# *Obesity and Late Stage Diagnosis of Breast Cancer in Nevada*

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*Office of Public Health Informatics and Epidemiology*

*Division of Public and Behavioral Health*

*Department of Health and Human Services*

**Brian Sandoval, Governor**

**Michael J. Willden, Director**

**Richard Whitley, MS, Administrator**

**Tracey Green, MD, Chief Medical Officer**

# *Table of Contents*

## PURPOSE

Cancer survival is closely tied to stage of cancer at diagnosis. Analysis of risk factors associated with late stage diagnosis of cancer could potentially decrease breast cancer mortality.

The goal of this report is to inform the Nevada Cancer Coalition and researchers of the effects of obesity on stage of breast cancer diagnosis in the state of Nevada. The findings and recommendations are intended to help guide future research and decision-making.

## SUMMARY

To study the effects of obesity on stage of diagnosis of invasive breast cancer, analysis of a linked data set containing Department of Motor Vehicle (DMV) and Nevada Central Cancer Registry (NCCR) records was conducted. DMV data files from 2005, 2008, 2010, and 2013 were matched with 2001-2010 incidence year records from NCCR. A total of 8,030 invasive breast cancer records were obtained. Records without a DMV record prior to diagnosis of cancer, males, and records with missing or incomplete data were excluded, leaving a total of 5,365 records for analysis. DMV records were used to calculate Body Mass Index (BMI), as a measure of obesity. Records were categorized as underweight (<20 BMI), normal weight (20-24.9 BMI), overweight (25-29.9 BMI), and obese (>30 BMI). NCCR records were used to obtain information regarding cancer stage, age at diagnosis, race, primary payer at diagnosis, and ZIP code at diagnosis. Information from the US Census 2007-2011 American Community Survey was used to obtain race specific median income for ZIP codes, which was then used as a proxy for socioeconomic status.

On univariate analysis, overweight and obese women were shown to have marginally significant higher odds of late stage diagnosis of cancer. After controlling for age, race, and primary payer at diagnosis, overweight and obese women were shown to have significantly higher odds of late stage diagnosis compared to normal weight women (overweight OR: 1.189 CI 1.041-1.359 and obese OR: 1.19 CI 1.014-1.397). These findings are similar to the findings of other studies.

Research has shown breast cancer screening can significantly reduce the odds of late stage diagnosis of breast cancer. Nevada's breast cancer screening rates are below national averages and Healthy People objectives. Therefore, a statewide screening and education program is recommended to increase screening for all women. Additionally, a program specifically targeting the overweight and obese population is recommended. An in-depth review of screening in Nevada and analysis of financial resources and feasibility is required to fully determine an appropriate screening program. Further study of differences in breast cancer mortality between normal and overweight/obese women is recommended. Additional research into the causes of late stage diagnosis of cancer is recommended.

## INTRODUCTION

Breast cancer is the most common cancer in Nevada women, accounting for nearly 29 percent of all female cancer cases. It is the third most common cancer in all Nevada residents, responsible for 13 percent of all cancer cases in the state. From 2005 to 2009, 7,412 Nevada women were diagnosed with breast cancer and 1,470 lost their lives to the disease.[1]

The most common form of breast cancer is ductal carcinoma. In ductal carcinoma, cancer begins in the cells that line the milk ducts in the breast. In lobular carcinoma, the second most common breast cancer, the cancer begins in the lobes of the breast. Lobes, or lobules, are the glands that make milk.[2]

To determine the extent of cancer in the body and guide treatment decisions, cancer is staged. Breast cancer stages range from 0 to IV. Stage 0 breast cancer is considered ductal carcinoma *in situ*, where cancer cells are within a duct and have not spread deeper into surrounding fatty breast tissue. Lobular carcinoma *in situ* is sometimes also classified as stage 0, but it is not considered to be a true breast cancer by most oncologists. Increased stages refer to more advanced disease, with stage IV classifying advanced cancer which has metastasized, or spread, to distant organs or lymph nodes far from the breast.[3] Early diagnosis and treatment of cancer can greatly increase the likelihood of survival, as survival rates for later stage cancers drop significantly compared to early stage cancer. For example, the five-year survival rate for breast cancer drops from 93 percent for stage 0 cancer to 15 percent for stage IV.[3]

Obesity has been shown to increase the risk of cancer in postmenopausal women.[4] In addition, obesity has been associated with late stage diagnosis of breast cancer[5-7] and larger tumors and higher rates of lymph node metastases.[8] Due to the increasing rates of obesity and the high prevalence of breast cancer, it is important to study factors which may impact breast cancer outcomes. To research the effect of obesity on breast cancer in Nevada, records from the Nevada Central Cancer Registry were linked with records from the Nevada Department of Motor Vehicles.

## METHODS

### *Data*

Information regarding cancer stage, age at diagnosis, residential ZIP code at diagnosis, primary payer, and race were obtained from the Nevada Central Cancer Registry (NCCR). Data was drawn from 2001-2010 incidence years. NCCR receives data from hospitals, outpatient facilities, and pathology laboratories on all reportable cancers in the state of Nevada. It operates under the standards set by the National Program of Cancer Registries and North American Association of Central Cancer Registries (NAACCR) and strives to achieve and maintain 95 percent complete case ascertainment within 24 months of diagnosis date. For 2000 to 2010 incidence data, NCCR has achieved a Gold Standard Certification from NAACCR eight times. Height and weight data or other measures of obesity are not included in NCCR case reports. Therefore, records from the Nevada Department of Motor Vehicles (DMV) were used to obtain height and weight information. DMV records were drawn from 2005, 2008, 2010, and 2013 data files. DMV records were matched with NCCR records using Centers for Disease Control and Prevention's Registry Plus™ Link Plus software.

**TABLE I** – CHARACTERISTICS OF STUDY SUBJECTS (*N*=5,365)

| Characteristic | *N* | % |
|---|---|---|
| Age (yr), mean (SD) | 59.3 (12.0) | |
| <50 | 1,212 | 22.6 |
| >=50 | 4,153 | 77.4 |
| Race | | |
| White | 4,322 | 80.6 |
| non-White | 1,043 | 19.4 |
| Socioeconomic status | | |
| Low | 233 | 4.3 |
| Middle | 4,249 | 79.2 |
| High | 883 | 16.5 |
| Payer | | |
| No insurance | 87 | 1.6 |
| Private insurance | 3,393 | 63.2 |
| Medicaid | 194 | 3.6 |
| Medicare | 221 | 4.1 |
| Medicaid/Medicare, NOS | 1,404 | 26.2 |
| Government | 66 | 1.2 |
| BMI[1], mean (SD) | 25.8 (5.0) | |
| Low | 89 | 1.7 |
| Normal | 2,676 | 49.9 |
| Overweight | 1,652 | 30.8 |
| Obese | 948 | 17.7 |
| Cancer stage | | |
| Localized | 3,634 | 67.7 |
| Regional | 1,644 | 30.6 |
| Distant | 87 | 1.6 |

[1]Body Mass Index ($kg/m^2$)

US Census data was used to determine median individual income by ZIP code. The 2007-2011 American Community Survey was used to obtain median income by race for ZIP code tabulation area. Though ZIP code tabulation areas do not directly coincide with postal ZIP codes, there was not enough information to geocode data for ZIP code tabulation area. Therefore, residential ZIP code at diagnosis was associated with ZIP code tabulation area from the US Census. Due to the small population and limited racial diversity of some ZIP codes, median individual income was not reported in the American Community Survey for some races. In these cases, the median individual income for the entire ZIP code was used in place of a race specific median individual income.

## *Study Subjects*

From the linked data set, 8,030 breast cancer records were extracted. There was no DMV record available prior to the diagnosis of breast cancer for 1,654 of the records, and they were excluded. Males and observations with missing or incomplete data were excluded, accounting for an additional 1,011 excluded records. A total of 5,365 observations were included in analysis.

## *Analysis*

The outcome variable of cancer stage was determined using SEER summary stage variables in NCCR. As dictated by NAACCR rules, cancers diagnosed prior to 2004 are staged according to the SEER *Summary Staging Manual 2000.* Cancers diagnosed January 1, 2004 and later are staged according to the Cancer Staging algorithm created with the Collaborative Stage Data Collection System. This variable was coded into a dichotomous variable of localized and regional/distant, representing early and late stage diagnoses, respectively. Stage I cancer was considered localized, and stage II, III, and IV cancers were considered regional/distant. Data was limited to invasive cancers; therefore, stage 0 cancers were not included in analysis.

The primary explanatory variable of obesity was quantified through Body Mass Index (BMI), a common measure of obesity. Height and weight data from DMV records was used to calculate BMI. BMI was calculated according to World Health Organization (WHO) criteria, as weight in kilograms divided by height in meters squared.[9] When there were multiple height and weight recordings prior to cancer

**TABLE II** – SUBJECT CHARACTERISTICS AND ASSOCIATED P VALUE CHI-SQUARE TEST ACCORDING TO BMI

| | Body Mass Index (kg/m$^2$) | | | | *P* chi-squared |
|---|---|---|---|---|---|
| | Low (<20) *N*=89 (%) | Normal (20-24.9) *N*=2,676 (%) | Overweight (25-29.9) *N*=1,652 (%) | Obese (≥30) *N*=948 (%) | |
| Age (years) | | | | | <.0001 |
| <50 | 32 (36.0) | 737 (27.5) | 290 (17.6) | 153 (16.1) | |
| ≥50 | 57 (64.0) | 1,939 (72.5) | 1,362 (82.5) | 795 (83.9) | |
| Race | | | | | 0.0613 |
| White | 71 (79.8) | 2,195 (82.0) | 1,307 (79.1) | 749 (79.0) | |
| non-White | 18 (20.2) | 481 (18.0) | 345 (20.9) | 199 (21.0) | |
| Socioeconomic status | | | | | <.0001 |
| Low | 4 (4.5) | 75 (2.8) | 89 (5.4) | 65 (6.9) | |
| Middle | 74 (83.2) | 2,114 (79.0) | 1,298 (78.6) | 763 (80.5) | |
| High | 11 (12.4) | 487 (18.2) | 265 (16.0) | 120 (12.7) | |
| Payer | | | | | <.0001 |
| No insurance | 1 (1.1) | 43 (1.6) | 29 (1.8) | 14 (1.5) | |
| Private insurance | 60 (67.4) | 1,836 (68.6) | 949 (57.5) | 548 (57.8) | |
| Medicaid | 6 (6.7) | 92 (3.4) | 62 (3.8) | 34 (3.6) | |
| Medicare | 16 (18.0) | 589 (22.0) | 518 (31.4) | 281 (29.6) | |
| Medicaid/Medicare, NOS* | 6 (6.7) | 88 (3.3) | 73 (4.4) | 54 (5.7) | |
| Government | 0 | 28 (1.1) | 21 (1.3) | 17 (1.8) | |
| Cancer stage | | | | | 0.68 |
| Localized | 61 (68.5) | 1,843 (68.9) | 1,099 (66.5) | 631 (66.6) | |
| Regional | 27 (30.3) | 788 (29.5) | 526 (31.8) | 303 (32.0) | |
| Distant | 1 (1.1) | 45 (1.7) | 27 (1.6) | 14 (1.5) | |

*NOS=Not otherwise specified.

diagnosis, the record closest to diagnosis was used. BMI was categorized according to WHO criteria[9]; underweight as less than 20 kg/$m^2$, overweight as 25 kg/$m^2$ to 29.9 kg/$m^2$, and obese as greater than or equal to 30 kg/$m^2$.

Due to low counts in many race categories, race was categorized as White and non-White. The variable of age was categorized as less than 50 and greater than 50. Race specific median income per ZIP code was used as a proxy of socio-economic status. Socio-economic status was categorized as low (<$35,000), middle ($35,000-$74,999), and high (>$75,000). NCCR provides information regarding primary payer at diagnosis, such as private insurance, Medicaid, Medicare, Veterans Affairs (VA), Tricare, and Indian Health Service. Payer at diagnosis was categorized as no insurance, private insurance, government health care (VA, Tricare, and Indian Health Service), Medicaid, Medicare, and Medicaid/Medicare not otherwise specified.

Statistical analysis was conducted using SAS version 9.3 for Windows. Descriptive statistics were calculated for the variables. Chi-squared tests were used to compare categorical variables. Univariate analysis was conducted using logistic regression. Those variables which were shown to have a significance of $p < .10$ on univariate analysis were included in model building. In model building, age and payer at diagnosis were shown to significantly impact the model. Multiple logistic regression was used to analyze variables in the final model. Though race was not shown to significantly impact the model, it was included because past research has shown race is a risk factor for stage of cancer diagnosis.[10] The final model included age, race, and payer at diagnosis.

**Table III** – OR AND 95% CI FOR BEING DIAGNOSED WITH REGIONAL/DISTANT STAGE WHEN COMPARED WITH NORMAL STAGE

| Variable | Unadjusted OR (95% CI) |
|---|---|
| Age | |
| <50 | 1 |
| ≥50 | .65 (.573-.736) |
| Race | |
| White | 1 |
| non-White | 1.165 (1.020-1.331) |
| Socioeconomic status | |
| Low | 1.241 (.932-1.652) |
| Middle | 1.084 (.934-1.257) |
| High | 1 |
| Payer | |
| No insurance | 1.549 (1.009-2.377) |
| Private insurance | 1 |
| Medicaid | 1.55 (1.158-2.075) |
| Medicare | .629 (.547-.723) |
| Medicaid/Medicare, NOS* | .789 (.586-1.063) |
| Government | 1.089 (.656-1.807) |

*NOS=Not otherwise specified.

## RESULTS

Descriptive data on the study subjects is shown in Table I. The mean age was 59.4 years, with a range of 24-95 years. Mean BMI was 25.8, with a range from 15.8 to 60.6. Chi-squared test was used to compare subject characteristics and cancer stage between low weight, normal weight, overweight, and obese women; results are shown in Table II. Significant differences were found between age groups, socioeconomic status, and payer at diagnosis. Obese and overweight women were more often older, lower economic status, and Medicare recipients.

On univariate analysis, significantly higher odds of late stage diagnosis were shown for non-White race (1.165, CI 1.020-1.331), no health insurance (1.549, CI 1.009-2.377), and Medicaid as primary payer (1.55, CI 1.158-2.075). Being 50 years or older (.65, CI .573-.736) and having Medicare (.629, CI .547-.723) were shown to be protective against late stage diagnosis, results are shown in Table III. Univariate analysis did not show a significant association between overweight/obese BMI and late stage diagnosis. However, as shown in Table IV, after controlling for age, race, and payer at diagnosis, overweight and obese groups had significantly higher odds of late stage diagnosis when compared to the normal weight group (1.189, CI 1.041-1.359 and 1.9, CI 1.014-1.397, respectively). Additional analysis was conducted using comparing BMI of less than 25 with greater than or equal to 25, similar higher odds of late stage diagnosis were shown (1.191, CI 1.059-1.339).

**TABLE IV** – OR AND 95% CI FOR BEING DIAGNOSED WITH REGIONAL/DISTANT STAGE IN OVERWEIGHT/OBESE WOMEN COMPARED WITH NORMAL WEIGHT WOMEN

| BMI | Localized | | Regional/Distant | | Unadjusted OR (95% CI) | Adjusted OR (95% CI)[1] |
|---|---|---|---|---|---|---|
| | *N* | % | *N* | % | | |
| Mean (SD) | 25.7 (5.0)[2] | | 25.9 (5.0)[2] | | | |
| Low | 61 | 68.5 | 28 | 31.5 | 1.016 (.644-1.6) | .965 (.61-1.528) |
| Normal | 1,843 | 68.9 | 833 | 31.1 | 1.0 | 1.0 |
| Overweight | 1,099 | 66.5 | 553 | 33.5 | 1.113 (.977-1.269) | 1.189 (1.041-1.359) |
| Obese | 631 | 66.7 | 317 | 33.4 | 1.112 (.949-1.301) | 1.19 (1.014-1.397) |
| <25 | 1,904 | 68.9 | 861 | 31.1 | 1.0 | 1.0 |
| >=25 | 1,730 | 66.5 | 870 | 33.5 | 1.112 (.992-1.247) | 1.191 (1.059-1.339) |

[1]ORs comparing regional/distant stage with localized stage, adjusted for age, race, and payer at diagnosis.
[2]p = .18 from Student's *t*-test.

### *Discussion*

In this study, overweight and obesity was significantly associated with increased odds of later stage of breast cancer at diagnosis. Adjusting for age, race, and payer at diagnosis did not drastically change the estimates of association. The results of this study are consistent with the findings of past studies.[5-7]

There are numerous possibilities for the difference in stage of diagnosis for overweight and obese versus normal weight individuals. Obese women may be less likely to engage in screening.[11, 12] Increased adipose tissue in obese women may impact the likelihood of cancer being detected or may have a biological effect on cancer growth.[13]

Though this analysis benefits from a large study size, there are several limitations due to the sources of data. First, BMI was assessed from self-reported DMV records. It is not possible to know the accuracy of reported height and weight. In addition, an individual's weight may have changed between license issuance/renewal and diagnosis of cancer. Second, NCCR records do not include information about potential known risk factors for breast cancer such as family history of breast cancer, menstrual or reproductive history, and hormone use. Additionally, there is no information regarding individual economic status; though NCCR has variables regarding occupation, the majority of records were incomplete. We attempted to control for socioeconomic status through census data. However, US Postal ZIP codes do not always coincide with the US Census ZIP code tabulation areas. Therefore, this analysis may not have accurately controlled for socioeconomic status or income status. These factors may be related to stage of cancer and our results may be biased due to these effects.

## RECOMMENDATIONS

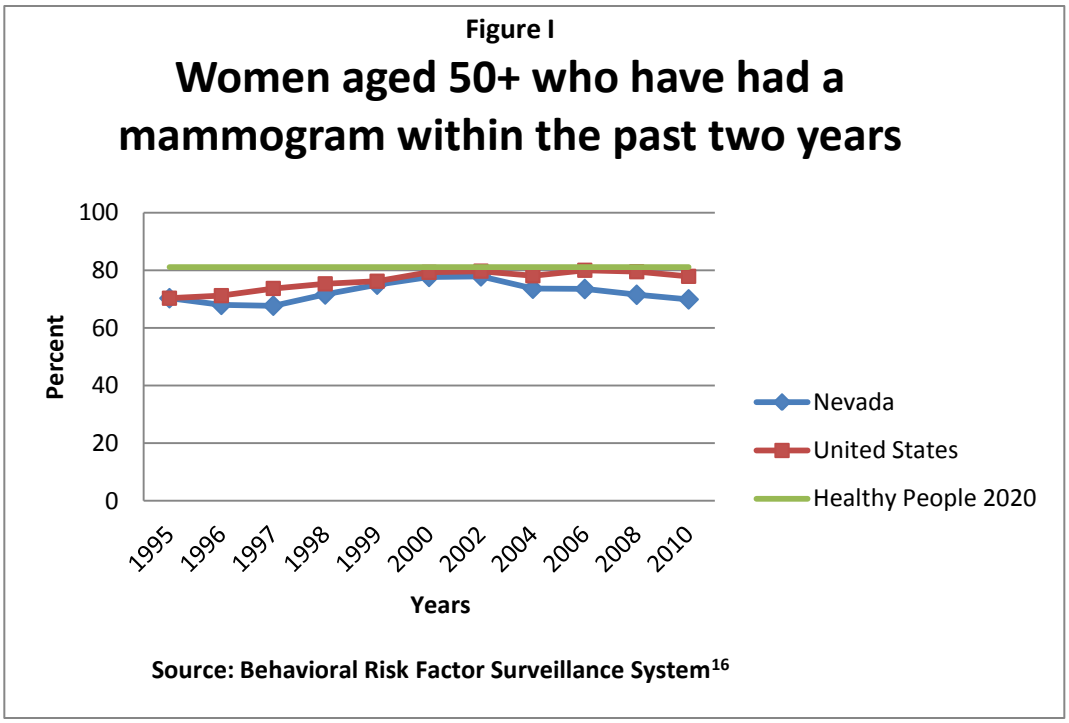
### *Screening*

Screening has been shown to have a significant impact on stage of cancer diagnosis; the odds of late stage diagnosis of breast cancer are higher for women who are not regularly screened.[14] The US Preventive Task Force (USPTF)[15] recommends biennial screening mammography for women aged 50-74; which is also the Healthy People 2020 objective. For women prior to age 50, the USPTF recommends the decision to start biennial screening mammography be an individual one, which should take patient context into account, including the patient's values regarding specific benefits and harms.

Review of breast cancer screening shows Nevada lags behind most of the United States. In 2010, Nevada ranked 48th out of the 50 states in the nation for women aged 50-74 who reported having a mammogram within the past two years.[17] Figure I shows screening rates for women aged 50 or older declined from a high of 77.7 percent in 2002 to a low of 69.9 in 2010. Data from 2012 shows the screening rate increased to 73.1 percent; however, survey methods and weighting have changed, so these results are not comparable to previous years.[16]

Due to the low overall screening rates, efforts should be made to increase screening for all women, not just those who are overweight or obese. Currently, efforts are focused on increasing breast cancer screening for low income and under or uninsured women through the Women's Health Connection and through Federally Qualified Health Centers. The Women's Health Connection is a federally funded program which provides free diagnostic and screening services for low income, uninsured and underinsured women. Nevada's Federally Qualified Health Centers provide a number of services, including primary and preventive care; serving mostly low income patients.

**Figure I**




**Source: Behavioral Risk Factor Surveillance System[16]**

Community based providers would benefit from partnering with the state and philanthropic organizations to secure funding to support breast cancer screening programs. Public health authorities may specifically target providers, women who meet the USPSTF recommendations for screening, or both. Both provider targeted interventions and interventions targeting women have proven to be effective.[18] Programs could range from educating providers on the importance of discussing mammography screening with their patients to a large public education campaign with community education sessions and television commercials. To properly assess the most appropriate and effective program, analysis of feasibility and funding are required.

Though increasing screening for all women in Nevada will likely increase screening among the overweight/obese population, programs specifically targeting overweight/obese women are also warranted. If a large screening program is not feasible, a smaller program targeting obese women may provide a feasible and beneficial option. Obese women have been shown to be less likely to engage in breast cancer screening.[10, 11] Therefore, specifically targeting this group should be considered. As suggested earlier, either provider-targeted or individual-targeted interventions may be used. A review of feasibility and financial resources will determine the most appropriate program.

### *Research*

As discussed previously, increasing breast cancer screening may reduce late stage diagnosis of breast cancer. However, a thorough review of breast cancer screening in the state is required before screening programs should be implemented. A statewide assessment of breast cancer screening is recommended. Currently, data is limited to sources such as the Behavior Risk Factor Surveillance System (BRFSS), which provide information such as screening rates. However, information such as individual barriers to screening and perceptions of the benefits of mammography, and provider recommendations, opinions, and mammography ordering rates are not available. An assessment of screening should aim to identify groups within the state with the lowest screening rates, the underlying causes of disparities in screening, and examine screening trends within the state. Information gained from this assessment can accurately guide program implementation.

This study has shown obese women have higher odds of later stage diagnosis of breast cancer. Though late stage diagnosis has been shown to decrease survival[3], this study does not directly show obese Nevada women have higher breast cancer mortality rates. Research into differing cancer outcomes between obese and normal weight women could be beneficial in determining the true impact obesity has on breast cancer in Nevada. Through linking this data set with death certificate records, mortality rates and long-term survival may be analyzed.

In addition to obesity, other factors within Nevada may be related to stage of cancer diagnosis. On univariate analysis, non-white race had higher odds of late stage diagnosis. A significant association was not shown on multivariate analysis. However, a more in-depth study of differences between races and stage of cancer diagnosis may find significant associations, as associations between cancer stage and race have been shown in previous studies.[10] On multivariate analysis, having Medicaid as the primary payer at diagnosis was significantly associated with higher odds of late stage diagnosis (1.53, CI 1.14-2.05), when compared to private insurance. This result is surprising, as the Women's Health Connection

provides no cost screening for Medicaid patients. Additional research into the cause of this association is warranted. Causes may include patients underutilizing available services, individual education and perceptions regarding screening, differences in provider recommendations for Medicaid patients, or some other cause. Information gained from additional research may help guide prevention strategies in the future.

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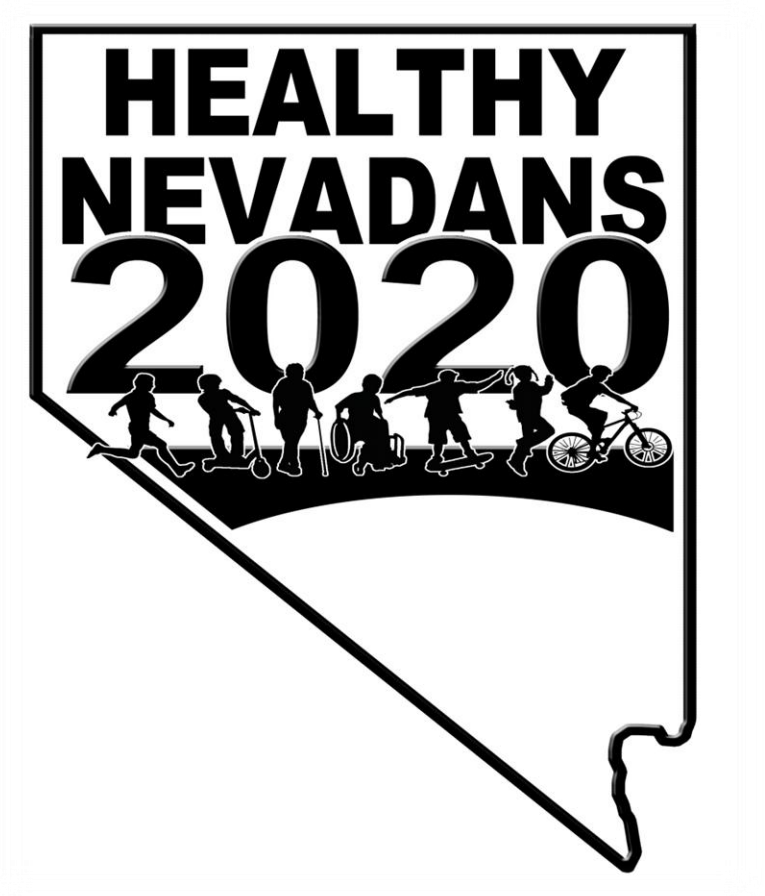
**COMMENTS, SUGGESTIONS, AND REQUESTS FOR FURTHER INFORMATION MAY BE ADDRESSED TO:**

OFFICE OF PUBLIC HEALTH INFORMATICS AND EPIDEMIOLOGY
4126 TECHNOLOGY WAY, SUITE 200
CARSON CITY, NV 89706
TEL: (775) 684-5911
FAX: (775) 684-5999

**COMPILED AND WRITTEN BY:**

PETER DIERINGER, HEALTH RESOURCE ANALYST

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