

Title: Spatiotemporal models to delineate West Nile virus transmission cycles as high-risk exposure areas at local scales

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Abstract

Various approaches are used to estimate density and clustering of unusual sightings of West Nile Virus (WNV) infected dead birds or human cases to delineate high-risk exposure areas. A significant and largely unmet need is to incorporate the temporal characterization of virus spread and locational information of all the components of transmission cycle, involving birds (reservoir), mosquitoes (vector), and humans (host) on a localized scale. Exposure areas involving all the three components of the WNV cycle in close proximity have higher potential to amplify an outbreak as compared to risk areas delineated by a single component only. In this paper, I developed two novel approaches to identify WNV cycles on micro scales. The first method, 'Nearest-Neighbor-Distance-Time' (NNDT) is based on calculated distance thresholds and the time required for the virus to be transmitted from one component to another in the cycle. The second method 'COMPOSITE' is an overlay of density estimation and spatiotemporal clustering of dead birds, mosquitoes, and human cases. I situated this research in the Twin Cities Metropolitan Area of Minnesota (TCMA). The NNDT method identified localized WNV transmission cycles with an area ranging from 5 to 150 sq miles. The years 2002 and 2003 had three such WNV cycles, followed by one, two, and five in 2004, 2005, and 2006 respectively. The COMPOSITE method also located several high-risk areas in the TCMA. In 2004 and 2006, the NNDT and COMPOSITE method identified two intense WNV transmission cycles at exact locations near North and South St. Paul region.

1. Introduction

West Nile Virus (WNV) is a vector-borne infectious disease spreading rapidly throughout the United States and infecting thousands of bird, human and animal lives. It is transmitted to humans and other mammals by mosquitoes that acquire the virus by feeding on infected birds (CDC 1999, Rappole *et al.* 2000, CDC 2002, MDH 2003). Most people infected with West Nile virus are asymptomatic or experience only a flu-like illness. In others, the virus causes West Nile fever (CDC 1999) and in some of these, the infected people develop West Nile encephalitis (inflammation of the brain) or meningitis (inflammation of the lining of the brain and spinal cord), both of which can be fatal (CDC 1999, Hayes *et al.* 2005, Grinev *et al.* 2006, Hayes 2007).

The geographic distribution of WNV has expanded since its discovery in Uganda in 1937 and now includes all continents save for Australia and Antarctica (Hayes 2007). In the United States, the virus first appeared in the Bronx borough of New York in 1999 (CDC 1999). Since then, this emerging virus has spread rapidly west and south causing seasonal epidemics and infecting thousands of people and native American wildlife population.

It is challenging to predict and explain the spread of WNV because it propagates via complex interrelationships between human, avian, and mosquito habitat systems coupled with environmental, built-environment, and anthropogenic risk factors (Brownstein *et al.* 2002, Ruiz *et al.* 2004, Gibbs *et al.* 2006). This complexity prompted both laboratory and field analysis of WNV (Theophilides *et al.* 2006). The laboratory analyses focused mainly on experiments that investigated the biological potential of mosquitoes and birds to acquire and transmit the virus (Komar 2003). The field analyses investigated the interaction of avian-human-environmental systems to explain the dynamics and spatiotemporal spread of the virus among birds, mosquitoes,

and humans (Cooke *et al.* 2006, Liu *et al.* 2006, Vaughan *et al.* 2006, Bolling *et al.* 2007, Cupp *et al.* 2007, Gleiser *et al.* 2007).

A significant part of the field analyses focused on identification of WNV high-risk exposure areas based on proxies for WNV presence and measurable environmental, socioeconomic, demographic, built environment, and anthropogenic factors (Chuang *et al.* 2007, Diuk-Wasser *et al.* 2007, Nielsen *et al.* 2007). This approach is significant for two reasons. First, public-health officials and mosquito control agencies can intervene with control measures and reduce the risk of infection among humans in the delineated high-risk areas. Second, delineation of high-risk exposure areas at various scales allow researchers to further investigate bird and mosquito habitat characteristics, their feeding behaviors, various environmental and anthropogenic risk factors at localized scales.

In this paper I develop two novel approaches to identify WNV transmission cycles in its entirety as exposure areas by focusing on the dynamics of birds, mosquitoes, and humans on local scales. I situated this research in the Twin Cities Metropolitan Area (TCMA) of Minnesota (Figure 1). The virus first reached Minnesota in 2002, creating epidemiological hotspots of WNV infections in 2003 (MDH, 2003) and 2007 saw one of the severest incidences of WNV in Minnesota. The increasing occurrence of warmer and wetter falls in Minnesota suggests that mosquito lifespan may increase, leading to increased incidence of WNV infections in the future (MDH 2005).

<Figure 1 somewhat here>

2. Background

Initial studies focusing on delineation of WNV high-risk area appeared with the measurement of densities of infected dead birds (Eidson *et al.* 2001a, Eidson *et al.* 2001b, Mostashari *et al.* 2003, Eidson *et al.* 2005). Density estimation results in a smoothed surface showing the spatial variation of local densities of points (in this case location of WNV-infected dead birds) at a user specified search radius. In simple terms, a smoothly curved surface is fitted over each point, where the density value is highest at the location of the point and diminishes with increasing distance from the point and reaching zero at the search radius or the kernel from the point (Diggle 1985, Berman *et al.* 1989). This approach, however, has a number of limitations. First, density estimation algorithms are not robust and select an arbitrary cutoff search radius to estimate density and identify high-risk areas for WNV. Second, density is highly susceptible to dead bird reporting due to confounding effects of population density, the varying level of interest of different communities to report dead birds, and absence of people in non accessible area to report dead bird locations (Mostashari *et al.* 2003). Third, density calculations assume uniformity of distribution of infected birds throughout the area, which can be at odds with the reality of ‘hotspot’ detection. Fourth, calculation of densities using kernel functions is subject to edge effects, resulting in inaccurate estimation of densities near the boundaries, although there are methods for edge correction (Theophilides *et al.* 2003). Fifth, delineation of high-risk areas for WNV based on only one component (dead birds or human cases) of WNV transmission cycle is incomplete and might be misleading given the multi-host nature of the disease. This can be problematic given that prevention and control strategies based on limited information can be ineffective and costly. Sixth, density measures ignore the biology and

ecology of WNV transmission cycle. Seventh, dead bird density approaches also did not account for the temporal characterization of virus transmission.

There is also a range of existing spatial and temporal models that are used to identify high-risk exposure areas of WNV (Daley *et al.* 1999). Though these methodologies attempted to overcome some of the limitations of density measures, they also have number of shortcomings. First, spatial and temporal process based models often assume *a priori* distributions, namely Poisson or binomial to locate clusters of WNV infected dead birds or human cases that does not map onto the complex interactions among birds, mosquitoes, and humans in a WNV transmission cycle. Second, similar to the density based approaches, these techniques typically center on a single host (usually dead birds or positive human cases) to identify exposure areas, likely missing exposure areas involving all the three components of the transmission cycle in close proximity that have a higher potential to amplify a WNV outbreak as compared to risk areas delineated by a single component only. There is limited research on methodologies that account for both spatial and temporal characterization of virus transmission as well incorporate multi-host ecological information of WNV to identify high-risk exposure areas.

In this paper, I address several of the above challenges in identifying WNV exposure areas by developing two methods that combine geographic principles, distance-time interactions, and ecological knowledge of WNV transmission cycles. The first method is 'Nearest-Neighbor-Distance-Time' (NNDT), which is based on the calculated distance thresholds and the time required for the virus to be transmitted from one component to another in the cycle. The second method is 'COMPOSITE', which combines density estimation approaches with the spatiotemporal clustering of dead birds, mosquitoes, and human cases. Together, these two approaches provide a new way to delineate WNV exposure areas at various scales.

3. Materials and Methods

3.1 Data Description

The study used three datasets for the years 2002 to 2006. First, the Metropolitan Mosquito Control District (MMCD) provided the location and the date of WNV infected dead birds (crows and blue jays) as reported by public. The raw data were later geocoded at the street level, verified, and cleaned with occasional field validation by MMCD staff. Second, MMCD also provided the location of WNV positive mosquito pools or traps designed to sample mosquitoes of different species for viral analysis on a weekly basis (MMCD 2004). Pool data included collection date, species type, and number of infected mosquitoes in the pool. Third, the Minnesota Department of Health (MDH) provided the location and the onset date of infected human cases by zip code. Because of confidentiality of human health-related data and the guidelines of the University of Minnesota's Institutional Review Board (IRB), I obtained WNV-infected human cases aggregated by zip codes. Table 1 details these data.

<Table 1 somewhat here>

3.2 Methods

In the following paragraphs, I will describe the methodology of NNDT and COMPOSITE, which were later used to delineate WNV transmission cycles at micro scale from the year 2002 to 2006 in the TCMA.

3.2.1 Nearest-Neighbor-Distance-Time (NNDT)

The 'Nearest-Neighbor-Distance-Time' (NNDT) method evaluated distance thresholds based on the spatial distributions of WNV infected dead birds, positive mosquito pools, and zip codes with infected human cases in the TCMA. Hence, the estimated distance thresholds generated by this method were 'local' in the sense that they were sensitive to sub-regional

variations in WNV incidence. Calculating NNDT involves: 1) calculating Euclidian distances to the nearest dead bird or mosquito pool location; 2) creating spider diagrams for these nearest neighbors centered on zip codes with human cases; and 3) categorizing spider diagrams by whether they were connected to both dead birds and mosquito pools, zip codes connected to either locations of birds or mosquito pools, and or connected to neither, 4) including the temporal thresholds to further categorize spider diagrams for the final WNV cycle delineation process.

First, I calculated Euclidean distances from the centroid of zip codes with at least one WNV-infected human case to the nearest location of a dead bird and a positive mosquito pool (Table 2). The maximum, minimum, and mean distances from the centroid of zip codes to the nearest location of a dead bird were highest for the year 2002 (Table 2). WNV cases were first identified in 2002 in Minnesota and there were 102 reports of infected dead birds. This is probably an undercount because this was the first year that WNV was detected in Minnesota and there was lack of general knowledge or awareness of the disease early in the year. When incidences of WNV peaked in the year 2003, the distances dropped significantly, where the minimum and mean distances of location of infected dead birds from the centroid of zip codes were 0.12 and 1 mile respectively. There was an apparent negative relationship between the distance measures and the number of dead bird reports. For example, in the year 2005, there were only 60 locations of dead birds and the mean distance from the centroid of a zip code to a nearest location of dead bird was as high as 4 miles. However, with the increase of locations of dead birds in the year 2006 (479 cases) the mean distance decreased significantly to 1.5 miles. This is somewhat expected given that, all other things being equal, an increase in incidence also increases the likelihood that a human case will have a bird case nearby.

<Table 2 somewhat here>

It was a challenge to tease out spatiotemporal patterns from the raw Euclidean distances from the centroid of zip codes to the nearest positive mosquito pools mainly because of the nature of mosquito abatement and surveillance programs conducted by the MMCD. The surveillance of *Culex* species mosquitoes, the main vector of WNV transmission, increased from 2002 onward. Given that the traps are inspected weekly (as noted above) temporal analysis of WNV positive mosquito pools will be biased in the sense that they are not gathered daily. However, since mosquito collection day and time are constant, these data can still be effectively used to delineate WNV high-risk areas.

In the second step, for each year, the mean distances from the centroid of zip codes to the nearest location of infected dead bird and mosquito pools were then used as the cut-off distances for *spider* diagrams. A spider diagram joins a single source feature to a set of nearest destination features (points, lines, and polygons) based on the user specified distance threshold. Here the centers were the centroids of zip codes with at least one WNV human case and destination features were locations of dead birds and positive mosquito pools. Figure 2 shows an example of a spider diagram for the year 2006. In the figure, the center of the spider diagram connected six locations of nearest dead birds and two mosquito pools by *spider legs*. Similar spider diagrams were generated for all zip codes with at least one human case from the year 2002 to 2006.

<Figure 2 Somewhat here>.

In the third step, the spider diagrams, centered on zip codes were categorized into 3 groups: spider diagrams connected to both dead birds and mosquito pools, spider diagrams connected to either locations of birds or mosquito pools, and spider diagrams connected to neither. The first category of spider diagrams (those with both dead birds and pools) were further divided based upon the temporal thresholds and epidemiology of transmission of WNV from

birds to mosquitoes, and then from mosquitoes to humans following the transmission route in a typical cycle. Spider diagrams centered on zip codes were selected only when they satisfied the temporal sequence of actual WNV infections, or when the reporting dates of the dead birds within the reach of the spider diagram (or '*web*') were 10-15 days prior, and the testing dates of mosquito pools were 5-7 days before that of the onset date of human cases located in that zip code. Finally, WNV transmission cycles were identified by drawing circles centered on the zip codes of selected spider diagrams and greater of the mean distances to locations of dead birds and mosquito pools as the radius in that particular *spider web*. Figure 3 shows the steps involved in the NNDT method.

<Figure 3. Somewhat here>

3.2.2 Composite

The COMPOSITE method combines a kernel-smoothing algorithm and spatiotemporal cluster analysis of WNV-infected dead birds, mosquito pools, and human cases. This involves three steps: 1) kernel density smoothing to visualize high and low-density regions of WNV-infected dead birds; 2) spatiotemporal cluster analysis of dead bird locations; and 3) overlaying the results of steps 1 and 2 on the spatial location of mosquito pools and infected human cases.

First, I used kernel density smoothing to visualize spatial locations of high and low-density regions of WNV-infected dead birds. The kernel width (the size of the moving window) ranged from 2 to 5 miles for the estimation of smoothed density maps of spatial distribution of infected dead bird locations from the year 2002 to 2006. Although density maps are quick and simple way to spatially locate hotspots, there is subjectivity in choosing the kernel width. In this study I estimated the kernel from the mean distances between the centroid of the zip codes with at least one WNV infected human case and the nearest location of a dead bird (Table 1). Another

drawback to standard kernel density smoothing is that it lacks the temporal characterization of virus amplification.

In the second step, in order to overcome the shortcomings of density smoothing, I supplanted the traditional density estimation procedure with a spatiotemporal cluster analysis of dead bird locations using a space-time scan statistic. To generate this statistic, a cylinder defines the scanning window; the circular or elliptical base of the cylinder signifies the geographical space and the corresponding height denotes the temporal window (Kulldorff 2005).

A cylindrical window with variable radius and height then scans the entire study area in space and time, so that for each possible geographical location, it also visits each possible time span. This process creates a number of overlapping cylinders. Here each cylinder reflects a potential space-time cluster and Monte Carlo simulation is performed to estimate the p-value to choose the cluster with maximum likelihood. The space-time scan statistic is used either for a single retrospective analysis using historical data, or for time-specific prospective surveillance, where the analysis is repeated for units of time, such as day, week, or month (Kulldorff 2005). The data used in this study had locations of dead birds with a temporal scale from the year 2002 to 2006 with granularity of a single day. Hence, I used a retrospective space-time scan statistic to detect spatiotemporal clustering of the locations of dead birds. The size of the spatial and temporal window ranged from 2 to 5 miles (same as that of the kernel widths used above) and 7 to 14 days respectively. The choice of maximum spatial and temporal window is based on the flight characteristics of two key species of birds, the Blue Jay and the America Crow. WNV research groups at the MMCD and the MDH confirmed that these cut-off choices were appropriate for capturing bird-mosquito dynamics because an infected bird generally flies about 2-4 miles over the course of the 10 to 14 days they tend to live after being infected by WNV.

In the final step, the outputs of the kernel density and space-time clustering steps were overlaid on locations of WNV positive mosquito pools and zip codes with human cases to provide a single visualization of the spatial locations of the entire WNV transmission cycles. Figure 4 shows the schematic diagram of COMPOSITE methodology.

<Figure 4 somewhat here>

4. Results

4.1 Nearest-Neighbor-Distance-Time

The NNDT method identified localized WNV transmission cycles with an area ranging from 5 to 150 sq miles. To recap, NNDT calculates distance to the nearest dead bird or pool locations, creates spider diagrams for these nearest neighbors, and categorizes spider diagrams centered on zip codes by the extent to which they are connected to birds and mosquito pools and the temporal threshold for transmission of virus in the cycle. The years 2002 and 2003 had three WNV cycles each, followed by one and two in 2004 and 2005 respectively, and five cycles in 2006 (Table 3). I further plotted all the cycles on a single map to highlight the temporal trends (Figure 4).

<Table 3. somewhat here>

<Figure 5. Somewhat here>

For the year 2002, three WNV transmission cycles were identified, all within a distance of 3 to 7 miles from the centroid of zip codes with positive human cases, and covering an aggregate area of about 255 sq miles. Per Figure 5, these cycles were located in the southwestern part of the metro area (Maple Plain, Minnetrista, Chaska, and Eden Prairie). WNV peaked in the year 2003 along with increased bird surveillance and testing of mosquito pools. Three local

WNV cycles were delineated within 1 to 3 miles from the zip codes with human cases. Compared to 2002, the 2003 cycles were much more intense and localized with 44 dead birds, 381 positive mosquitoes, and 7 human cases within an area of approximately 90 sq miles mainly centered on the densely populated areas of Minneapolis and South St. Paul (Golden Valley, Edina, and South St. Paul).

Interestingly, there were no overlapping cycles in 2002 and 2003 because the spread of WNV infection shifted from less-populated suburban areas to more densely populated urban areas. There were two possible reasons for this spatial shift. The first is the habitat characteristics of different mosquito species. According to the reports of pool inspection at the MMCD, there was significant increase in *Culex tarsalis* mosquitoes in 2002, which are typically found in open prairie grasslands and dry short grasses that are common in the southwest metro. This increased vector population likely led to the formation of WNV transmission cycles in the southwest metro area. Conversely, in 2003, there were more *Culex restuans* species, which were predominantly found in urban areas, exemplified by the delineation of WNV transmission cycles in Minneapolis and St. Paul. A similar outbreak of WNV occurred in the urban areas of Chicago in 2003 (Ruiz *et al.* 2004). A second reason lies with data collection. By 2003, public understanding of WNV in Minnesota was widespread, in part due to the news in the local media of infections and deaths the previous year, advertisements and precautionary measures issued by MDH. Greater awareness could create a higher rate of reporting of dead birds, which could increase the number of dead bird locations in areas of greater population (i.e., urban areas). In addition, MMCD also increased the frequency of testing of mosquito-breeding sites for WNV infection between 2002 and 2003.

Only one WNV transmission cycle was located in the year 2004. This particular cycle was unique in its characteristics than the cycles identified in the previous years. It was formed in a very small area of 5 sq miles, where the virus was transmitted from infected birds (8) to mosquitoes (25) and finally to humans (2) in North St. Paul (Location A in figure 5). The Euclidean distances from the human case (centroid of the zip code) to the nearest dead bird was approximately 0.35 miles and 1 mile to the WNV positive mosquito pool. Identification of a transmission cycle in such a small area could be useful to investigate further and understand the potential causal factors of WNV infection. It would also allow researchers to investigate very detailed social and environmental characteristics that determine WNV incidences, such as land cover, population characteristics, presence of stagnant water features, or efficiency of mosquito abatement programs.

The WNV cycles identified in 2005 and 2006 had similarities to those of 2003. The two 2005 cycles shared similar spatial locations in that they were urban, with 17 dead birds, 35 infected mosquitoes and 4 human cases within a combined area of approximately 200 sq miles. In 2006, five WNV transmission cycles had total area of about 130 sq miles and were similar to the 2003 cycles in that they were smaller and intense. The Euclidean distances of dead birds and positive mosquito pools from the human cases located at the centroid of the zip codes were all within a close proximity of 1 to 3 miles and had relatively large combined figures of 102 infected dead birds, 1129 infected mosquitoes, and 8 human cases. The 2006 cycles, like those of 2003 and 2004, were in urban areas of Minneapolis and St. Paul (Brooklyn Park, Minneapolis, Richfield, and South St. Paul).

Temporal analysis of the 2002 to 2006 WNV transmission cycles identified the following trends. In spatial terms, after 2002, the location of the cycles shifted from the suburban western

and southwestern TCMA area to densely populated areas near the cities of Minneapolis and St. Paul. Of these areas, South St. Paul was identified as exposure area for 2003, 2005, and 2006 (Location B in figure 5), and may therefore be an important location for further investigation to identify the causal factors of WNV activities.

In terms of temporal dynamics, the number of birds with reporting dates after the onset date of a human case was very low to negligible i.e., on average the number of dead birds declined from 12 cases before, to one or two cases after the human onset date. This is likely because of localized reduction in bird population due to either bird die-offs or migration, leaving mosquitoes to feed on dead-end hosts like humans and other mammals namely horses. There is also evidence that the WNV cycle reached its peak 10-15 days prior to the onset of human illness and by the time humans developed WNV symptoms, the transmission of virus was disrupted in that area due to lack of substantial number of infected birds.

4.2 Composite

COMPOSITE produces a map that illustrates the spatial congruence of density of dead bird locations, spatiotemporal clusters of birds; positive mosquito pools, and zip codes with at least one WNV positive human case. I created composite maps for 2002 to 2006 to visualize and delineate WNV transmission cycles at local scales, but for the purpose of explanation, I will focus on the years of 2002 and 2004.

In 2002, a hotspot of infected dead birds was located in southern Minneapolis including smaller cities like St. Louis, Hopkins, and Richfield (Figure 6). Retrospective space-time clustering located a statistically significant spatiotemporal cluster right in the middle of high density of dead bird locations (Figure 6 inset). This space-time cluster has a radius of one mile and a p-value of 0.012, signifying that this area had more WNV-infected dead birds than

surrounding areas. This conforms well onto the fact that there were two zip codes with at least one infected human case close by and a positive mosquito pool with 392 infected mosquitoes within 4 miles of both the center of the dead bird hotspot and spatiotemporal cluster center. The COMPOSITE map of 2004 identified two hotspots of infected dead birds, one in the southwest and the other in North St. Paul (Figure 7). The second hotspot of dead birds (inset) shows formation of a WNV transmission cycle at a small scale that included two spatiotemporal cluster centers, a zip code with at least one positive human case, and a nearby positive mosquito pool with 25 infected mosquitoes. The COMPOSITE maps for 2002 and 2004 highlights the spatial correspondence of bird density, spatiotemporal clusters of birds, mosquito pools, and zip codes in a way that helps one visualize a WNV transmission cycle in its entirety that captures birds, mosquitoes and humans at a micro scale.

<Figure 6 somewhat here>

<Figure 7 somewhat here>

4.3 Comparison of NNDT and COMPOSITE results

The NNDT and COMPOSITE methodologies are complementary, as they delineated WNV transmission cycles as exposure areas at similar spatial locations for the years 2002, 2004, and 2006. In 2002, both NNDT and COMPOSITE identified a WNV transmission cycle in Eden Prairie, located south of Minneapolis (Figure 5 and Figure 6). This WNV cycle included two infected dead birds, 392 positive mosquito pools, and two human cases within an area of 50 sq miles. The number of WNV incidences among birds, mosquitoes, and humans were lower in the year 2004, but both the approaches located a WNV cycle in North St. Paul. This cycle was

smaller than that delineated in 2002, with 8 infected dead birds, 25 positive mosquito pools, and one human case within an area of only 5 sq miles.

In 2006, TCMA experienced higher numbers of incidences for all the components (birds, mosquitoes, humans) of WNV transmission cycle. Among the five micro scaled WNV transmission cycles delineated by the NNDT method, the spatial locations of three cycles were similar to the locations of cycles obtained by the COMPOSITE approach (Figure 8). First area, Richfield, located south of Minneapolis, had a cycle with 44 infected dead birds, 243 positive mosquitoes, and two human cases. Second, both the methods delineated a cycle in Brooklyn Park in northwest Minneapolis, with two infected dead birds, 55 infected mosquitoes, one human case, and covering an area of about 10 sq miles. The third common cycle was delineated near North St Paul with 63 infected dead birds, 68 positive mosquitoes, and 2 human cases.

<Figure 8 somewhat here>

5. Conclusion

This study improves our ability to identify WNV exposure areas. NNDT and COMPOSITE use geographic information techniques to delineate high-risk areas or WNV transmission cycles in their entirety on a local scale, thereby moving away from use of arbitrary “critical” density or clusters of a single component (birds, mosquitoes, or humans) of the WNV transmission cycle. These methods recognize that WNV is transmitted to humans by infected mosquitoes that acquire the virus by feeding on infected birds. Thus high-risk exposure areas for virus transmission will only be effectively delineated by including information from all the components, birds (reservoir), mosquitoes (vectors), and humans (hosts). NNDT is a novel combination of geographic principles, distance-time interaction, and ecological knowledge of

WNV transmission cycle that focuses on delineating cycles in their entirety by examining birds, mosquitoes, and humans at a micro scale. The COMPOSITE method is a useful compliment to NNDT that allows visualization of the entire WNV cycle and providing more contexts on the spatial dimensions of WNV.

Furthermore NNDT demonstrated how Euclidean distances among the location of infected dead birds, positive mosquito pools, and infected human cases infuses a ‘local’ dimension that is combined with the ‘global’ knowledge of the time required for the virus to be transmitted from one component to another in the cycle. NNDT is therefore a quantitative methodology in which the relationship between the distances of spatial location and temporal thresholds of the transmission of virus from one component to another within a cycle is used to delineate exposure areas. The COMPOSITE methodology, on the other hand, provides a simple and effective visualization of the entire WNV cycle at various scales. COMPOSITE brings together the results of density estimation, spatiotemporal clustering of dead birds, mosquitoes, and human case onto a single map with which we can visualize high-risk exposure areas for WNV. The combination of NNDT and COMPOSITE can be used as an effective way to understand WNV cycles, which is an important topic of research as well as providing a tool for the efficient and effective targeting of remediation and control efforts.

The use of NNDT and COMPOSITE methodologies have provided evidence that dead bird reports are an essential part of the delineation of WNV cycles at localized scale. The cycle peaks 10-15 days prior to the onset of human illness, a period that is consistent with the epidemiology of the virus transmission from bird to mosquito and then to human in the same approximate time frame. Temporal analysis of the delineated cycle at local scales also showed evidence of substantial reduction in the reporting of dead birds after the 10 -15 days window

either due to localized reduction in bird population or migration or both. This indicates a signal of reduction in amplification activities due to lack of abundant reservoir (bird) population and virus proliferation ceases further with the onset of human illness. These findings can influence remediation and control strategies. For example, preventive strategies such as insecticide spraying may be best concentrated during the temporal window of 10-15 days after the reporting dates of WNV-infected dead birds because by the time humans develop WNV symptoms in an given area, the risk of further amplification of WNV disease may have subsided and thus widespread spraying of insecticide will have little or no effect. More efficient allocation of resources allows for a better balance between the need for mosquito eradication and desire to limit the environmental impacts of excessive insecticide usage.

Delineation of WNV cycles at local scales also advances our understanding of the complexity of avian-mosquito-human environmental systems on a micro scale. Both the NNDT and COMPOSITE methodologies, for example, delineated a WNV transmission cycle in North St. Paul in 2004. The cycle remained active for 12-16 days prior to the date of human illness and then subsided with substantial decrease in dead bird reporting. These dynamics point to the need to investigate the predilection of mosquitoes to feed on birds or humans, and their feeding behavior, over discrete periods of time. The delineation of WNV cycles and their components at micro scale helps such localized investigations by prompting questions such as “Why did a WNV cycle occur here” or “What environmental and neighborhood characteristics catalyze WNV transmission cycles?”

This paper mainly concentrated on developing novel methodologies to visualize and delineate WNV transmission in its entirety at micro scale. Future research directions include investigation of the complex avian-mosquito-human and environmental interrelationships that

create WNV high-risk exposure areas. Another direction is understanding the extent to which methods such as NNDT and COMPOSITE can be used to understand WNV in other areas of the world where the disease is well entrenched given that the characteristics of transmission cycle and their component varies significantly from one region to another.

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Table 1. Data

Year/ Component	2002	2003	2004	2005	2006	Resolution	Temporal Scale, Resolution	Attributes	Source
Dead birds	102	285	125	60	479	Point	2002-2006, Day	X/Y, Date reported	MMCD
No. of Mosquitoes (No. of Pools)	1101 (5)	388 (17)	26 (2)	161 (14)	1549 (90)	Point	2002-2006, Day	X/Y, Collection date, Trap type, Species, No. of mosquitoes	MMCD
Human Cases	13	26	6	7	15	Zip Code	2002-2006, Day	Onset date	MDH

Table 2. Nearest neighbor Euclidean distances from the centroid of zip code with at least one WNV-infected human case (miles)

Year	Distance to Nearest Dead Birds			Distance to Nearest Positive Mosquito Pool		
	Maximum	Minimum	Mean	Maximum	Minimum	Mean
2002	15.0	1.0	4.0	22.0	1.5	12.0
2003	6.0	0.12	1.0	23.0	1.0	7.0
2004	6.0	0.4	3.0	23.5	0.9	12.0
2005	8.0	0.75	4.0	15.5	10.0	9.9
2006	6.0	0.15	1.5	11.0	0.9	3.4

Table 3. West Nile Virus incidences at a micro-scale, 2002-2006

Year	No. of Cycles	No. of infected dead birds	No. of positive Mosquitoes	No. of positive Human Cases	Range of Cycle area in sq miles
2002	3	5	1705	5	50 to 150
2003	3	44	381	7	5 to 50
2004	1	8	25	2	5
2005	2	17	35	4	50 to 150
2006	5	102	1129	8	7 to 35

Figure 1. Study Area

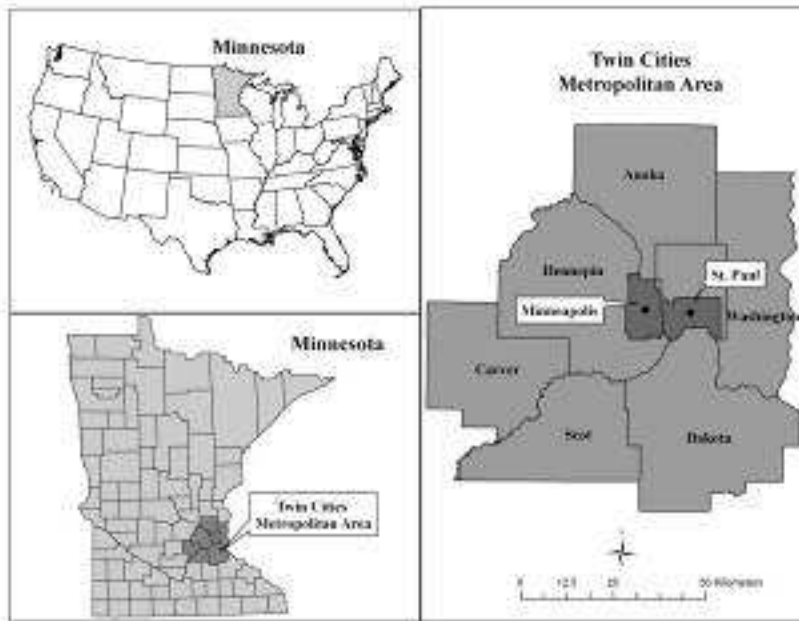


Figure 2. An Example of Spider Diagram, 2006

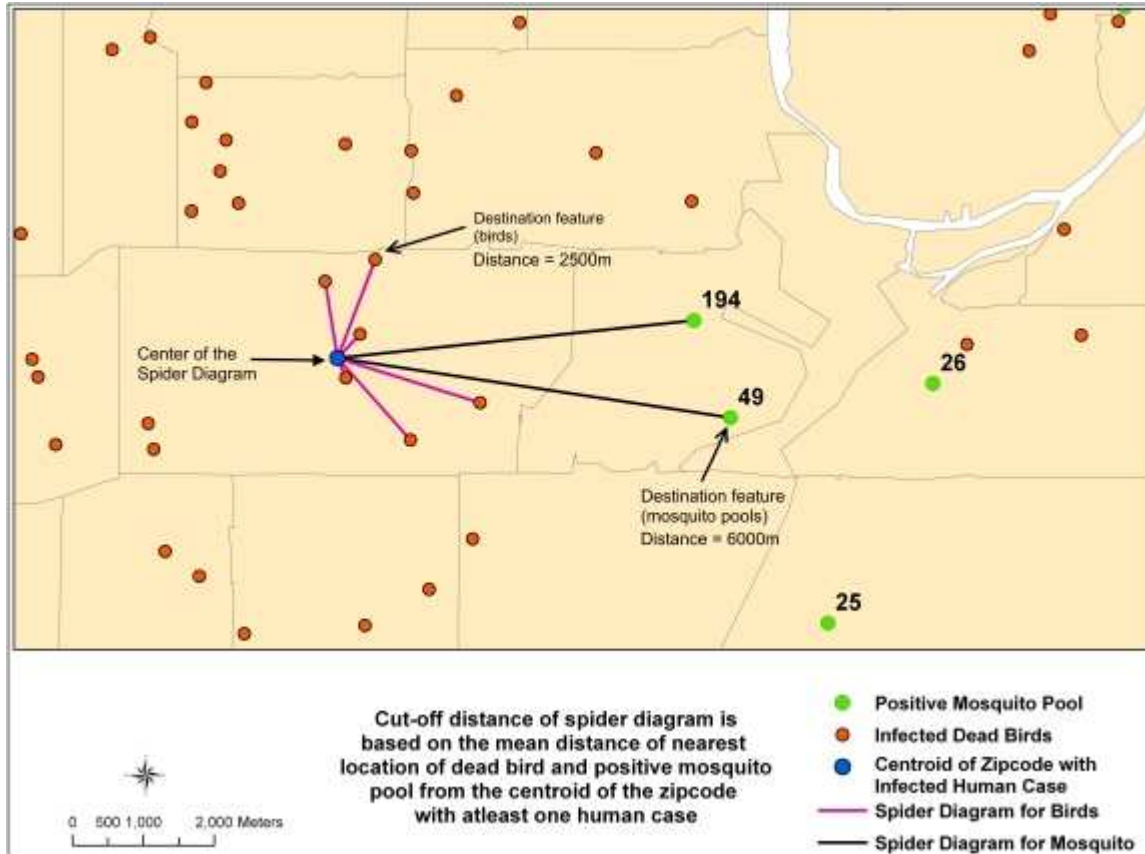
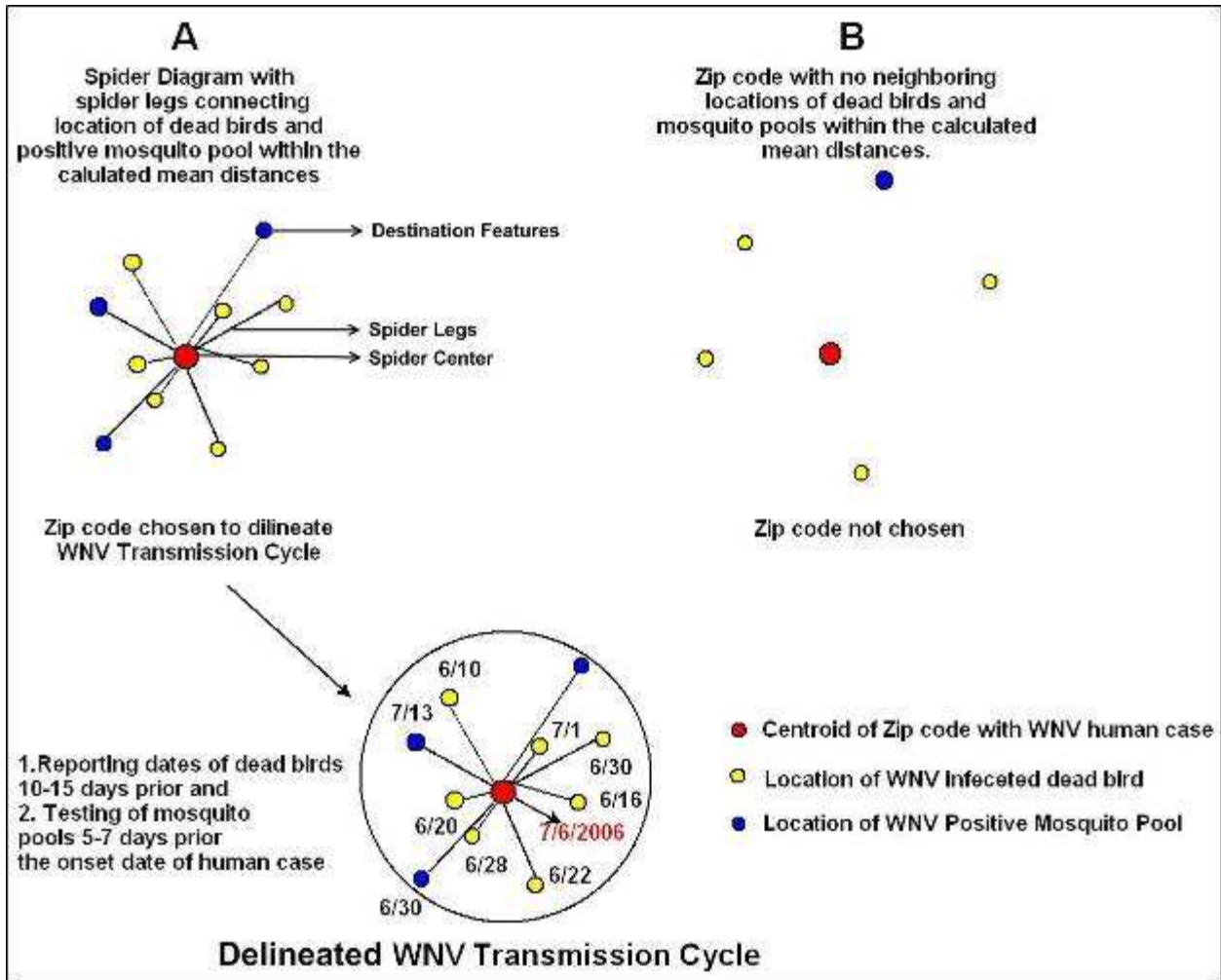


Figure 3. A Schematic Diagram of Nearest-Neighbor-Distance-Time (NNDT) methodology



4. Figure 4. A schematic diagram of COMPOSITE methodology

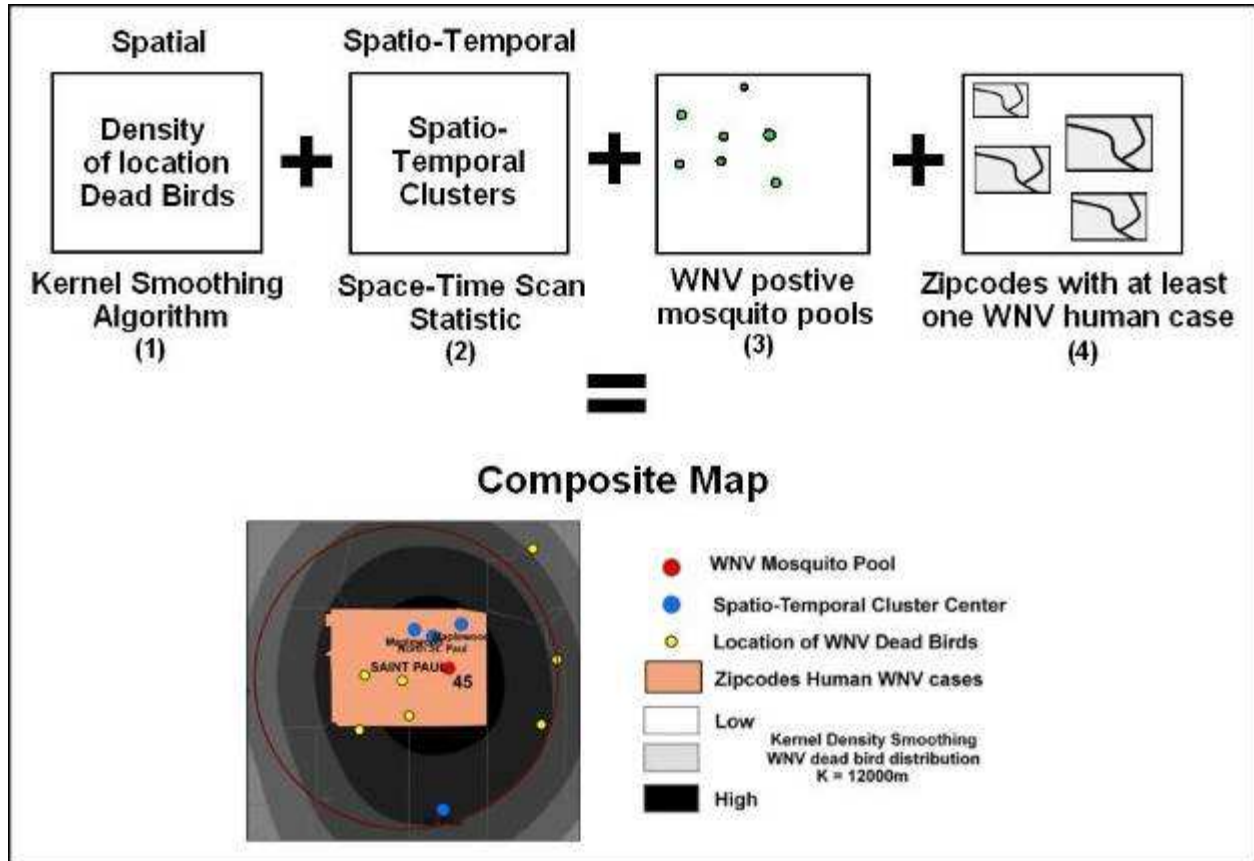


Figure 5. Location of delineated WNV transmission cycles at local scales, 2002-2006, TCMA, Minnesota

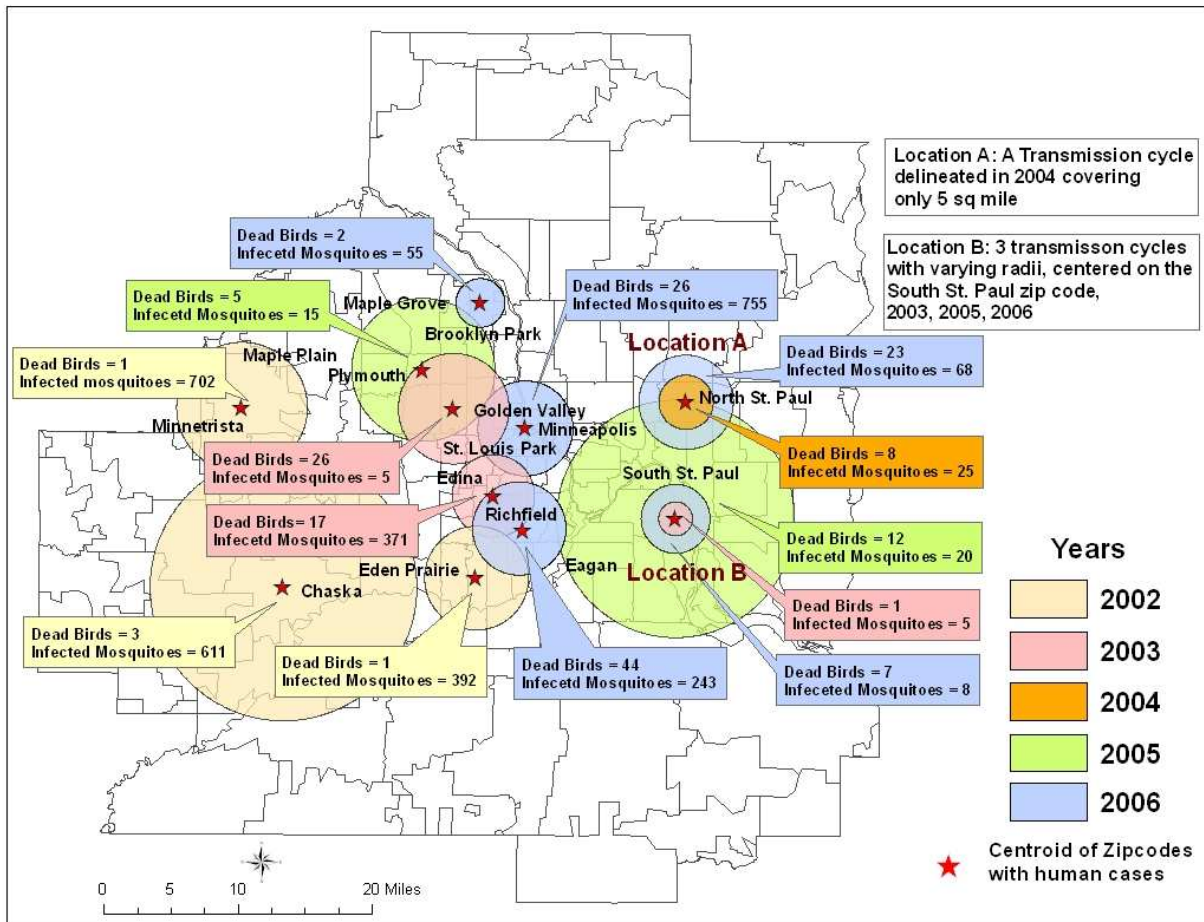


Figure 6. Formation of a West Nile virus transmission cycle at local scale, 2002

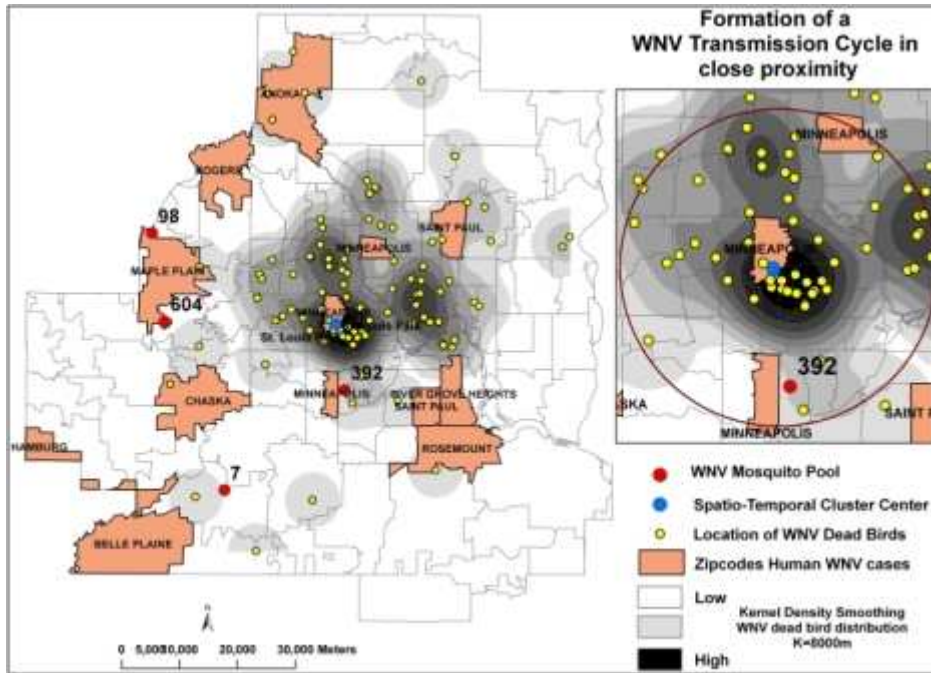


Figure 7. Formation of a West Nile virus transmission cycle within a distance of 1.25 miles near North St Paul, 2004

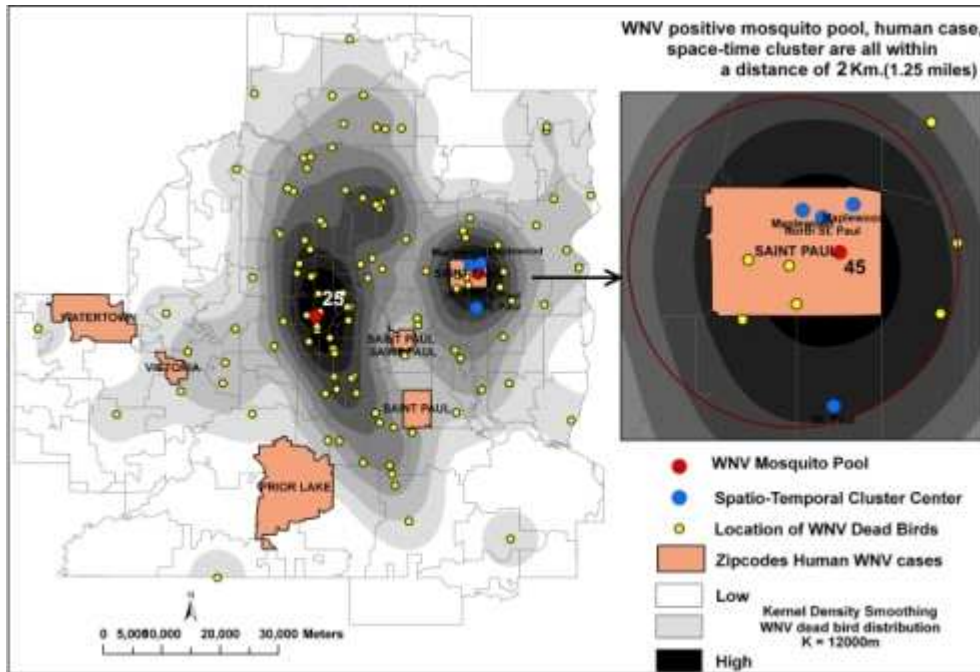


Figure 8. Comparing the WNV delineated exposure areas by NNDT and COMPOSITE methodologies, 2006

