assigning a single value for the spatial and temporal scales associated with each k requires a distillation of these distributions. The technique proposed here to do this is a variation on the mean nearest neighbor distance proposed by Clark and Evans [48]. The approach involves computing the average spatial and temporal distances across all pairs of events that comprise the set of k nearest neighbors for all events in the dataset. This is expressed mathematically in Equations 4 and 5.

$$\hat{S}_k = \frac{\sum_i^n \sum_j^n (a_{ijk}^s d_{ij}^s)}{nk} \tag{4}$$

$$\hat{T}_k = \frac{\sum_i^n \sum_j^n (a_{ijk}^t d_{ij}^t)}{nk} \tag{5}$$

The spatial average for level k is shown in Equation 4 and the temporal average in Equation 5. Here a^s_{ijk} and a^t_{ijk} refers to adjacency in space and time, respectively, at level k between events i and j; defined previously in Equation 1. Terms d^s_{ij} and d^t_{ij} refer to the Euclidean distance between events i and j in space and time, respectively.[3] Essentially, these equations average the times and distances for the sets of k nearest neighbors associated with each observation in the dataset. The average spatial and temporal distance associated with a unique level of k (i.e. ΔJ_k), can be determined using Equations 6 and 7.

$$\hat{S}_{\Delta k} = \frac{\sum_i^n \sum_j^n (a^s_{ijk} d^s_{ij} - a^s_{ijk-1} d^s_{ij})}{n} \tag{6}$$

$$\hat{T}_{\Delta k} = \frac{\sum_i^n \sum_j^n (a^t_{ijk} d^t_{ij} - a^t_{ijk-1} d^t_{ij})}{n} \tag{7}$$

5.1.1 Example Using Burkitt's Lymphoma Data

To establish spatial and temporal scales associated with space-time interaction for the Jacquez test, significant interaction must first be detected. To test for interaction in the Burkitt's Lymphoma data, a combined J_k test was run for each of the four time periods specified in the Williams et al. [23] study: 1961-65, 1966-70, 1971-75, and 1972-73. The combined J_k test is employed to establish if space-time interaction is present in the data across a range of values for k because the exact scale of the interaction is not known. As described previously, when assessing the significance of results across a range of values for k, the combined test must be employed to account for the problems introduced by multiple testing. In the combined tests run here, k assumed all values in the range from 1 to 10. This range has been used in the literature previously to establish significance using the Jacquez test [8, 30]. The pseudo-significance of the tests for each period are shown in Table 2. The results from the combined Jacquez test mimic the conclusions reported by Williams et al. [23] generated using the Knox test. The table shows that two periods, 1961-65 and 1972-73, exhibit significant space-time interaction whereas the other two periods do not.

[Table 2 about here.]

Given that significant space-time interaction was observed for the periods 1961-65 and 1972-73 up to and including the scale of $k = 10$, it was necessary to establish the values of k, beyond k=10, for which interaction was no longer detected. This value was determined by increasing the value of k iteratively in steps of 1. For each increase in the value of k the significance of the cumulative J_k was calculated. This process was repeated until the test statistics for individual levels of k were consistently no

[3]While Euclidean distances are employed throughout this study, alternative measures of distance could be substituted depending on the context.

longer significant. By examining the spatial and temporal distances associated with the highest value for k which proved to be significant (determined using Equations 4 and 5) the approximate spatial and temporal scales at which the interaction occurs can be established. The results of this analysis are shown in Figure 2 for 1961-65 (top) and 1972-73 (bottom). The figures on the left link the different levels of k to particular distances in space (kilometers), while those on the right link the different levels of k to particular times (in days). Approximate boundaries for the scale of interaction are denoted by dashed lines in each of the figures.

[Figure 2 about here.]

5.1.2 Comparison with Knox Results

To corroborate the scales of interaction diagnosed by this enhancement to the Jacquez test the results were compared to the original results reported by Williams et al. [23] established via the Knox test. While the results of the two tests will not align exactly because the distances and times reported by the enhanced Jacquez are averages across all kth nearest neighbors and the Knox test was only calculated at set intervals, similarity in the results provides a method of verifying the utility of the proposed enhancement.[4]

In the original analysis by Williams et al. [23], the Knox test detected significant interaction for the 1961-65 period for most combinations of threshold distances and times less than the critical values of 360 days and 40 kilometers. Similar results were found with the combined Jacquez test. Values for the cumulative J_k statistic for this subset of the data remain significant up to $k = 19$. As Figures 2a and 2b show, the average spatial distance between cases associated with this level of k is ≈ 31 kilometers and the average temporal distance is ≈ 307 days. Examination of the 1972-73 period reveals similar agreement of the enhanced Jacquez with the results reported by Williams et al. [23]. The Knox revealed significant interaction for critical spatial distances between 5 and 40 kilometers, and critical temporal distances between 90 and 180 days. The cumulative Jacquez test produced significant clustering for values of k between 6 and 31, which correspond to a spatial scale between 14 and 34 kilometers and a temporal scale between 40 and 174 days using the enhancement described above. The relative agreement between the results of the two tests is an indication of the effectiveness of this proposed enhancement to the Jacquez test.

5.2 Visualization

As mentioned previously, one of the shortcomings of the Jacquez test is the lack of visual output associated with the results. This issue is largely a by-product of the

[4] In their original exploratory analysis of the Burkitt's lymphoma dataset Williams et al. [23] employed critical spatial distances of 2.5, 5, 10, 20, and 40 kilometers, and critical temporal distances of 30, 60, 90, 120, 180 and 360 days for the Knox test.

global nature of the test statistic. However, by visualizing the links between events and their k nearest neighbors common in both space and time, the user can gain a better understanding of when and where significant interaction occurs within a dataset. This section explores different methods of visualizing this information.

5.2.1 Space-Time Cube

To start, the links produced by the enhanced Jacquez statistic are visualized in a three-dimensional space-time cube. The cube was implemented using the R environment for statistical computing [49] and the Scatterplot3D library [50]. An illustration of this cube with the Burkitt's Lymphoma cases from 1961-65 is shown in Figure 3. The x- and y-axes of the cube correspond to the spatial coordinates of the cases while the z-axis or height of the cube corresponds to the temporal dimension. Events are plotted in space and time along with the mutual nearest neighbor linkages comprising the J_5 statistic, visualized as bold black lines.

The user is able to rotate the cube to explore the cases and their interaction with one another. In examining these cases in the space-time cube, a number of centers of interaction are apparent. However, it is difficult to gauge the proximity of cases in this implementation of the cube because the user has no sense of perspective. This lack of perspective is recognized as one of the issues with this visualization approach [51, 52]. The disorientation may be mitigated somewhat by utilizing the cube in conjunction with maps and other graphical displays to best highlight trends in data [53].

[Figure 3 about here.]

In exploring the results as presented in the space-time cube, it became apparent that most information was actually gleaned from a quasi-areal perspective (seen mainly as a map) or from a side view where either the x- or y-axis is placed horizontally in front of the user while the z-axis remains vertical. Consequently, the best static method to display this information is in a multi-paned graphic comprised of four elements: the space-time cube, a conventional map of space-time linkages, a slice of the space-time cube with the y-axis of the plot in the traditional horizontal location of the x-axis and time in the vertical location of the y-axis, and a slice of the space-time cube with the x-axis in its traditional location and time in the location of the y-axis. These elements are shown in Figure 4.

[Figure 4 about here.]

An examination of the linkages identified as Cluster 1 in the space-time cube (Figure 4d) reveals the utility of this multiple perspective approach. If the user were to consider only the static space-time cube presented in Figure 4d, the projection effect resulting from viewing three-dimensional phenomena on a two-dimensional surface (i.e. computer screen or paper) [53], may lead the user to believe that this cluster of linkages is close in space to Clusters 2 and 3. However, when the clusters in the cube are considered in conjunction with the map (Figure 4a), x-axis profile (Figure 4c), and y-axis profile (Figure 4b), it becomes obvious that this cluster is quite distant from Clusters 2 and 3. This multi-paned perspective also helps to identify that Cluster 1 is located between Clusters 2 and 3 in time. Based solely on the view afforded by the static space-time cube however, it may appear Cluster 1 occurs after the other two clusters in time.

This example clearly demonstrates that multiple perspectives are needed to fully understand the distribution of the links generated by the Jacquez test. This visualization approach is similar to the dynamic linking techniques advocated by Andrienko et al. [52], which enables users to translate the three-dimensional visualization of phenomenon in the space-time cube to a two-dimensional map, or similar frame of reference, without losing their orientation. Although more interactive and dynamic approaches, such as that developed by Andrienko et al. [52], may prove more useful for exploring the Jacquez results, a key advantage of the technique presented in this paper is that it effectively visualizes three-dimensional phenomena on a two-dimensional surface and is thus more relevant for print media.

5.2.2 Comparison with Knox Visuals

Finally, as part of the work to visualize the results of Jacquez test, the results are compared to those of the Knox test. Given that the Knox results are not conventionally visualized in a space-time cube, the comparison was made using the linkages as they are represented on a conventional map. To visualize the results of both tests, the data from 1961-1965 are used and the Jacquez linkages are shown for J_5. For the Knox test, critical thresholds of 13 kilometers (space) and 90 days (time) were used to approximate the distance and time associated with a average spatial and temporal distance associated with the links for J_5 according to Figure 2. These maps are shown in Figure 5.

The comparison reveals general consistency between the location of links identified by the two tests: both identify strong interaction in the northwest portion of the study area and weaker interaction in the southern portion. It is apparent that the Jacquez test identifies more space-time links than the Knox test. This is due to the more robust nearest neighbor approach of the Jacquez, which is unconstrained by the set thresholds of the Knox test and thereby adjusts the definition of adjacency based on event concentration. Its nonlinear nature also allows it to detect a greater number of links in areas with a more dispersed concentration of events (i.e. the southern part of the study area). Generally though, there is visual agreement between the two tests, which corroborates the findings from Section 5.1.2. After exploring the results using the different perspectives offered by the space-time cube, however, it is apparent that plotting the results using only a map as a visual aid tells only part of the interaction story.

[Figure 5 about here.]

5.3 Incorporating Population Shift

Having addressed the issues of ambiguous spatial and temporal scales of interaction, and visualization of the Jacquez test results, this section focuses on the last of the three shortcomings associated with this test: population shift bias. As discussed above, heterogenous changes in the underlying population from which events are drawn can artificially inflate the α values for a test of space-time interaction and lead to an increase in Type I errors if the changes are not reflected in the probability distribution used to assess the significance of the results [11]. Here, a method is demonstrated that illustrates how to conduct statistical inference for the Jacquez test in study areas that experience such heterogeneous population growth (or contraction). The method follows the general framework provided by Kulldorff and Hjalmars [11], but differs in that it does not base inference on a standard probability distribution (e.g. Poisson or Normal as in the case of the Knox test). Instead, a Monte Carlo method is employed to account for the fact that the exact probability distribution for the Jacquez test is unknown[8]. Unlike standard Monte Carlo approaches to significance testing for space-time interaction however, the reference distribution does not come from a permutation of the observed data. Instead the reference data are simulated based on knowledge of the underlying population and its dynamics through time. The steps for conducting an unbiased test of space-time interaction, outlined by Kulldorff and Hjalmars [11], are described below as adapted for the Jacquez test.

Step 1: Generate N random event datasets such that each contains the same number of events, λ, as the observed data. The events in the simulated datasets must be distributed randomly throughout the study area and time period of interest based on probabilities proportional to the population at all given location and time combinations (for an extended explanation see [11]). To achieve this, there must be an estimate of the spatial and temporal distribution of the underlying population across the study area throughout the time period of interest. Although an exact and continuous measure of the underlying population throughout time is more than likely unavailable, reasonable discrete estimates can be made based on population information available through time for defined spatial units. For our example, population estimates were derived for the counties in the West Nile district for the periods 1961-65 and 1972-73 based on the methodology described in Section 4.

Step 2: Calculate the test statistics for the observed and N simulated datasets. Here, the J_k statistics for $k = 1$ through 25 for the period 1961-1965 and $k = 1$ through 35 for the period 1972-1973 were calculated.[5] A combined test across multiple values of k could also be specified and either formulation of the test, the cumulative or the k-specific measure (J_k or ΔJ_k) could be used.

[5]These values of k correspond to the range of values over which significant interaction was identified in Section 5.1.1.

Step 3: Finally, the pseudo-significance of the Jacquez test statistic for the observed data is determined by ranking it within the distribution of test statistics for the N simulated datasets. The number of statistics greater than the observed value is tallied. This number, c, is then inserted into Equation 3 to get the unbiased pseudo p-value for the combined Jacquez test.

The result of this process for the Burkitt's Lymphoma data for the 1961-1965 and 1972-1973 periods are presented in Figure 6. The pseudo p-values generated by the unbiased generation approach are compared to the pseudo p-values generated by the biased permutation approach originally advocated by Jacquez (for both, $N = 999$). The results show that for these data, there is very little difference in the results generated by the unbiased and biased methods of assessing pseudo-significance. However, as anticipated from the results provided by Kulldorff and Hjalmars [11] and Mack and Malizia [22], the unbiased values are slightly higher than those provided by the biased estimation across most values of k where significant interaction was observed.

[Figure 6 about here.]

The small difference between the p-values for the unbiased and biased version of the test reflect the slightly heterogeneous growth of the underlying susceptible population. By not accounting for this growth, the original test for space-time interaction is minimally biased, with an associated p-value lower than it should be due to the population shift. Even after accounting for this bias, though, by adjusting for the heterogenous growth in the underlying population, the statistic still remains significant at an α level of 0.05 for most values of k. In this example, the difference in results produced by the two methods is minimal because of the small population shift during the relatively short time periods examined here. Population shift bias becomes more of a problem when more dramatic heterogenous population change occurs over longer time periods [11] or when the population changes occur in short time periods examined using a high number of temporal intervals [22]. In these situations, the user should take care to assess significance of the Jacquez results using the unbiased approach to avoid increasing the likelihood of Type I errors.

As a brief illustration of this point, we compare the results for the biased and unbiased versions of the Jacquez test using space-time event data randomly generated within the hypothetical populations created by Mack and Malizia [22]. Their study quantified potential population shift bias in three population movement scenarios for an artificial metropolitan area. Approximately 33% of the metropolitan population concentrated daily in work, shopping and entertainment areas in their low movement scenario, 54% in the medium movement scenario and 78% in the high movement scenario.[6] Here, we generate a random set of space-time events ($\lambda = 100$) within the population of each scenario and test the data for space-time interaction ($N = 999$) over a range of k (1

[6]The reader is referred to the original study for a full explanation of the movement scenarios and the geography of the hypothetical metropolitan area.

to 15) using the biased and unbiased versions of the Jacquez test. The differences in p-values estimated by the biased and unbiased tests for the data generated within each scenario are compared in Figure 7.

[Figure 7 about here.]

Figure 7a shows a minimal difference between the biased and unbiased p-value estimates for the low population movement scenario. However, as the population movement increases, greater differences can be observed between the two versions of the test. The gap between the biased and unbiased p-values widens for the medium movement scenario (Figure 7b) and expands further in the high movement scenario (Figure 7c). The positive relationship between the difference in p-values and degree of population movement is further illustrated in Figure 7d, which plots the differences across all scenarios for each value of k. Collectively, these results further illustrate the necessity of employing the unbiased version of the Jacquez test for situations where heterogenous population changes may underly an event pattern.

6 Discussion and Conclusions

The Jacquez test for space-time interaction has been shown to be quite powerful and has demonstrated greater flexibility over other tests of space-time interaction. The test is particularly relevant for studies where the suspected interaction is nonlinear or does not conform well to the explicit thresholds presumed by other tests. Despite the advantages associated with this test however, it has been utilized in practice less frequently than other tests of space-time interaction. Potential reasons for this limited application are the ambiguity associated with diagnosing the spatial and temporal scale at which interaction occurs for a k nearest neighbor based test statistic and the limited visual output of the test.

However, with the three enhancements developed in this study the utility of this test is greatly improved. These enhancements better contextualize the test's results in terms of real world distances and times, provide tools to visualize the results, and ensure the results are free of population shift bias. The additional information gleaned from these enhancements combined with the visualization tools help make the Jacquez test results more relevant and easily interpreted. Additionally, by accounting for population shift bias, the specificity of the test has been increased. In spite of these contributions however, future research is necessary to expand upon the visualization of the enhanced Jacquez test results presented in this study.

While our work presents a key first step in visualizing the results, additional efforts could be directed at visualizing the results in a more intelligent dynamic space-time cube. Specifically, the cube could be made to interact with the map and perspective views presented here, through dynamic linking and brushing techniques [52, 53]. Implementation of these tools would mitigate the abstraction of the cube. Further work also needs to be invested in developing methods for the space-time cube to allow for the display of a greater number of observations. Although the dataset employed in this study was small, orientation issues are still present when rotating the cube. This problem will only be compounded with the use of larger datasets or examining linkages generated by a larger value of k. However, the inclusion of more ancillary data within the cube itself may assist with this problem. Such improvements may help move the cube beyond a simple results visualization tool into the realm of a visual analytic tool to investigate potential causality and provide explanations for observed interaction [54].

Along with improvements in visualization, further work remains on the decomposition of the Jacquez results in terms of the spatial and temporal scales associated with each level of k. While this work presents an average of the distances and times associated with different levels of nearest neighbor linkages, additional techniques for summarizing these distributions of spatial and temporal data should be explored. Simple extensions might include the use of the median distance and time between nearest neighbor events, in place of the mean. Additional work might also explore the variability within the distribution of distances associated with each level of k in space and examine how it changes through time (and vice versa). This may yield a more complete picture of the scale of interaction.

However, the manner in which the spatial and temporal scale of interaction is diagnosed in this study certainly provides useful information that can be used to approximate the scale of space-time interaction. This information can be used in a comparative context to evaluate the results of other tests for space-time interaction. Alternatively, this scale information might also be used to better inform the selection of critical space and time thresholds for the computation of the Knox test, or the space and time subintervals necessary for the computation of the space-time K function. Such information obtained from the enhanced Jacquez test would be particularly beneficial if the researcher has no prior knowledge of the scale of interaction, and would thus reduce the subjectivity associated with the selection of spatial and temporal thresholds needed by other tests.

Although additional work remains, the enhancements presented in this study represent a series of useful techniques that transform the Jacquez test into a complete, descriptive, informative metric that can be used as a stand alone measure of global space-time interaction. Not only do these enhancements address some of the suggestions for the Jacquez test made by prior studies, such as the development of an unbiased Jacquez test [11], but these enhancements open the door to increasingly sophisticated evaluations and visualizations of space-time interaction.

7 Acknowledgements

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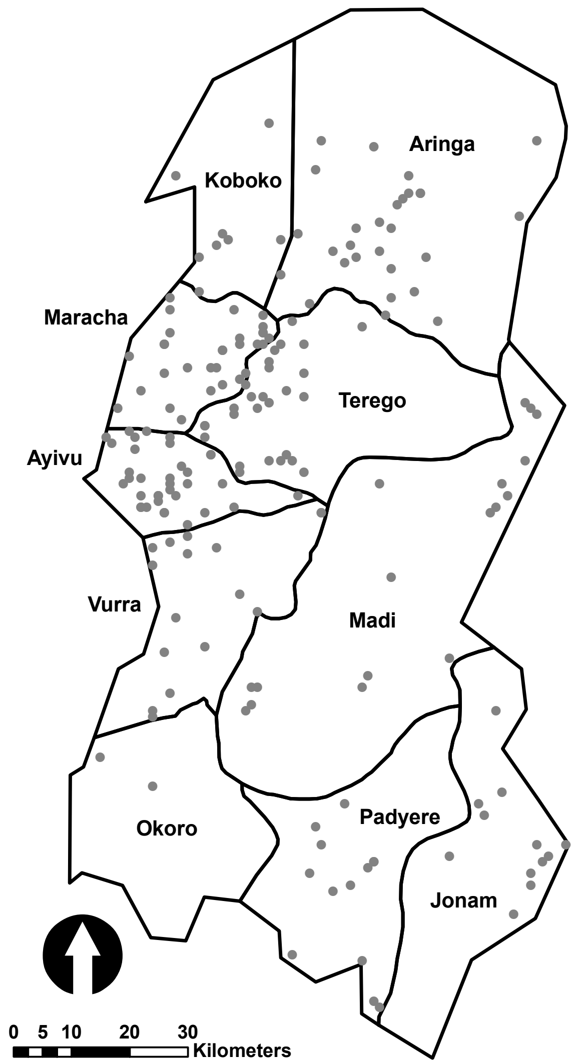
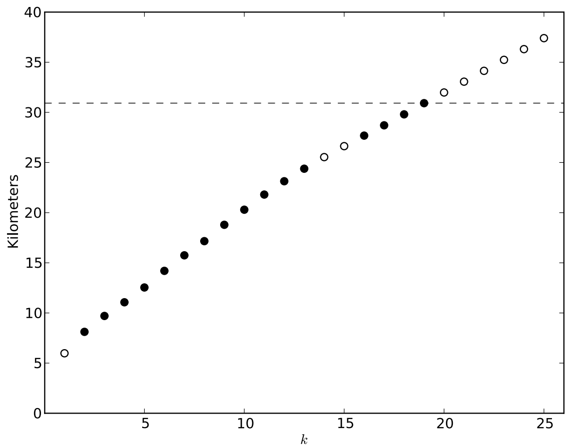
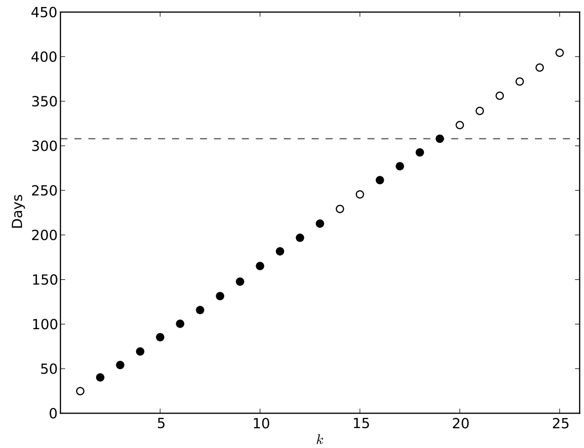


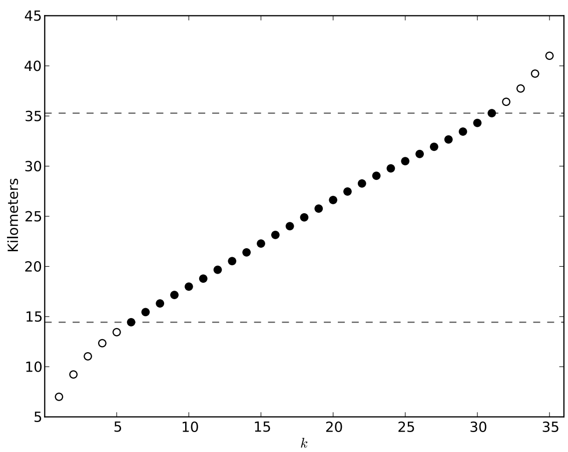
Figure 1: West Nile district of Uganda. Cases of Burkitt's Lymphoma between 1961 and 1975 are shown as grey dots.



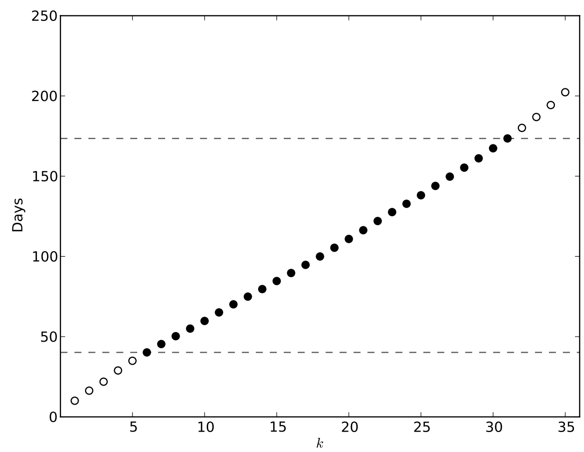
(a) 1961-65 spatial scale.



(b) 1961-65 temporal scale.



(c) 1972-73 spatial scale.



(d) 1972-73 temporal scale.

Figure 2: A collection of plots to contextualize the J_k results for the 1961-1965 and 1972-1973 time periods. The pseudo-significance of test statistics is determined via the traditional permutation approach (using 999 permutations) and is denoted by filled circles. The dashed lines denote the approximate scale of observed space-time interaction.

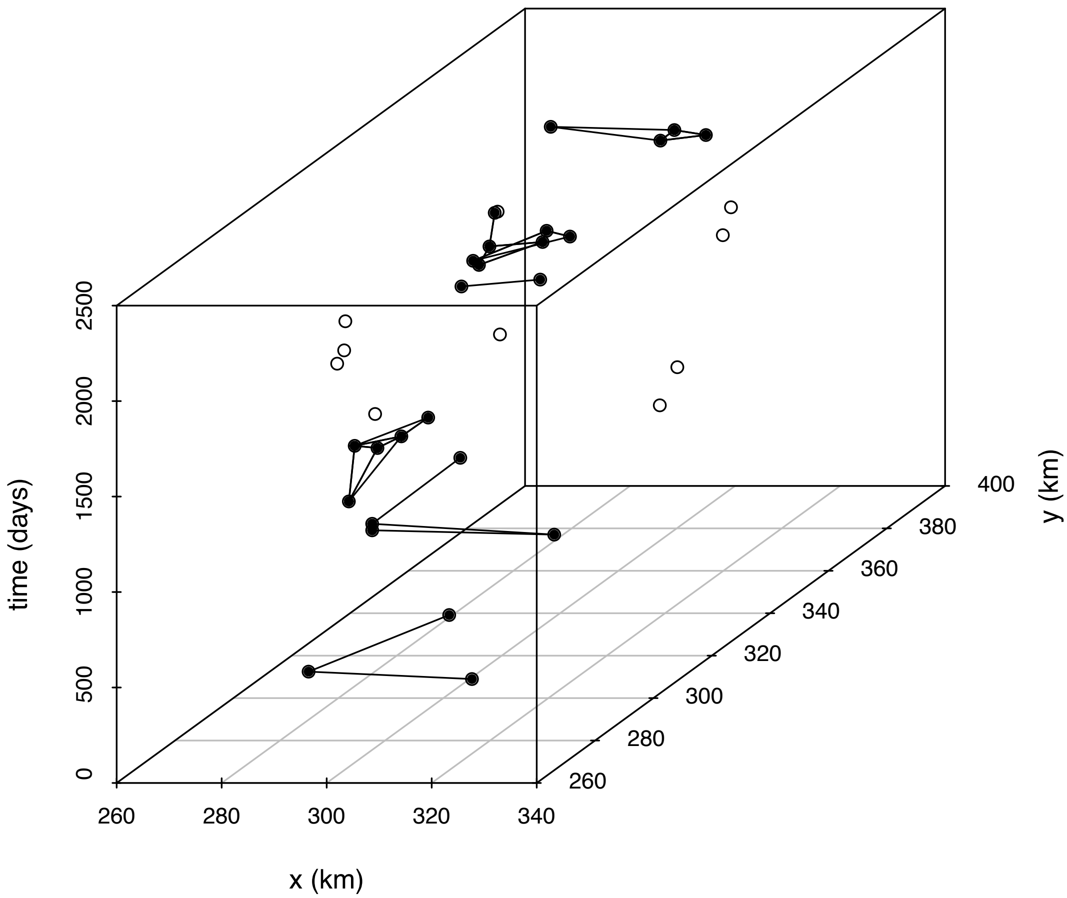


Figure 3: Space-time cube of cases for 1961-65 and connections for J_5.

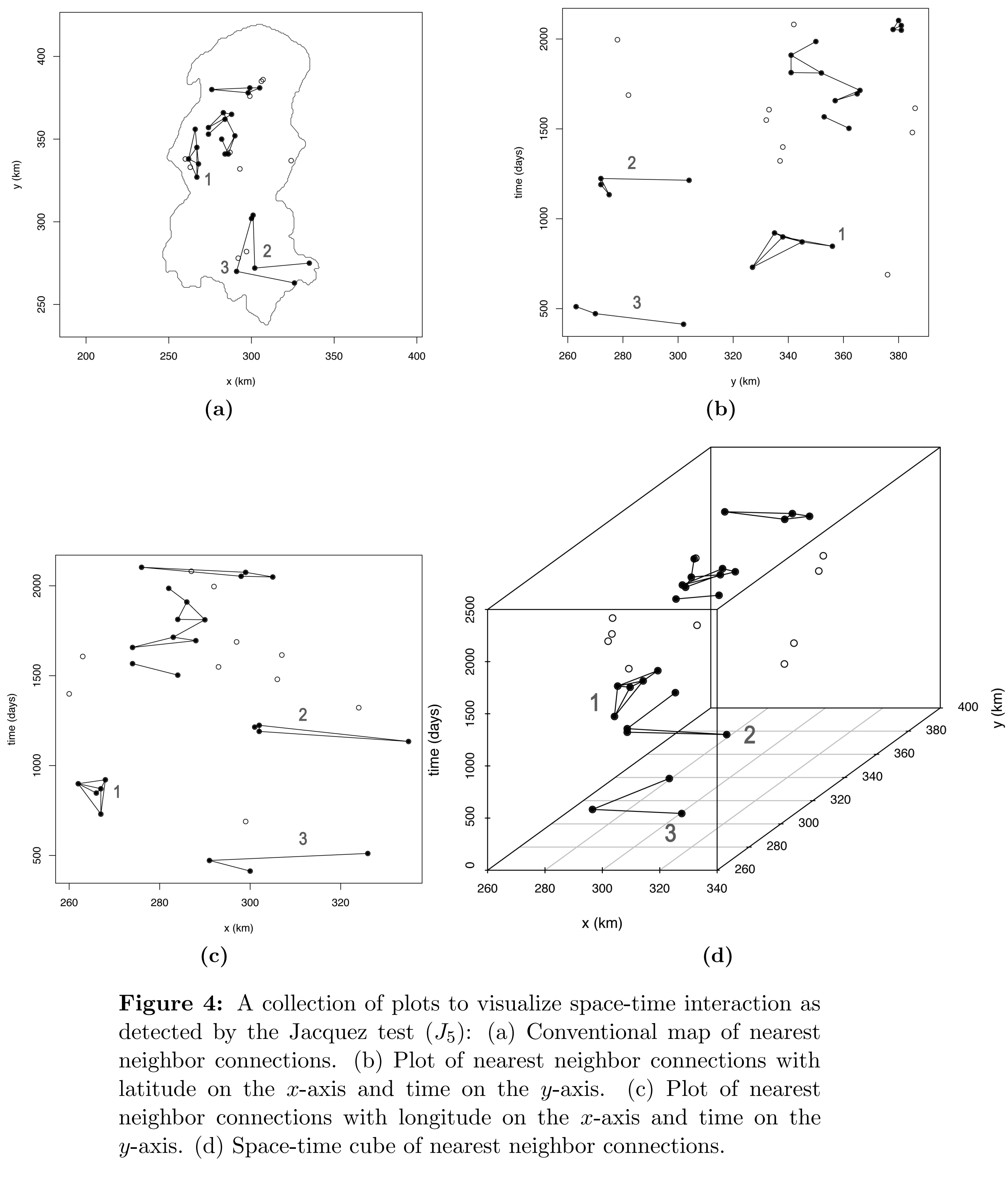
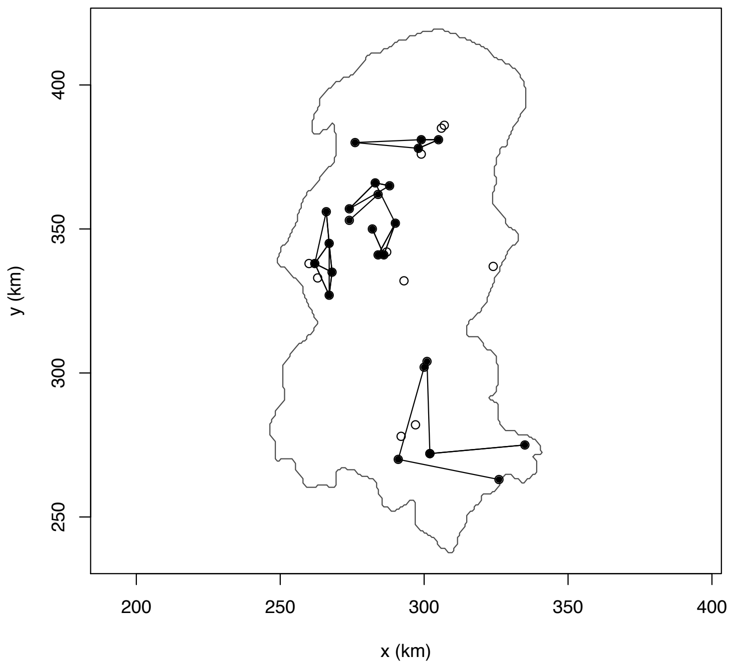
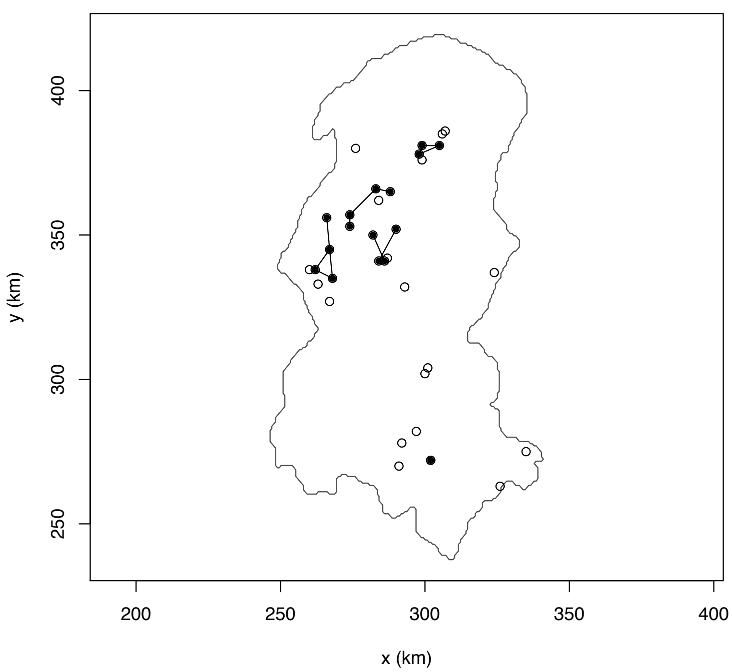


Figure 4: A collection of plots to visualize space-time interaction as detected by the Jacquez test (J_5): (a) Conventional map of nearest neighbor connections. (b) Plot of nearest neighbor connections with latitude on the x-axis and time on the y-axis. (c) Plot of nearest neighbor connections with longitude on the x-axis and time on the y-axis. (d) Space-time cube of nearest neighbor connections.

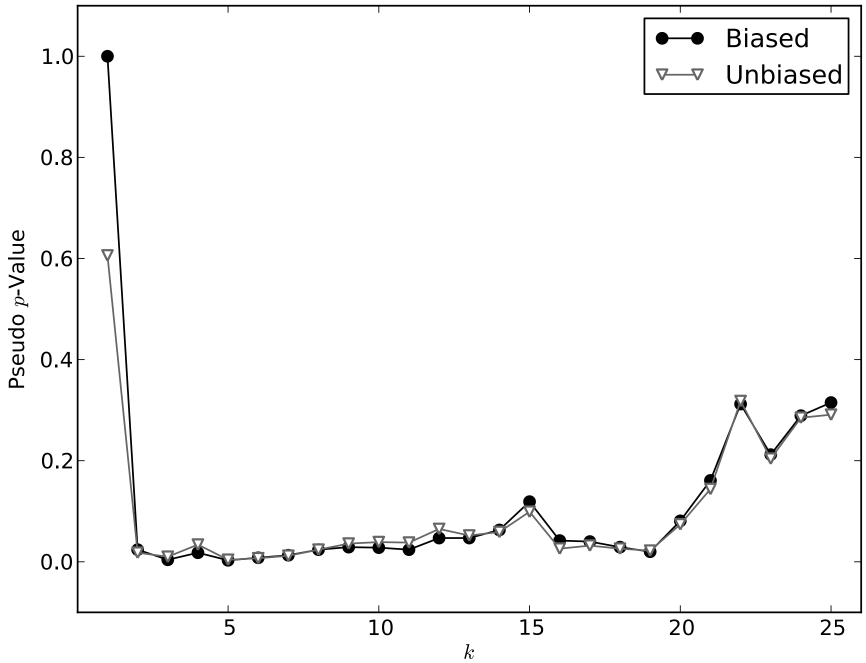


(a) Jacquez links.

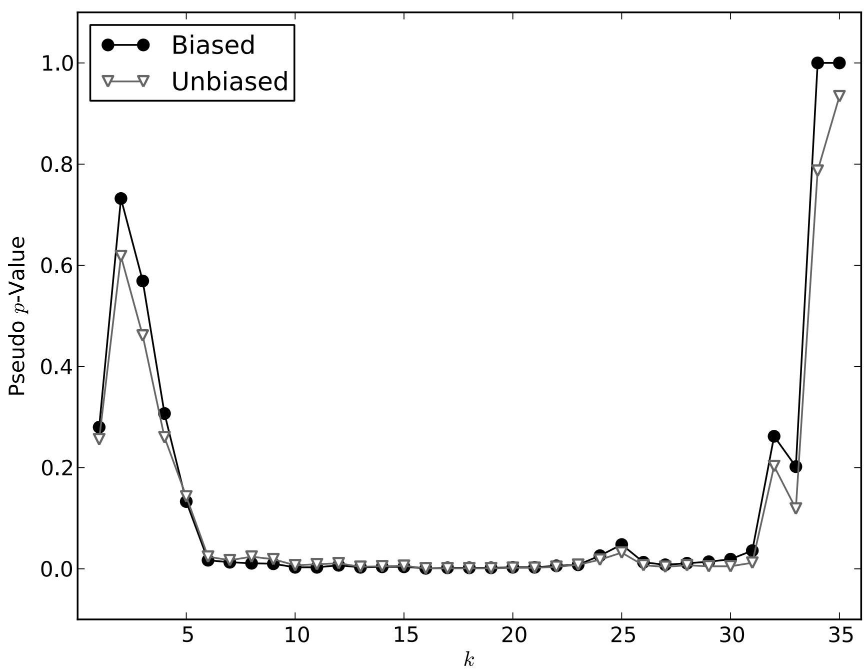


(b) Knox links.

Figure 5: A comparison of the locations of significant linkages identified by the Jacquez ($k = 5$) and Knox (space = 13 km, time = 90 days) tests.



(a) 1961-65.



(b) 1972-73.

Figure 6: A comparison of the biased and unbiased combined Jacquez test results

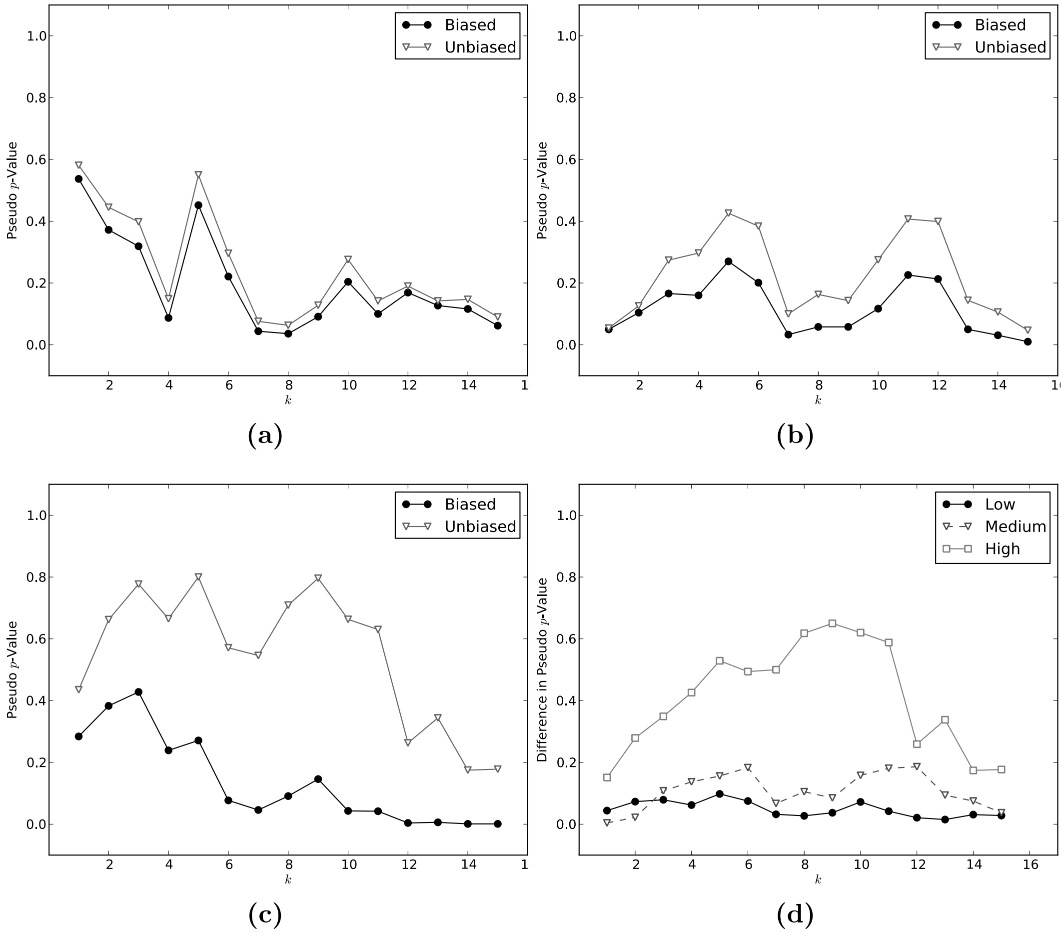


Figure 7: A comparison of biased and unbiased J_k test results for the three population movement scenarios described by Mack and Malizia [22]. This includes plots of results for the (a) low movement, (b) medium movement and (c) high movement scenarios as well as (d) the difference in results across all scenarios.

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		Population		
County	Cases	1961	1975	% Change
Koboko	9	23,081	48,918	112
Aringa	31	42,265	67,018	59
Maracha	25	48,545	67,089	38
Terego	34	44,134	66,483	51
Ayivu	36	57,108	89,645	57
Vurra	14	28,114	39,721	41
Okoro	4	50,839	100,753	98
Padyere	12	48,747	96,606	98
Jonam	13	27,138	69,125	155
Madi	15	29,628	60,237	103

Table 1: Population trends and cases of Burkitt's Lymphoma in the West Nile District derived from Williams et al. [23].

Period	Cases	Statistic	p-value
61-65	35	10.484	0.001
66-70	72	2.513	0.571
71-75	81	3.004	0.498
72-73	37	7.452	0.005

Table 2: Results for the combined Jacquez test (J_k) across the study time periods based on 999 permutations.