

**Rural-Urban Continuum as a Potential Geographic Correlate of Breast and Prostate Cancer Mortality: A Case Study of Nevada, USA**

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**ABSTRACT**

**Background:** Incidence rates and mortality rates associated with female breast cancer and prostate cancer have decreased through time. This analysis examined purported differences in metro, urban, and rural counties as potential geographic correlates of cancer mortality.

**Methods:** We obtained Nevada mortality rates, US mortality rates, and Nevada county-based mortality rates from the Institute for Health Metrics and Evaluation (1980-2014). Rural-Urban Continuum Codes were obtained from SEER. Mortality distributional curves were compared using a Bonferroni-adjusted KS test.

**Results:** Breast and prostate cancer mortality declined regardless of geography. For breast cancer, mortality did not differ between metro and urban counties ( $D = 1.01$ ,  $P = .771$ ), but both exceeded rural counties ( $D = 1.75$ ,  $P = .012$ ;  $D = 2.30$ ,  $P < .001$ ),

respectively. All geographic areas showed a plateau or increase in recent years, wherein rural rates exceeded metro in 2013-2014. For prostate cancer, mortality for urban counties always exceeded metro and rural counties ( $D = 3.56$ ,  $P < .001$ ;  $D = 3.52$ ,  $P < .001$ ), respectively, though metro and urban rates did not differ ( $D = 1.40$ ;  $P = .117$ ). Like breast cancer, there were increases across all geographies in recent years of data.

**Conclusions:** Directly incorporating geography in cancer mortality studies provides a unique view of spatial associations for understanding population-health impacts.

**Impact:** Little is known about the potential association of geography and cancer mortality, particularly in areas of the Mountain West. This study provides a novel investigation and serves as a hypothesis-generating study for population health management.

**KEYWORDS:**

Breast Cancer; Prostate Cancer; Cancer Screening; Cancer Mortality; Geography

**INTRODUCTION**

Individuals living in rural areas may not have equivalent access to health care when compared to those living in urban or metropolitan areas. Evidence suggests that populations residing in rural areas experience more challenges and additional barriers in accessing health care.<sup>1,2</sup> Additionally, disparities within rural areas exist for gender, racial/ethnic groups, and socioeconomic status, which may serve to exacerbate this issue.<sup>3</sup> Current studies indicate that disease incidence and mortality, including cancer, may be associated with geography (a term used herein to describe the associated features of patient location, population density, and distance to adequate healthcare), thereby influencing prognosis, treatment, and outcome. Collectively, rurality has been linked to disparities in both morbidity and mortality, some of which is linked to obesity and physical inactivity, which serve as correlative negative health behaviors for a myriad of chronic health conditions.<sup>4-6</sup>

Lack of availability of certain health-related services and differential outcomes related to health disparities in rural areas has been examined in some detail.<sup>7</sup> Relative to cancer, rural preventative screening may not always be available, and demographic population characteristics may be associated with these findings. As may be expected, screening rates for rural populations are generally lower than for more populated areas, though

interestingly, African American women are not as negatively impacted as their Caucasian or Hispanic counterparts in this regard.<sup>7</sup> However, screening by itself is insufficient in that research on African American women also has shown rurality was related to lack of knowledge regarding diagnosis, and hence to a reduced use of available post-screening support services.<sup>8</sup> Rurality has also been linked to advance-stage diagnosis, which additionally negatively impacts survival outcome for these populations.<sup>9</sup>

Because of rurality, access to care continues to be an issue and includes the entire cadre of medical providers (i.e., physicians, dentists, para-professionals, etc.).<sup>10</sup> This may directly or indirectly be reflected in the level of service provided, with more aggressive medical procedures being associated with rural status.<sup>11</sup> It has been reported that women in rural areas are more likely to receive mastectomies versus breast-conserving options (e.g., lumpectomy followed by radiation therapy).<sup>12</sup> Likewise, prostate cancer radiotherapy has been shown to be less likely in rural populations, which may be related to reduced diagnosis of early-stage disease, lack of radiotherapy facilities due to its capital costs, and both age and income disparities in rural communities.<sup>12, 13</sup>

Though demonstrable differences in healthcare delivery exist among different countries, cancer disparities related to patient location are not limited to just the United States. For example, countries like China are challenged with increasing populations and inadequate health care infrastructure, particularly in rural areas. The current cancer registry in China only covers 13% of its population, which may affect the necessity for control and screening programs, early diagnosis, and treatment programs.<sup>14</sup> Similarly, largely rural states, like Nevada, have historically lacked the infrastructure to maintain a cancer registry sufficient to understand the associations of patient location with cancer screening and mortality, particularly through time. Rurality, and more generally patient location, are potential confounders of cancer incidence and mortality and should be an important consideration in the study of population-based studies of cancer. Further, changes in the spatial landscape of populations plays a critical role in population health management.

Data suggest that incidence and mortality associated with female breast cancer and prostate cancer have shown favorable downward trends through time, with mortality rates for breast cancer for the US dropping from over 37/100K to less than 26/100K and prostate cancer mortality rates dropping from over 36/100K to less than 25/100K since 1980. Examination of Nevada data, however, suggests that mortality rates for both cancers has been elevated above the US average by approximately 2/100K for

the last two decades. Further, mortality rates for metro vs non-metro areas suggest potential geographic disparities in mortality. The objective of our analysis was to examine purported differences in metro, urban, and rural counties in Nevada as potential geographic correlates of cancer mortality. Nevada is unique in its changing population landscape through time, with large expanses of frontier and rural areas surrounding pockets of very large populations (e.g., Las Vegas). Additionally, Nevada, much like other Mountain West States, is often regarded as a keystone state for many negative health outcomes, with disparities both in diseases and among the socio-demographically diverse population; many examples are highlighted in the long-running *America's Health Rankings* annual reports.<sup>15</sup> Hence, Nevada is an interesting case study for population health management, and several new studies are beginning to examine cancer through population-based analyses in the state, though data are still often limited.<sup>16-18</sup>

## MATERIALS AND METHODS

### Data Sources and Recoding

We retrieved Nevada statewide mortality rates, US mortality rates, and Nevada county-based mortality estimates from the Institute for Health Metrics and Evaluation, Global Health Data Exchange (1980-2014). All data were age-adjusted.<sup>19,20</sup>

Additional data on decadal Rural-Urban Continuum Codes (RUCC) were obtained from NCI/SEER for decades starting in 1974 through 2013, and these were matched to counties in Nevada to obtain a temporal representation of cancer mortality as a function of county population to develop correlative associations of geography and mortality rates. RUCC classifications extend from 1 (largest, metropolitan classification) to 9 (smallest, rural classification).<sup>21</sup> Counties within Nevada were re-coded as either “metro” (RUCC classes 1-3), “urban” (RUCC classes 4-7), or “rural” (RUCC classes 8-9). RUCC data are updated each decade (1974, 1983, 1993, 2003, and 2013) according to demographic data, including population size and proximity to a metropolitan area. Because of shifting demographics, particularly in a state such as Nevada with a strong and itinerant mining industry, many counties change RUCC classification through time, allowing investigation of mortality trends both through time and as a function of population size (Appendix A; Fig. 1;).

Because we used secondary data, this research was reviewed and exempted by the Institutional Review Board (Protocol: 1337899-1).

### Geographic and Statistical Analyses

Data were analyzed after recoding into RUCC categories to differentiate metro, urban, and rural counties based on decadal classification. Our main interest was to explore trends based on available data using geography as a potential correlate of mortality rate. Because we were interested in understanding how rates may be related to geographic location, temporal trends were plotted as mean rates for each classification type and plotted simultaneously to develop data visualizations. These mortality distributional curves were compared using a Bonferroni-adjusted Kolmogorov-Smirnov test with exact p-values among the three geographic designations to determine if there were, in fact, any differences in classifications without making implicit assumptions about how such differences may occur (i.e., location or scale).<sup>22,23</sup> Additionally, we were interested in examining potential trends in incidence and mortality rates in instances when counties change status through time (e.g., urban-to-metro, rural-to-urban, etc.). Visual examination and discussion of trends in these plots is provided.

### RESULTS

Nevada is predominantly urban and rural, though the majority of the population live in and around two large, urban centers in Washoe County (e.g., Reno) and Clark County (e.g., Las Vegas). Like many western states, the counties in Nevada are extraordinarily large and often have small, fluctuating population centers surrounded by large areas of uninhabited land. Nevada counties readily demonstrate these fluctuations in population size through time (Fig. 1).

In both female breast cancer and in prostate cancer, mortality rates have decreased, presumably as a function of both preventative screening and due to advances in treatment, and this is seen for both the US average and for Nevada specifically. Because of changes in population sizes, and hence denominators associated with age-adjusted mortality rate estimates, fluctuations in estimated rates are noticeable for Nevada compared to the US (Appendix B; Fig. 2).

Mortality rates demonstrated this general temporal decline regardless of geography, though interesting comparative trends in RUCC curves exist (Fig. 3). For female breast cancer, mortality did not differ between metro and urban counties ( $D = 1.01$ ,  $P = .771$ ), but both exceeded rural counties ( $D = 1.75$ ,  $P = .012$ ;  $D = 2.30$ ,  $P < .001$ ), respectively. All geographic areas showed a plateau or slight increase in the most recent years of data, wherein rural mortality rates exceeded metro in 2013-2014 (Fig. 3). For prostate cancer, mortality rates for urban counties always exceeded metro and rural counties ( $D = 3.56$ ,

$p < .001$ ;  $D = 3.52$ ,  $P < .001$ ), respectively, though metro and urban incidence rates did not differ ( $D = 1.40$ ;  $P = .117$ ). Similar to female breast cancer, there were increases across all geographies in the most recent years of data, with rural mortality rates exceeding metro from 2010-2014 (Appendix C; Fig. 3).

Changes in county RUCC designation relating to population fluctuations through time provide a means to track mortality as populations shift geographically. Though there are too few examples of changing RUCC designation among Nevada counties to permit a sophisticated statistical examination, general trends warrant preliminary investigation for the purposes of hypothesis generation. Four counties provide sufficient data among the study years for examination – Carson City, Lyon County, Storey County, and Nye County – the last of which demonstrated all three classifications. In cases where higher designations went to lower designations (Carson City: Urban-to-metro; Lyon County: Rural-to-urban; and Storey County: Rural-to-metro), the general decreasing trend in rates is notable for female breast cancer. For Nye County (Rural-to-metro-to-urban), increasing trends in female breast cancer mortality during rural designation were followed by strongly decreasing trends for metro, and were then followed by increasing trends for urban (Appendix D; Fig. 4). For prostate cancer, there were marked increases in rates at the county level regardless of RUCC designation followed by decreases as designations changed; an interesting trend for prostate cancer, and similar to that observed in female breast cancer, is seen for Nye County, with latest years of data showing a mortality rate increase (Appendix E; Fig. 5).

### DISCUSSION

The impact of cancer as an important contributor to mortality in the US cannot be overstated. During the period covered by this study, 1980-2014, over 19 million cancer deaths occurred in the US; however, there was a decrease in cancer mortality of around 20%.<sup>20</sup> This decrease in mortality, however, was not uniform across the country. In fact, there are many areas where high cancer mortality rates are concentrated, such as female breast cancer and prostate cancer in the southeast, particularly in the Mississippi Valley.<sup>20</sup>

The contribution of patient location concomitant with population density and access to adequate healthcare and its impact on cancer mortality, though well-studied and documented in some areas of the country, is not well understood in

the Mountain West. Rurality plays a major role for many reasons, including access to specialty medical professionals (e.g., radiation oncologists/medical oncologists), access to screening, and access to funding.<sup>4,7,9,10,12</sup> Additionally, health disparities related to age, race, and gender also impact incidence and mortality rates, and are generally associated with rurality as well.<sup>1,2,24</sup>

Geography is an important correlate of access to resources and given its relationship to many known disparities and access issues, may play a significant role in the incidence and mortality of certain cancers, particularly for patients who are located in areas with fewer medical resources for screening and/or treatment. Investigation of cancer mortality comparing Nevada as a whole to the US showed general decreasing trends through time as would be predicted based on what is known about cancer rates in general (Appendix B; Figs. 2a,b).<sup>20</sup> However, such comparisons may inadvertently mask important differences when examining state-level data. Hence, evaluation at the county-level, where rurality may be directly assessed, is an important consideration in the context of this analysis and in the context of the provision of healthcare across disparate geographies when trying to implement healthcare management plans and policies. It should be noted, however, that even the county level may be too coarse. For example, Clark County, Nevada, which is the home to Las Vegas, is over 8,000 mi<sup>2</sup>, with large expanses of federal lands and frontier landscapes surrounding large, metropolitan areas. Hence, data evaluation for even smaller spatial scales is important, but such data are often not readily available.

Curves in both female breast and prostate cancer displayed similar downward trends, compared to the state-level data when accounting more specifically for geography (Appendix C; Figs. 3a,b), with reductions in mean annual mortality rates of 10-15/100K. However, important differences in rural, urban, and metro curves can be directly examined to gain an understanding of the relationship of patient location and mortality. Interestingly, rural Nevada counties showed lower mortality rates in female breast cancer compared to both urban and rural areas. This is perhaps related to medically necessary migration to areas with better treatment options requiring specialists such as radiation, medical, and surgical oncologists, and where palliative care and hospice are available; these specialists/services are generally found more readily in the urban and metro areas of the state. Prostate cancer, on the other hand, showed a different trend, with the highest mortality rates in the urban counties. This trend potentially indicates that mortality rates for prostate cancer are

less related to geography at this scale, perhaps owing to the long, chronic natural history of this disease, making migration to surgical and radiation facilities in metro areas less necessary.<sup>25</sup>

One of the more interesting aspects of accounting more directly for geography is the examination of temporal changes in county populations through time. For female breast cancer, trends showed a general decrease in rates as counties changed status (Appendix D; Fig. 4), with the exception of Nye County, which showed an increasing rural trend in rates followed by decreasing trends in these rates until 2008, when mortality rates once again increased while the county was designated as urban. Interestingly, prostate cancer showed increasing trends in mortality rates in some counties followed by decreases as expected. Again, a general increase in mortality rates in Nye County after 2008 can be observed. Clearly the increases may be explained by random error in the mortality estimates, but to see this increase in two cancer types across sexes is certainly worth further exploration. One potential area to examine further is the impact of an increased incidence rate for both female breast cancer and for prostate cancer from 2000-2002 in Nevada. This increase in incidence rates may be related to a number of factors, including inadequate screening programs, but whatever the case, the time delay between that incidence rate increase and the increase in mortality rates for these cancers in some geographies provides a plausible explanation for the rise in mortality after 2008. Certainly, more years of data will allow this to be parsed more specifically.

A confounding issue relevant for cancer screening and its presumed relationship with mortality is the actual impact of screening on the absolute mortality rate. Survival after screening, for example, may not be accurately reflected by examining screening data because of potential lead-time bias. That is, having an earlier diagnosis may change the course of treatment, but may not, ultimately, lead to differences in length of life after diagnosis. Additionally, the potential over-diagnosis of cancer that leads to unnecessary mitigating treatments brings into question the impact of false-positive rates and their relationship to predicting mortality from advance-stage disease.<sup>26</sup> Further research on these issues will be important to address purported associations between incidence and mortality.

Understanding disparities in different geographic areas provides an opportunity to develop specific interventional strategies. For example, providing periodic screening activities in rural areas, providing access to specialists through telehealth opportunities, and providing access to data

systematically to understand trends is sorely needed in Nevada. Now that Nevada has its first accredited School of Public Health and has opened its second School of Medicine, the hope is that targeted healthcare strategies, educational opportunities, and specialist training will converge to address health disparities and disease disparities in the State. Recent studies of breast reconstruction surgeries for female cancer patients in Nevada have utilized teams of plastic surgeons, public health faculty, medical residents, and graduate/medical students in an attempt to understand cancer in this state and the Mountain West, and these studies highlight the importance of utilizing interdisciplinary teams to address cancer from population health and population management perspectives.<sup>17,18</sup>

### **Study Strengths**

How geographic location, as a function of access to care and population density, impacts disease burden is a necessary and substantial component of research in population-based healthcare. This study utilized existing county-based data to provide an initial assessment of cancer and its relationship to geography, which is a novel approach in studies in the Mountain West.

### **Study Limitations**

Results of any exploratory study come with caveats, and this investigation is no exception. We relied on estimates of mortality provided county-wise that were derived from an important paper on the topic.<sup>20</sup> Certainly errors in estimation are important to consider in that regard, and some differences in temporal trends may be related to such errors. However, we based our results and explanation on general trends across decades of time, likely ameliorating the impact of error to some degree. Additionally, it should be noted that Nevada, like many states in the Mountain West, has extraordinarily large counties, which may mask more micro-level geographic correlations that can be examined in states with more numerous county partitions. We plan to explore this in future research.

### **CONCLUSIONS**

Our study provides some evidence of the importance of considering rural-urban continuum in exploring mortality rates for female breast and prostate cancers and provides an initial exploration of data relevant for understanding health disparities related to geography for the population of Nevada. Mortality estimates may seem paradoxically higher in metro and urban areas compared to rural areas because patients likely travel to these geographies to

obtain more sophisticated and complex tertiary care, hence potentially increasing mortality estimates for these areas. Further research needs to be conducted to expand our understanding of the potential of correlating cancer mortality with geography. Regardless, however, understanding the spatial context of disease within the framework of changing landscapes provides an interesting backdrop for population health management in largely rural states.

### **ACKNOWLEDGEMENTS**

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### **DISCLOSURES**

*The authors declare no potential conflicts of interest.*

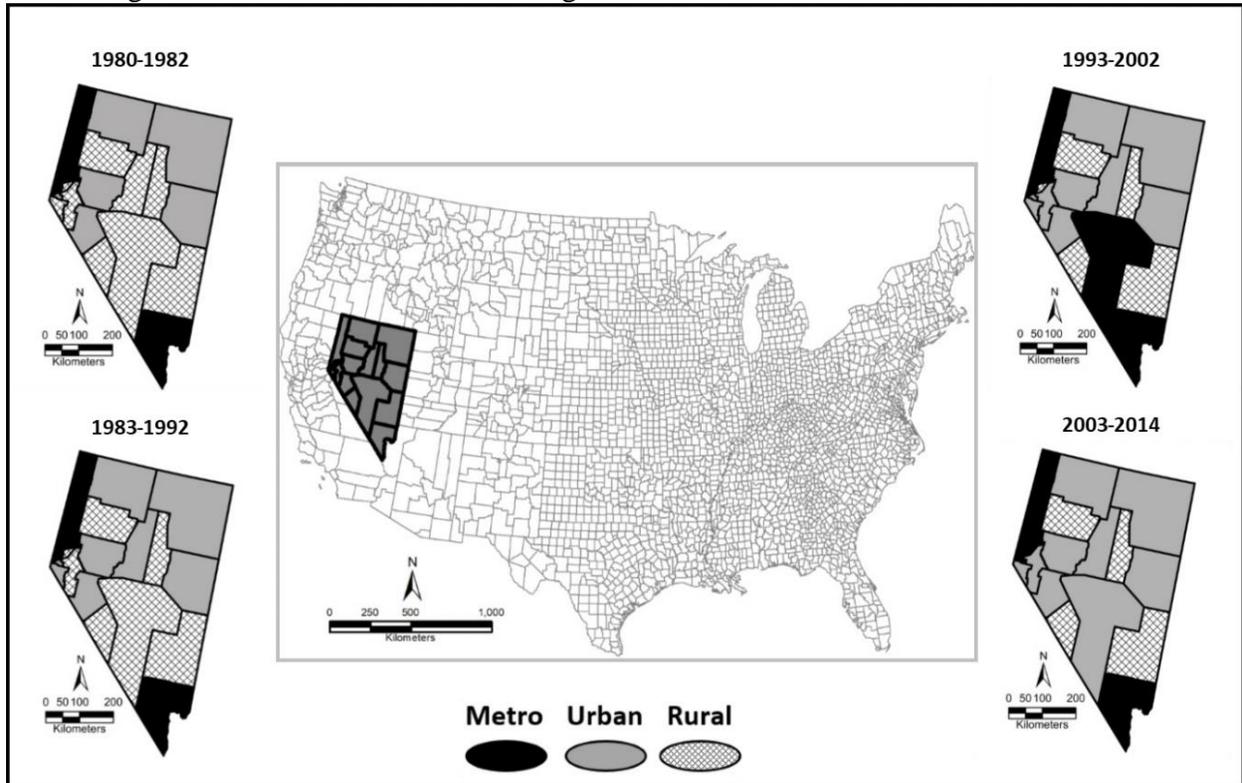
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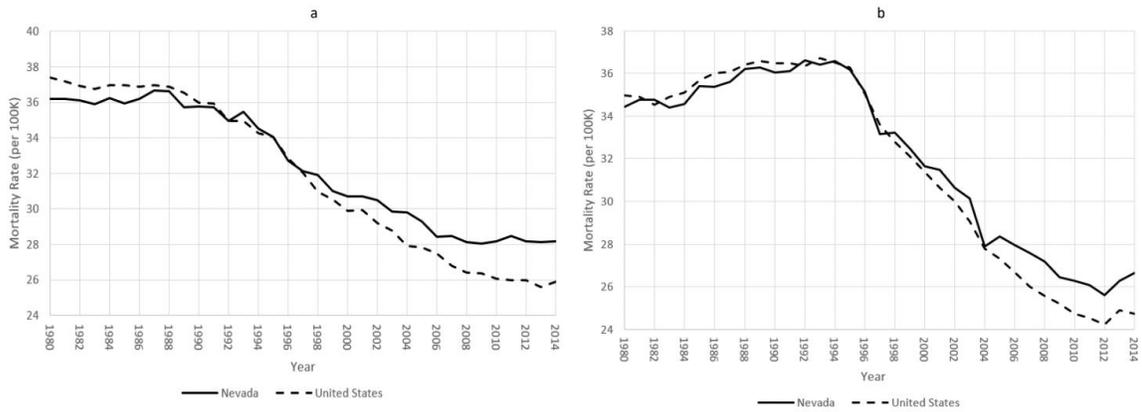
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**APPENDIX**

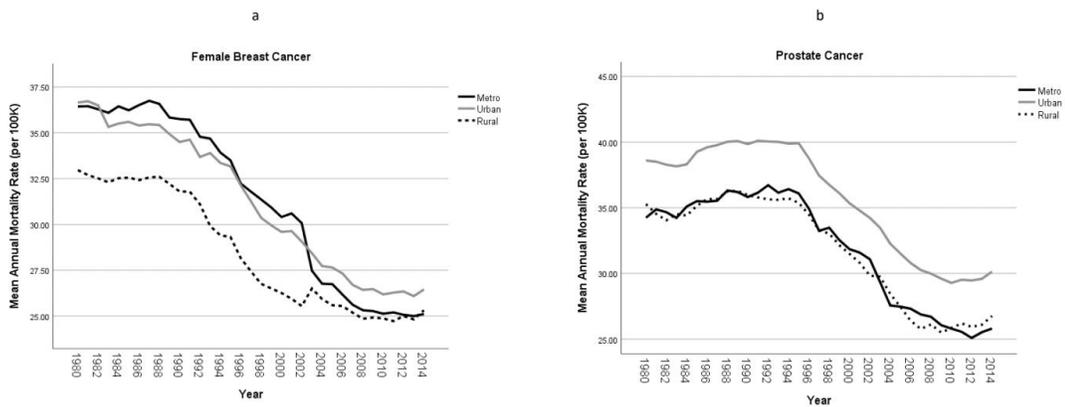
A. Figure 1. RUCC classification through time in Nevada



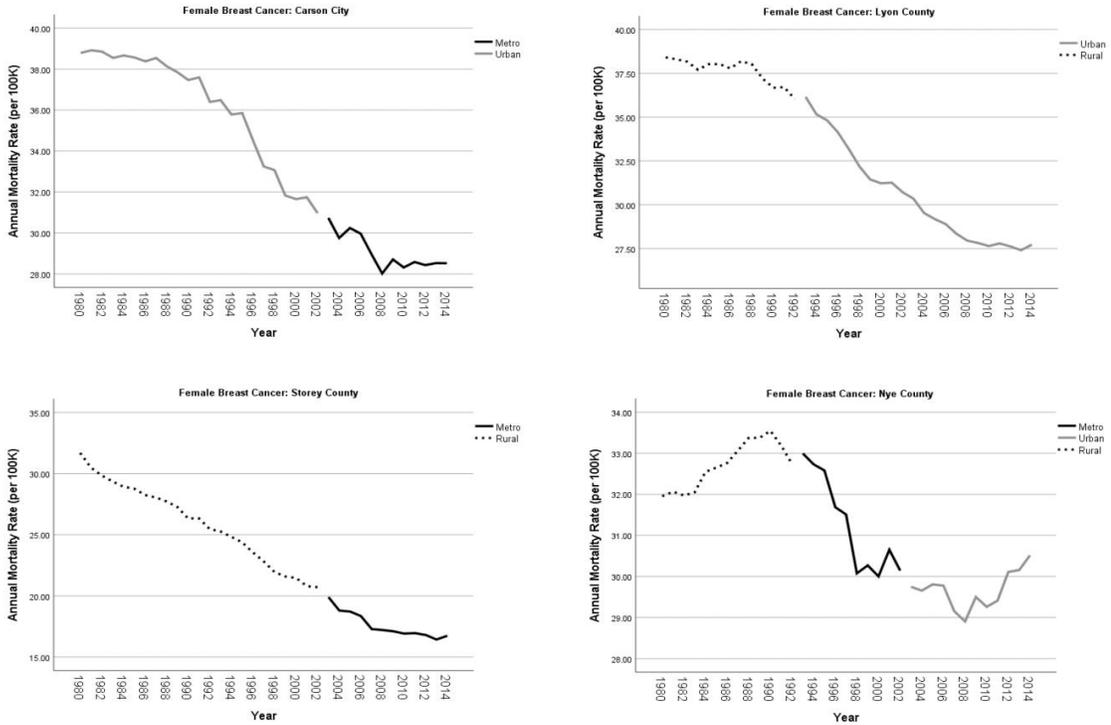
B. Figure 2. Fluctuations in estimated rates for Nevada compared to the US



C. Figure 3. Mortality rates for Female Breast Cancer in Rural, Urban, and Metro areas in Nevada from 2010-2014



D. Figure 4. Female Breast Cancer mortality rates across NV counties: Carson City: Urban-to-metro; Lyon County: Rural-to-urban; and Storey County: Rural-to-metro from 1980-2014



E. Figure 5. Prostate cancer rates at the county level: Carson City: Urban-to-metro; Lyon County: Rural-to-urban; and Storey County: Rural-to-metro from 1980-2014

