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Analysis of Diagnosed vs. Expected Cancer Cases In Residents of the Vasquez Boulevard/ I-70 Superfund Site Study Area

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EXECUTIVE SUMMARY

This study presents the findings of cancer occurrence in neighborhoods in the Vasquez Boulevard and I-70 (VBI70) Superfund Site in north-central Denver. Studies conducted by the U.S. Environmental Protection Agency (EPA) have shown high levels of arsenic and lead in soil at some homes in the Swansea, Elyria, Clayton, Cole, and southwest Globeville neighborhoods.

This study was conducted at the request of citizen representatives of the Colorado People's Environmental and Economic Network (COPEEN) and the Clayton, Cole, Elyria, and Swansea Neighborhood Coalition (CEASE) to conduct a review of cancer rates in their community. In Colorado, investigation of cancer occurrence is possible by using data available form the Colorado Central Cancer Registry (CCCR), which is based at the Colorado Department of Public Health and Environment. All cancers are reported to the Cancer Registry with the exception of non-melanoma skin cancers.

The study design used in this analysis focuses on a numerical summary of cancer incidence in neighborhoods within the VBI70 Superfund Site study area. The results aid in determining whether the number of certain types of cancer is greater than would be expected for the age, gender, race and ethnicity of the study population. The study does not make detailed examinations of individual cases and does not allow conclusions to be made about causal association between exposure and any single cancer or group of cancers.

This study examined all cancers diagnosed and reported to the state Cancer Registry from 1982 to 1998 for a geographic area matching the Superfund Site boundary (Census Tracts 35.00, 36.01, 36.02 and a small portion of 16.00). Cancer rates from the rest of the Denver metropolitan area over the same time period were used as standards for estimating the expected number of cancers.

The primary focus of this study was to evaluate the occurrence of lung and bladder cancer, based on the strong association reported in the epidemiological literature between arsenic exposure and these types of cancer. Non-melanoma skin cancer, which has also been reported to occur at higher rates in arsenic-exposed communities, was not investigated because only melanoma skin cancer is reported to the Cancer Registry. At the community's request, the number of all tumor sites combined ("All Cancers Combined") was also investigated. Additional analysis was done to investigate the potential association between the level of arsenic in soil and observed increases in specific types of cancer.

For cancer types with an established association with arsenic exposure -lung and bladder- the outcome of this study was mixed, with a statistically higher than expected number of lung cancers observed, but no elevation in bladder cancer. Additional statistical analyses did not detect an association between the occurrence of lung cancer and high levels of arsenic in the soil of homes where individuals with lung caner lived.

The findings of this study suggest that there is a generally higher than expected rate of cancer in the VBI70 study area, based on observed elevations of several additional types of cancer-- pancreas, breast, cervical, colorectal, "other pharynx" (cancers of the tonsil, oropharynx, and hypopharynx, including pyriform sinus), larynx, brain and other nervous system cancers (brain/ONS), and multiple myeloma. There is no established association between these specific types of cancers and arsenic exposure, however, and it is believed that these cancers are predominantly associated with other known risk factors, such as smoking,

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dietary habits, alcohol consumption, viral infections, or other predisposing genetic factors or family history.

Among these cancer types, none were statistically elevated in both genders (males and females individually). "Other pharynx" cancer occurred at statistically high levels in males only. Six cancer types (breast, pancreas, colorectal, cervix, larynx, and multiple myeloma) were statistically elevated in females only. Brain and other nervous system cancers were diagnosed in elevated, but not statistically high, numbers in both males and females, which resulted in a statistically high number of cancers when combined across both genders. Certain cancers were statistically elevated in specific race/ethnicities, but there was no consistent pattern or evidence of any one group that was more consistently impacted than another. There also was no evidence of a clustering of elevated numbers of cancer in any one neighborhood. Rather, pancreas, breast, and "other pharynx" cancers were statistically high in Census Tract 35.00 only, and larynx and brain/ONS cancers were high in Census Tract 36.01 only. In Census Tract 36.02, multiple myeloma was the only type of cancer that occurred at a statistically elevated level for the time period studied. Cervical and colorectal cancers were not statistically high in any of the geographic areas individually, but slight increases in the numbers diagnosed in females in each tract for all age groups resulted in a statistical elevation, when cases reported from the three census tracts were combined ("Entire Study Area").

Many or most of the lung and laryngeal cancers reported from these neighborhoods are likely related to smoking. This conclusion is based on a review of Cancer Registry medical abstracts and the large number of these individuals reported to be smokers. Other factors, such as exposure to carcinogens in an occupational setting or other chemical exposures from indoor or ambient air, may also contribute to the overall individual and population risk. For lung cancer, the possibility of some effect from exposure to arsenic in soil cannot be ruled out by this analysis, but any such effect would likely be small compared to the smoking effect.

Tobacco use is also recognized as an important risk factor for several of the other types of cancers that were elevated among segments of the study population. Colorectal, "other pharynx", cervix, and pancreas cancer all have an established association with smoking. Cancer Registry records showed that, among these cancer types, 57 to 100 percent of all cases with known smoking status were reported to be smokers. Therefore, smoking is likely to be a significant risk factor in those diagnosed with these types of cancer, although other factors may have also played a role. For example, excessive use of alcohol was noted for several individuals diagnosed with "other pharynx" cancer, which is a recognized risk factor for this disease. A review of the epidemiological literature revealed that none of these cancer types has an established association with exposure to arsenic.

Three of the cancer sites reported at statistically elevated levels-- breast, brain/ONS, and multiple myeloma-- do not have known associations with smoking. Elevations in each of these cancers were detected at statistically high levels in different census tracts. The elevation in multiple myeloma was seen in females in Census Tract 36.02 (9 cases diagnosed compared to less than 3 expected), with most of the excess cases occurring in older individuals over the age of 65. The age distribution of these cases was consistent with the typical age distribution reported in the epidemiological literature for this disease. The primary risk factor for multiple myeloma identified by the American Cancer Society is increasing age, with few occupational or chemical associations noted, although some evidence of increased risk for farmers and workers in petroleum-related industries does exist.

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The number of breast cancer cases in Census Tract 35.00 was statistically high, a finding partly attributed to a higher proportion of second breast tumors, particularly in Hispanic women. Fifteen of the 69 cases reported occurred in women under the age of 45, a finding that may suggest the potential for genetic predisposition or family history of breast disease. Other plausible contributing factors would include a high number of extended families with similar predisposing factors living in this same census tract, a higher proportion of individuals with a higher overall risk of developing breast cancer than is typical of the comparison population, and longer than average residency for people in this community, resulting in a higher likelihood of diagnosing multiple primaries while an individual resides in the same census tract.

Brain/ONS cancer was reported at levels statistically higher than expected in Census Tract 36.01. Six of the nine cancers in this tract occurred in individuals under the age of 20, with a greater proportion of one specific histologic cell type—glioblastoma-- reported for these six cancers, compared to the cell type distribution for the rest of the Denver metropolitan area. For children, a higher risk of developing certain types of brain tumors has been associated with parental employment in agricultural, electricity, or motor vehicle related occupations, and for maternal employment in the textile industry. Studies of other communities with general environmental exposures to arsenic have not detected an increased risk for developing brain or other nervous system cancers.

This study did reveal that several tumor types, most notably tumors of the breast and cervix, were detected at a later, more invasive disease stage when survival may not be as good as that achievable with early detection. This finding may indicate poor access to medical care in this community.

The findings of this report will be communicated to the Comprehensive Cancer Control Section at the Colorado Department of Public Health and Environment to improve cancer control strategies in these Denver neighborhoods within the VBI70 study area to encourage educational efforts and outreach to these communities to better characterize the presence of known and potential cancer risk factors.

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INTRODUCTION

The Vasquez Boulevard and I-70 (VBI70) Superfund site is an approximately four-square-mile area located in north-central Denver. The site is composed of several neighborhoods including Swansea, Elyria, Clayton, Cole and southwest Globeville. Studies conducted by the U.S. Environmental Protection Agency (EPA) indicate that elevated levels of arsenic and lead occur in the soil of many residential properties in these neighborhoods. The source of these high concentrations of arsenic and lead in soil has not yet been determined, but may be associated with historical releases from a cadmium refinery or two other smelters which previously operated in the area. Arsenic levels in soil may also be associated with other sources such as past use of arsenical pesticides for common household practices such as control of crab grass, orchard pests, or household pests such as ants and termites.

This study was conducted in response to a request from representatives of the Colorado People's Environmental and Economic Network (COPEEN), the Clayton, Cole, Elyria, and Swansea Neighborhood Coalition (CEASE), and the community's technical advisor, Dr. Michael Kosnett, to examine cancer statistics routinely collected by the Colorado Central Cancer Registry (CCCR) for residents living in the vicinity of the VBI70 Superfund Site. Cancers diagnosed in Colorado are reported to the Colorado Central Cancer Registry at the Colorado Department of Public Health and Environment.

Cancer is a general term applied to a wide variety of different diseases characterized by uncontrolled growth and spread of abnormal cells. These diseases are common within the population, and therefore remain at the forefront of public health concern. Over 16,000 new cases of cancer are registered annually in Colorado, and Coloradons have, on average, an individual lifetime risk of developing cancer of approximately one chance in three[1]. Whether an individual develops cancer during his or her lifetime may be greatly influenced by a variety of factors, many of which are not currently understood. We do know that the development of cancer is a complex, multistage[2] process involving both external factors, such as chemical, radiation, and viral exposure, and internal factors, including hormonal, immune conditions, and inherited mutations. Unfortunately, this complexity and its associated latencies (the time period between the initiation of the cancer and subsequent diagnosis), often limit scientific efforts to identify causative factors or combinations of factors. We may, however, monitor incidence rates of cancer to be alert to significant differences from the expected background rates. This, in turn, allows investigation of statistical deviations with respect to potential environmental associations and provides information about whether an unusual number of cancer cases have occurred in a particular neighborhood.

This study assessed the incidence of cancer in the VBI70 area, defined as Census Tract 35.00-- including a small portion of Census Tract 16.00-- Census Tract 36.01, and Census Tract 36.02. This study also includes an investigation of soil arsenic concentrations in the census tracts studied to further characterize possible exposures at homes where cancer cases were diagnosed.

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1 The cumulative lifetime risk of cancer in Colorado is 1 in 2 for males and 1 in 3 for females.

2 The development of cancer, or carcinogenesis, is believed to be a multistage process involving replication of damaged DNA, reduced control of cell division and function, and transformation into a malignant tumor.

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METHODS

The study design used was an analysis of the number of cancers diagnosed in the Vasquez Boulevard/I-70 area compared to a "typical" or expected number of cancer cases based on rates in the general Denver metropolitan area. In Colorado, surveillance of cancer incidence is possible using data collected by the Central Cancer Registry at the Department of Public Health and Environment. The Cancer Registry maintains an incidence-based registry of all cancer cases, except non-melanoma skin cancers, reported at hospitals and other medical facilities. Data from incidence-based registries provide several benefits compared to mortality-based data. Because incidence-based registries identify each case at the time a diagnosis of cancer is reported, rather than at the time of death, a more complete count of all cancers that have occurred, regardless of survival, is available. Incidence data will not be affected by differences in survival across cancer types and sites, whereas mortality data are susceptible to bias from differences in treatment and access to health care, particularly when more readily treatable types of cancer, such as breast, prostate or thyroid cancer, are being compared. In addition, medical records used to compile incidence-based registry statistics typically have more detailed information on cancer diagnoses, from sources such as pathology reports, than is collected on death certificates, which are used to compile mortality statistics.

The epidemiological study design used is descriptive and ecological. The descriptive element provides a numerical summary of disease frequency, whereas the ecological component examines entire communities or populations, rather than individuals. Ecological studies have been conducted frequently in communities adjacent to potential environmental exposures, since they are efficient and can be completed within a reasonable period of time. Theses types of studies are usually viewed as exploratory and hypothesis-generating, because the analyses made are for large or small groups of people, rather than for individuals. A weakness inherent in studies in which the analysis is at the group level, rather than the individual, is that information on potential confounders, such as lifestyle behaviors, occupation, genetic predisposition, or residential history, is lacking or limited and the data cannot be fully examined for their effects. Another weakness of ecological studies is that, because potential exposure to an individual is not actually measured, geographical area of residence is used as a surrogate measure of exposure. The use of geographical area raises the likelihood of exposure misclassification, which reduces the ability of the study to observe a statistically significant difference between groups. Lastly, the design of this cancer incidence analysis does not allow conclusions to be made about causal association between exposure and any single cancer or group of cancers. The study design and results only aid in determining whether the number of certain cancers is greater or less than expected, whether that difference is statistically significant, and whether additional study would be useful.

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Choice of Study Area and Population Estimates

For this study, cancer diagnosis counts were compared to expected counts for Census Tracts 35.00, 36.01, and 36.02, covering the time period of 1982-98. Descriptive epidemiological studies of incident cancer cases are usually based upon residence within a given census tract, recognizing that the boundaries of the census tract may, in some cases, define the exposure area imprecisely. However, census tract data provide the most accurate, up-to-date population counts as well as age, gender, and racial composition, factors that can influence cancer rates in an area. For this study, the boundary of the census tracts selected matches the area of interest within the VBI70 Superfund Site project boundary quite closely (see Figure 1).

U.S. Census counts of population for the three census tracts by age, race/ethnicity, and sex for 1980, 1990, and 2000 were obtained from a number of sources, as described below.

Population data for 1980 for each census tract, stratified by age, race/ethnicity, and sex, came from two sources: (1) Table 8 of the 1980 Census STF2 file provided by the Colorado Department of Local Affairs, Division of Local Government (State Demographer's Office) and (2) Tables P-1, P-2, P-3, P-6 and P-7, 1980 Census of Population and Housing, Census Tracts, Denver-Boulder, Colo. SMSA, PHC80-2-138. Since estimates of non-Hispanic whites and non-Hispanic blacks by age and sex were not provided directly in the 1980 Census, these data were computed by a series of calculations using these tables. The full, detailed population counts for census tracts by race/ethnicity, age, and sex for 1980 were then printed and stored in the Colorado Central Cancer Registry.

Population data for 1990 for each census tract, by age, race/ethnicity, and sex, were obtained from the Colorado Department of Local Affairs, Colorado Division of Local Government (State Demographer's Office). These data were obtained from the "Modified Age-Race-Sex (M.A.R.S.)" file prepared by the State Demographer's Office using 1990 Census data. These census tract population files are stored in the Colorado Central Cancer Registry.

Population data for 2000 for these three census tracts by age, race/ethnicity, and sex were obtained from the U.S. Census Bureau website, www.census.gov. Since the 2000 Census allowed individuals to check more than one race and population tables were not provided for every possible combination, population counts for non-Hispanic whites, which represented 7.5 percent of the total in this area, and non-Hispanic blacks, which represented 20.4 percent of the total, were selected from tables where only one race was checked. Hispanic counts were selected from the "Hispanic" tables, and represented 69.5 percent of the total. Population counts for all other races combined, which also included counts where two or more races were checked, were calculated by subtracting the non-Hispanic white, non-Hispanic black, and Hispanic counts from the total counts for the three census tracts. The category of all other races combined represented 2.6 percent of the total population.

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Population estimates for the intercensal years from 1982-1998 by race/ethnicity, sex, and age were then calculated by linear interpolation between the 1980, 1990, and 2000 Census counts. Census Tract 35.00 had a population of 6,708 in 2000, and its boundaries are the Denver-Adams County line, Colorado Boulevard, East 40th Avenue, Walnut, 38th Street and the South Platte River. A small portion of Census Tract 16.00, just southwest of 38th Street, was address-matched to the area included in the VBI70 Superfund Site project boundary (see Figure 1). This portion of Census Tract 16.00 was included with Census Tract 35.00 for this analysis. This small section is defined as Arkins Court and the 3500, 3600, and 3700 blocks of Delgany Street. Census Tract 36.01 had a population of 5,662 in 2000, and its boundaries are Walnut Street, E. 40th Avenue, York Street, Martin Luther King Boulevard, and Downing Street. Census Tract 36.02 had a population of 5,172 in 2000, and its boundaries are East 40th Avenue, Colorado Boulevard, Martin Luther King Boulevard, and York Street. The full study area had a population of 17,542 in 2000, which represents approximately 0.7 percent of the total population for the Denver metropolitan area.[3] The boundaries of the study area were the Denver-Adams county line, Colorado Boulevard, Martin Luther King Boulevard, Downing Street, Walnut Street, 38th Street, and the South Platte River, in addition to Arkins Court and the 3500, 3600, and 3700 blocks of Delgany Street. A small portion of the VBI70 Superfund Site, west of the South Platte River and south of I-70 (southwest Globeville) was not included in this study because that area has been studied in the past as part of an investigation of cancer in residents living near the Asarco Globe Plant. Cancer incidence there was within expected statistical limits for all cancer types evaluated, which included lung, bladder, liver, kidney, prostate, and larynx cancer, for the time period 1980-1990.

Cancer Types Selected for Study

The cancer types selected for an investigation of incident cancer cases are typically based on a known association between a specific type or types of cancer and the exposure of concern. For this study, a request was made by members of COPEEN, CEASE, and their technical advisor to compile data from the Cancer Registry for lung, bladder, and skin cancer, based on numerous human epidemiological studies in Mexico and various Asian and South American populations showing an association between exposure to high levels of arsenic in drinking water and these specific types of cancers (NRC, 1999). Of these three tumor sites, data were available from the cancer registry for lung and bladder cancers only. While the Cancer Registry routinely collects data on all melanoma skin cancers, nonmelanocytic basal and squamous cell carcinomas, the cell types that are associated with arsenic exposure, are only reported if the case is at an advanced stage at diagnosis, meaning the cancer has already spread to the lymph nodes or another organ in the body. For the VBI70 area, since only one case was reported that fit that description, analysis of skin cancer was not possible.

3 – VBI70 population represents approximately 0.1%, 3% and 5%, respectively, of the total Anglo, Hispanic and Black population for the Denver metropolitan area.

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In addition, due to concerns expressed in the past by residents living within this study area, counts for all tumor sites combined ("All Cancers Combined") were compiled for each census tract to determine whether the total number of cancers diagnosed was higher than expected, based on population-specific rates from the Denver metropolitan area as a whole. Based on the initial finding of an elevated number of all cancers types combined, it was determined through further investigation that several specific cancer types had more cases diagnosed than expected in some of the census tracts studied. The additional cancer sites evaluated were pancreas, breast, cervix, colorectal, "other pharynx", larynx, brain and other nervous system, and multiple myeloma. These data are presented in this investigation even though there is no known association between arsenic exposure and these additional cancers.

All cancer sites are categorized in the CCCR according to the International Classification of Diseases for Oncology (ICD-O) anatomic site and histology codes.

Time Period of Study

This study evaluates cancers diagnosed from 1982 to 1998, the last year for which complete case counts were available at the time the study began. All the cancer cases diagnosed between 1982 and 1998 in the study area were identified and registered with the State's Central Cancer Registry according to standard procedures followed for all Colorado cancer cases. This identification process involved searching hospital medical charts, pathology laboratory records, and examining death certificate information. The address at the time of diagnosis for each case was used to assign residence within the census boundaries. U.S. Census counts of population for the three census tracts by age, race, and sex for 1980 and 1990 were obtained from the Colorado Division of Local Government (State Demographers Office). Population data for the area by age, race, and sex for 2000 were obtained from the U.S. Census Bureau website.

Calculation of Diagnosed to Expected Ratios

Cancer rates from the Denver metropolitan area-- excluding the census tracts that comprise the study area-- for the time period 1982-1998 were used as standards for calculating expected numbers of cancers for the study area. This area provides a large population base to generate reliable cancer rates. In addition, complete age-specific rates by race and sex are available from the Cancer Registry for the entire Denver metropolitan area. Each diagnosed case is coded to a census tract based on the address of the patient at the time the cancer was diagnosed. The Denver metropolitan area is defined as six counties, comprised of Adams, Arapahoe, Boulder, Denver, Douglas, and Jefferson.

Cancer rates from the Cancer Registry for men and women of comparable race groups and ages were used to calculate the expected number of cancers for each census tract within the study area. A cancer rate is the annual average number of new cancer cases diagnosed per 100,000 population for a particular time period. To calculate the expected number of cancers, the population in each census tract area, stratified by age, sex, and race, was multiplied by the cancer

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rate for each age, sex, and race group in the Denver metropolitan comparison population. This method assures that any differences found are not due to differences in demographic composition. For example, census tracts with a higher proportion of elderly individuals would be expected to have higher cancer rates, since incidence of most cancers increases dramatically with increasing age.

A diagnosed-to-expected ratio was then calculated by dividing the number of cancers diagnosed in the area by the number of expected cases. This ratio is called a standardized incidence ratio, or SIR. If the SIR was greater than 1, then more cancer cases than expected were reported in the area. When this occurred, the next step was to look more closely at that relationship. It was important to know if that ratio could have been higher by chance alone, so a confidence interval was calculated for the ratio. The confidence interval has a lower number, or a minimum value, called a lower confidence limit, and a higher number, or a maximum value, called the upper confidence limit. It is common to use a 95 percent confidence interval, which means that we are 95 percent sure that the true ratio is within the range between the lower and higher values. If the ratio is greater than 1 but the confidence interval includes the number 1, then the ratio is within expected statistical limits. If the confidence interval does not include the number 1, then the ratio is statistically significant at the $p<.05$ level, meaning there is less than a 5 percent chance that the higher number of diagnosed cancers is due to chance alone. A statistically significant elevated ratio means that there were more diagnosed cases than expected and the result probably did not happen by chance.

Because the estimate of expected cancers was based on the larger Denver metropolitan area population, this estimate will be a central tendency, or average number, of expected cases for the time period 1982-1998. Cancer rates for specific populations, such as smaller cities, towns, or neighborhoods, will likely be either somewhat higher or lower than the "expected average". Smaller populations tend to show greater variability. The variability of small populations is statistically reflected in the 95 percent confidence interval for the ratio of diagnosed-to-expected cases. Confidence intervals for small populations are generally wider than for large populations. When the expected number of cancer cases is small, slight increases can result in large diagnosed- to-expected ratios. For example, if only one case of cancer is expected in a small population in a given year, and two were actually diagnosed, the ratio would show a doubling of cases. But, in this situation, twice the number of expected cases would be within expected statistical limits. Statistical testing was not done on ratios with fewer than three diagnosed cases, because of the inherent variability of such small numbers.

When statistically significant elevations of diagnosed-to-expected ratios were observed, other data recorded in the cancer registry abstract were also reviewed. The abstract data reviewed included occupation, smoking history, and cell type. These data help to characterize potential exposure commonalities among the cases, including the presence of important known risk factors for certain cancers, and separation of particular anatomical categories of cancer into cell types. Lastly, for cervical cancer, the frequency of *in situ* and invasive disease diagnoses was noted. The relative frequency of disease stage may suggest late access to preventive medicine.

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Tests of Statistical Significance

The statistical significance of the standardized incidence ratio (SIR), the number of diagnosed cases divided by the expected number, was tested by treating the observed number as a Poisson variate in respect to its expected frequency. Confidence intervals for these ratios were calculated and examined for statistical significance using published tables (Bailar, 1964). Due to the large number of comparisons being made, the probability level of 0.05 was used as a cutoff to determine significance. Ratios having a 95 percent confidence interval that bracket the value 1.00 were not considered statistically high or low.

Analysis of Soil Arsenic Concentration Data

Because yards within the VBI70 site containing unusually high concentrations of arsenic do not occur in any predictable geographic pattern, additional analysis was done to investigate whether soil arsenic concentrations were higher at homes where cancer cases occurred compared to all other homes. Many homes in the study area have had their yards tested by EPA to determine the levels of arsenic in their soil. An electronic file containing soil measurements for approximately 3,000 properties within the study area was reviewed, so that the arsenic concentrations in the soil of homes of bladder, lung, and selected breast and brain cancer cases could be matched by address and then compared to soil arsenic concentrations of all homes tested within the study area. Chi-square tests were used to compare soil arsenic concentrations in the census tracts studied.

Additional statistical analysis was done for residences where lung cancers were diagnosed, due to the established association between lung cancer and arsenic exposure. Cases were stratified into two groups, those with average soil concentrations below 150 mg/kg[4] and those with an average concentration at or above 150 mg/kg. The stratification break-point for the soil arsenic concentration (150 mg/kg) was selected to provide the highest possible soil arsenic level for which adequate data were available, to allow for statistical comparison between the "high" and "low" categories. Relative risks were calculated to test whether there was a relationship between higher soil arsenic concentrations and occurrence of lung cancer for each census tract. Similar statistical tests were not conducted for homes of residents diagnosed with bladder cancer, or select subpopulations with statistically elevated numbers or unusual distributions of breast or brain cancer, due to the small number of properties with a soil arsenic concentration above 150 mg/kg at residences where those individuals lived at the time of diagnosis.

4 mg/kg = milligrams per kilogram. This is a standard unit of measurement used to express chemical concentration in soil and can be interpreted here as milligrams of arsenic per kilogram of soil.

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FINDINGS

Tables 1-4 display the findings for the cancer types that are the primary focus of this study: bladder, lung, and all cancers combined. These tables display the number of diagnosed cancers in the study area during 1982-98 compared to the number that would be expected based on the population of male and female residents in the areas studied, stratified by race and age. Tables 5-20 display similar information for several additional cancers – pancreas, colorectal, cervix, breast, "other pharynx", larynx, brain and other nervous system, and multiple myeloma – that had statistically high ratios of diagnosed-to-expected cases for a particular gender or census tract in the study area or had a pattern of high ratios not necessarily beyond statistical limits. Cancer rates from the Cancer Registry for men and women of comparable race groups and ages were used to calculate the expected number of cancers for the areas. The ratios of diagnosed-to-expected cases along with the 95 percent confidence intervals for these ratios provide information about the relative rate of cancer in these areas. Note that diagnosed/expected ratios and confidence intervals are displayed with rounding to two decimal points. In Tables 1,5,and 6 where the displayed lower bound of a confidence interval rounded to 1.00, the third decimal was considered when determining that the confidence interval did not include 1.00, thus resulting in a statistically significant ratio.

Table 21 provides a summary of all statistically significant findings for each census tract, stratified by gender.

Tables 22-24 display statistical summaries and comparisons of soil arsenic concentrations for the entire study area and for individual census tracts, compared to arsenic levels at homes where cancer cases were diagnosed.

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All Cancers Combined. Table 1 shows that the overall numbers of cancers diagnosed in the study area during 1982-98 were statistically higher than the expected numbers calculated. There were 942 cancers diagnosed, compared to about 882 cancers expected, for a ratio of 1.07. The ratio of diagnosed-to-expected cancers in the study area was 1.07 for males and 1.06 for females, both of which were within expected statistical limits. For one Census Tract, 35.00, there were 186 cancers in females diagnosed, compared to about 154 cancers expected, for a statistically high ratio of 1.21. Most of the elevation seen in female cancers in Census Tract 35.00 was due to higher ratios for pancreas, colorectal, cervical, and breast cancer, as described in Tables 5-12.

Table 1 - Number of Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	166	161.57	1.03	(0.88-1.20)
Tract 36.01	152	139.88	1.09	(0.92-1.27)
Tract 36.02	168	151.30	1.11	(0.95-1.29)
Study Area	486	452.75	1.07	(0.98-1.17)
Females				
Tract 35.00	186	153.38	1.21*	(1.04-1.40)
Tract 36.01	133	129.64	1.03	(0.86-1.22)
Tract 36.02	137	145.77	0.94	(0.79-1.11)
Study Area	456	428.78	1.06	(0.97-1.16)
Both Sexes				
Tract 35.00	352	314.95	1.12*	(1.00-1.24)
Tract 36.01	285	269.51	1.06	(0.94-1.19)
Tract 36.02	305	297.07	1.03	(0.91-1.15)
Study Area	942	881.53	1.07*	(1.00-1.14)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.

* Ratio is statistically high at p=.05 level.

** Ratio is statistically high at p=.01 level.

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Bladder Cancer. Table 2 shows that the overall numbers of bladder cancers diagnosed in the study area during 1982-98 were not statistically higher than the expected numbers calculated. There were 20 bladder cancers diagnosed, compared to about 28 cases expected, for a ratio of 0.72. Ratios of diagnosed-to-expected cancers were 0.79 for males and 0.55 for females in the study area, both also within expected statistical limits. Nine of 20 cases, or 45 percent, had a recorded history of smoking and two were non-smokers. Limiting the calculation to the 11 cases with registry information available for smoking status, nine of 11 cases, or 82 percent, were smokers. A review of occupational data from CCCR abstracts and death certificates showed a variety of occupations listed with no particular job pattern. See Soil Arsenic Concentrations section for analysis of arsenic soil levels at homes of residents diagnosed with bladder cancer.

Table 2 - Number of Bladder Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed To Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	7	9.45	0.74	(0.30-1.53)
Tract 36.01	7	5.67	1.24	(0.50-2.55)
Tract 36.02	2	5.27	0.38	NC
Study Area	16	20.38	0.79	(0.45-1.27)
Females				
Tract 35.00	0	3.06	0.00	NC
Tract 36.01	0	2.04	0.00	NC
Tract 36.02	4	2.16	1.85	(0.50-4.73)
Study Area	4	7.27	0.55	(0.15-1.41)
Both Sexes				
Tract 35.00	7	12.50	0.56	(0.22-1.15)
Tract 36.01	7	7.71	0.91	(0.36-1.87)
Tract 36.02	6	7.43	0.81	(0.30-1.76)
Study Area	20	27.64	0.72	(0.44-1.12)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

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Lung Cancer. Table 3 shows that the overall number of lung cancers diagnosed in the study area during 1982-98 was statistically higher than the expected number calculated. There were 135 lung cancers diagnosed, compared to about 107 cases expected, for a statistically high ratio of 1.26. Most of the lung cancer elevation was due to the elevation seen in males, where 88 cases were diagnosed, compared to about 67 cases expected, for a statistically high ratio of 1.32. The statistically high ratio of 1.56 in Census Tract 36.01 for both sexes was due mostly to the high ratio of 1.65 among men. The ratio among women in this census tract was 1.40, which was within expected statistical limits.

Table 3 - Number of Lung Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	26	21.74	1.20	(0.78-1.75)
Tract 36.01	34	20.61	1.65**	(1.14-2.31)
Tract 36.02	28	24.33	1.15	(0.77-1.66)
Study Area	88	66.68	1.32*	(1.05-1.63)
Females				
Tract 35.00	15	13.25	1.13	(0.63-1.87)
Tract 36.01	17	12.16	1.40	(0.81-2.24)
Tract 36.02	15	14.95	1.00	(0.56-1.66)
Study Area	47	40.36	1.17	(0.86-1.55)
Both Sexes				
Tract 35.00	41	35.00	1.17	(0.84-1.59)
Tract 36.01	51	32.76	1.56**	(1.16-2.05)
Tract 36.02	43	39.28	1.10	(0.79-1.48)
Study Area	135	107.04	1.26*	(1.06-1.49)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.

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Table 4 shows that there were 42 lung cancers diagnosed among white, non-Hispanics in the study area during 1982-98, compared to about 27 cases expected, for a ratio of 1.57, which was statistically significant. Ratios of diagnosed-to-expected cases for the other race/ethnic groups were all within expected statistical limits. Ratios displayed by age showed values above 1.00 for every age group, but only the 55-64 age group had a statistically high ratio of 1.50, 43 cases compared to about 29 expected.

Table 4 – Number of Lung Cancer Diagnoses by Race and by Age Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	42	26.84	1.57**	(1.13-2.12)
Hispanic	26	25.81	1.01	(0.66-1.48)
Black	67	52.98	1.27	(0.98-1.61)
Age				
35-44	5	2.18	2.29	(0.74-5.36)
45-54	11	7.97	1.38	(0.69-2.47)
55-64	43	28.67	1.50*	(1.09-2.02)
65-74	47	41.04	1.15	(0.84-1.52)
75+	29	26.62	1.09	(0.73-1.56)
Total	135	107.04	1.26*	(1.06-1.49)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.

Because smoking is known to be the primary cause of lung cancer, a review of CCCR abstracts was undertaken to determine smoking status for lung cancer cases. This review established that 77 percent of the 135 lung cancer cases in the study area had a recorded history of smoking, although smoking status could not be determined from the available records for some of the cases. Including only the 107 cases with information recorded on smoking status, 97 percent were smokers. Although smoking history was not available

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for 9 of the 34 male lung cancer cases diagnosed in Census Tract 36.01, all of the males in this census tract, for whom smoking status could be determined, were smokers.

A review of occupational data from Cancer Registry abstracts and death certificate records indicated a variety of jobs were held by individuals diagnosed with lung cancer, representing a mix of professional, technical, homemaker, skilled and unskilled laborers. Some job types did indicate the potential for work in industries associated with an increased risk for developing lung cancer. These included work as a stone mason, plasterer, auto mechanic, metal work, mining, wood worker, and construction work with asbestos. There were no uncommon histological types recorded, and the distribution of types of lung cancer in the study area was comparable to the rest of the Denver metropolitan area. The cases included the major forms of lung cancer: squamous cell carcinoma (27 percent vs. 24 percent in the Denver metropolitan area), large cell carcinoma (11 percent vs. 10 percent), small cell carcinoma (19 percent vs. 18 percent), adenocarcinomas (30 percent vs. 32 percent), and all other types (13 percent vs. 16 percent).

See Soil Arsenic Concentration section for more analysis of arsenic soil levels at homes of residents diagnosed with lung cancer.

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Pancreas Cancer. Table 5 shows that the 11 pancreatic cancers diagnosed among males in the study area were close to the expected number of about 12. However, there were 18 pancreatic cancers diagnosed among females in the entire study area during 1982-98, compared to about 11 cases expected, for a ratio of 1.70, and there were 14 cases among males and females combined in Census Tract 35.00, compared to about eight cases expected, for a ratio of 1.83. Both of these ratios were statistically significant. The Census Tract 35.00 elevation was due to females having a statistically higher ratio of 2.64, while the ratio for males was near one.

Table 5 - Number of Pancreas Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	4	3.85	1.04	(0.28-2.65)
Tract 36.01	5	4.04	1.24	(0.40-2.89)
Tract 36.02	2	4.48	0.45	NC
Study Area	11	12.37	0.89	(0.44-1.59)
Females				
Tract 35.00	10	3.79	2.64*	(1.27-4.85)
Tract 36.01	2	3.23	0.62	NC
Tract 36.02	6	3.58	1.68	(0.61-3.65)
Study Area	18	10.60	1.70*	(1.00-2.68)
Both Sexes				
Tract 35.00	14	7.64	1.83*	(1.00-3.07)
Tract 36.01	7	7.27	0.96	(0.39-1.99)
Tract 36.02	8	8.06	0.99	(0.43-1.95)
Study Area	29	22.97	1.26	(0.85-1.81)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

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Table 6 displays pancreatic cancer findings for females by race/ethnicity and age. Ratios of diagnosed-to-expected cases for the individual race groups were all within expected statistical limits. Ratios displayed by age showed a statistically higher ratio of 2.41 in the 75+ age group. Smoking is a risk factor for pancreatic cancer, and according to CCCR abstracts, six of the 18 female pancreatic cases, or 33 percent, had a reported history of smoking. Examining only abstracts with recorded information about smoking status, six of 10 cases, or 60 percent, were smokers. In the 75+ age group, two of the 10 cases, or 20 percent, were smokers. Using only abstracts with recorded information about smoking status, two of five cases, or 40 percent, were smokers.

Table 6 – Number of Pancreas Cancer Diagnoses by Race and by Age Compared to the Expected Number in Census Tract 35.00, 36.01, and 36.02, 1982-98, Females

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	6	2.65	2.26	(0.83-4.93)
Hispanic	7	3.10	2.26	(0.91-4.65)
Black	5	4.68	1.07	(0.35-2.50)
Age				
45-54	3	0.65	4.65	(0.96-13.60
55-64	4	1.79	2.23	(0.61-5.71)
65-74	1	3.82	0.26	NC
75+	10	4.15	2.41*	(1.16-4.43)
Total	18	10.60	1.70*	(1.00-2.68)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

A review of occupational data from Cancer Registry abstracts and death certificate records for females diagnosed with cancer of the pancreas indicated a variety of jobs held, with no pattern of occupations associated with higher risk for developing pancreatic cancer, such as chemists, coal gas workers, or those in the metal, leather-tanning, and textile industries. The distribution of cell types was similar to the rest of the Denver metropolitan area, with 72 percent of cases being adenocarcinomas, compared to about 66 percent of cases in the Denver metropolitan area.

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Colorectal Cancer. Table 7 shows that the count of 129 diagnosed cases of colorectal cancer in the entire study area during 1982-98 was close to the expected count of about 114, resulting in a ratio of 1.13. Among males there were 57 colorectal cancers diagnosed, compared to about 59 expected, for a ratio of 0.97. However, among females there were 72 cases diagnosed, compared to about 56 cases expected, for a ratio of 1.29, which was statistically high.

Table 7 - Number of Colorectal Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	15	21.32	0.70	(0.39-1.16)
Tract 36.01	17	18.43	0.92	(0.54-1.48)
Tract 36.02	25	19.01	1.32	(0.85-1.94)
Study Area	57	58.76	0.97	(0.73-1.26)
Females				
Tract 35.00	26	18.70	1.39	(0.91-2.04)
Tract 36.01	23	17.06	1.35	(0.85-2.02)
Tract 36.02	23	19.92	1.16	(0.73-1.73)
Study Area	72	55.68	1.29*	(1.01-1.63)
Both Sexes				
Tract 35.00	41	40.02	1.03	(0.74-1.39)
Tract 36.01	40	35.49	1.13	(0.81-1.54)
Tract 36.02	48	38.93	1.23	(0.91-1.64)
Study Area	129	114.44	1.13	(0.94-1.34)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.

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Due to the statistically high ratio for female colorectal cancer in the study area, more detailed analysis was conducted on these cases. Smoking is considered a potential risk factor for colorectal cancer, and 21 out of 72 female colorectal cancer cases, or 29 percent, had a known history of smoking, according to Cancer Registry abstracts. Limiting this calculation only to cases where smoking status was available, 21 out of 37 cases, or 57 percent, were smokers. Colorectal cancer is generally not viewed as an occupational disease, although there have been reports of some increased risk to workers in the auto manufacturing industry and mixed results in workers exposed to asbestos. A review of occupational data from Cancer Registry abstracts indicated a variety of jobs listed for those diagnosed with colorectal cancer with no particular pattern evident.

The distribution of colorectal cancer cell types in females was similar to Denver metropolitan area findings, with 99 percent of cases being adenocarcinomas, compared to about 92 percent of the Denver metropolitan area cases. The distribution of anatomic sites within the colon and rectum was similar to that seen in the Denver metropolitan area, with close to half of all cases being "right" sided, meaning from the cecum through the splenic flexure, about one-fourth being "left" sided, meaning the descending colon and sigmoid colon, and about one-fourth from the rectum and rectosigmoid junction.

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Table 8 displays colorectal cancer findings for females in the entire study area by race/ethnicity and age. Ratios of diagnosed-to-expected cases for the individual race/ethnic groups, though above 1.00, were all within expected statistical limits. Ratios displayed by age showed elevations in the 55-74 age range. Although the 55-64 and the 65-74 age-group ratios were within expected statistical limits, combining the two groups resulted in 44 cases, compared to about 30 expected, for a statistically high ratio of 1.49. In this 55-74 age range, 17 out of 44 cases, or 39 percent, were recorded as smokers in CCCR abstracts, with smoking status not recorded for some individuals. Limiting this calculation to cases with known smoking status, 17 out of 22 cases, or 77 percent, were smokers.

Table 8 – Number of Colorectal Cancer Diagnoses Among Females by Race and by Age Compared to the Expected Number in Census Tract 35.00, 36.01, and 36.02, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	21	13.96	1.50	(0.93-2.30)
Hispanic	18	13.81	1.30	(0.77-2.06)
Black	33	27.41	1.20	(0.83-1.69)
Age				
35-44	3	1.47	2.04	(0.42-5.95)
45-54	4	3.45	1.16	(0.32-2.97)
55-64	17	10.57	1.61	(0.93-2.57)
65-74	27	18.91	1.43	(0.94-2.08)
75+	21	20.75	1.01	(0.62-1.55)
Total	72	55.68	1.29*	(1.01-1.63)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.

* Ratio is statistically high at p=.05 level.

** Ratio is statistically high at p=.01 level.

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Cervix Cancer. Table 9 shows that the ratio of 1.44, resulting from 44 cervical cancers diagnosed compared to about 31 cases expected in the study area during 1982-98, was statistically higher than expected. Individual census tracts had elevated ratios, though within expected statistical limits.

Due to the statistically high ratio for cervix cancer in the study area, more detailed analysis was conducted on these cases. Almost half (48 percent) of the cervical cancers in the study area were invasive, while only 31 percent of cervical cases in the Denver metropolitan area for this time period were invasive, indicating a problem with late detection in the study area. The distribution of cancer cell types among the *in-situ* cancers in both the study area, with 65 percent carcinomas and 35 percent squamous cell carcinomas, and in the Denver metropolitan area, with 58 percent carcinomas and 40 percent squamous cell carcinomas, were similar. However, the distribution of cell types among the invasive cases appeared different. In the study area, squamous cell carcinomas accounted for 53 percent of invasive cases, compared to 72 percent in the Denver metropolitan area. For adenocarcinomas the differences were smaller, 29 percent in the study area and 23 percent in other Denver metropolitan areas. For all other cell types, the percentages were 19 percent in the study area vs. 6 percent in the Denver metropolitan area. All of these cell type differences were dependent on small case counts in the study area, where each case of the 23 *in-situ* cases or the 21 invasive cases represents close to 5 percentage points. Thus, a change of only 1 or 2 cases can affect study area percentages by 5-10 percentage points.

Smoking is considered a risk factor for cervical cancer, and 11 out of 44 cervical cancer cases, or 25 percent, had a known history of smoking, according to Cancer Registry abstracts. Limiting this calculation only to cases with information about smoking history recorded, 11 out of 18 cases, or 61 percent, were smokers.

Table 9 - Number of Cervix Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Females				
Tract 35.00	16	11.91	1.34	(0.77-2.18)
Tract 36.01	16	9.53	1.68	(0.96-2.73)
Tract 36.02	12	9.10	1.32	(0.68-2.30)
Study Area	44	30.53	1.44*	(1.05-1.94)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.

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Table 10 displays cervical cancer findings by race/ethnicity and age for the study area. The ratio of 2.56 among non-Hispanic whites, resulting from 11 cases diagnosed compared to about 4 cases expected, was statistically high. For Hispanics, the number of cases was very close to the expected. The ratio of 1.57 among Blacks, with 15 cases diagnosed compared to about 10 expected, was within expected statistical limits. Ratios displayed by age for all races combined showed the most elevations in the 45-54, 55-64, and 65-74 age range. These ratios were close to 2.00. Each age category was within expected statistical limits, but combining these three age groups together resulted in a statistically significant ratio of 2.12, resulting from 21 cases compared to about 10 expected.

Table 10 – Number of Cervix Cancer Diagnoses by Race and by Age Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	11	4.31	2.56**	(1.28-4.57)
Hispanic	17	16.22	1.05	(0.61-1.68)
Black	15	9.58	1.57	(0.87-2.58)
Age				
15-19	1	0.25	4.03	NC
20-24	4	2.59	1.55	(0.42-3.95)
25-34	11	9.83	1.12	(0.56-2.00)
35-44	6	6.43	0.93	(0.34-2.03)
45-54	7	3.30	2.12	(0.85-4.37)
55-64	7	3.49	2.01	(0.81-4.13)
65-74	7	3.14	2.23	(0.90-4.60)
75+	1	1.50	0.67	NC
Total	44	30.53	1.44*	(1.05-1.94)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.

* Ratio is statistically high at p=.05 level.

** Ratio is statistically high at p=.01 level.

NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

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Female Breast Cancer. Table 11 shows that the count of 133 breast cancers diagnosed in the study area during 1982-98 was close to the approximately 125 cases expected. However, there were 69 breast cancers diagnosed among females in Census Tract 35.00, compared to about 47 cases expected, for a ratio of 1.47, which was statistically significant. Due to the higher ratio in Census Tract 35.00, several additional analyses of these data were done.

Table 11 - Number of Female Breast Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Females				
Tract 35.00	69	46.89	1.47**	(1.15-1.86)
Tract 36.01	27	36.89	0.73	(0.48-1.07)
Tract 36.02	37	41.31	0.90	(0.63-1.24)
Study Area	133	125.08	1.06	(0.89-1.26

Note: *Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.*
** Ratio is statistically high at p=.01 level.

First, the distribution of cell types in Census Tract 35.00 was similar to that seen in other Denver metropolitan area breast cancers during 1982-1998. The top three cell types in the census tract accounted for over 90 percent of the cases. These included infiltrating ductal carcinoma, (80 percent vs. 72 percent in the rest of the Denver metropolitan area), lobular carcinoma (9 percent vs. 8 percent), and medullary carcinoma (3 percent vs. 1 percent).

Second, breast cancer findings by race/ethnicity and age for Census Tract 35.00 are shown in Table 12 on the next page. The ratio of diagnosed cases to expected cases was elevated for non-Hispanic whites, though within expected statistical limits. For Blacks, the number of cases was less than expected. However, the ratio of 1.75 among Hispanics, with 36 cases diagnosed compared to about 21 expected, was statistically high. Ratios displayed by age for all races combined showed elevations in the 25-44 age range and in the 75+ age groups.

Third, the number of second breast cancers was checked to examine the contribution of multiple breast cancers on these elevated ratios. Cancer cases are counted statistically as independent, primary cancer diagnoses, such that one person with more than one primary cancer may account for two or more case counts. In the entire Denver metropolitan area for 1982-98, the time period

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of this study, about 5 percent of primary breast cancers were second or later diagnoses in the same individual. However, in Census Tract 35.00, 10 of the 69 breast cancers, or 14 percent, were second tumors, a percentage high enough to elevate the ratio of diagnosed-to-expected breast cancers above expected statistical limits.

The effect of multiple breast cancer diagnoses was also seen in the Hispanic data where 7 of 36 breast cancers, or 19 percent, were second tumors. This finding is in agreement with some research which suggests that Hispanic women generally have higher rates of multiple primary tumors (Fox, 1998). However, Denver metropolitan area data for 1982-98 showed about 7 percent of Hispanic cases to be second tumors, very close to the rate of 5 percent for the rest of the Denver metropolitan area for all race/ethnicity groups combined. Likewise, the elevated ratios seen in the 25-44 age groups were partly explained by multiple tumors where 4 of 15 breast

Table 12 – Number of Female Breast Cancer Diagnoses by Race and by Age Compared to the Expected Number in Census Tract 35.00, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	31	23.96	1.29	(0.88-1.84)
Hispanic	36	20.47	1.76**	(1.23-2.44)
Black	2	2.16	0.93	NC
Age				
25-34	5	1.38	3.63*	(1.17-8.48)
35-44	10	4.96	2.02	(0.97-3.71)
45-54	6	7.84	0.77	(0.28-1.67)
55-64	12	9.45	1.27	(0.65-2.22)
65-74	17	12.72	1.34	(0.78-2.14)
75+	19	10.49	1.81*	(1.09-2.83)
Total	69	46.89	1.47**	(1.15-1.86)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

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cancers, or 27 percent, were second tumors. Also, in the 75+ age group, 2 of 19 breast cancers, or 11 percent, were second tumors. Compared to the more common value of 5-7 percent of cases being second tumors, these higher percentages of second tumors in Hispanics and in the 25-44 and 75+ age groups were enough to elevate the diagnosed-to-expected case counts above statistical limits for this study population.

Multiple breast tumor data in Census Tract 35.00 were also checked to compare the percentage of tumors diagnosed bilaterally, meaning tumors occurred in both breasts, to the percentage for the Denver metropolitan area. In the census tract, 9 of 10 women, or 90 percent, with multiple tumors were diagnosed bilaterally, which is very close to the Denver metropolitan area data, showing a rate of 89 percent.

Fourth, among the 69 breast cancer cases diagnosed in Census Tract 35.00, about 59 percent were detected "early" (either *in situ* or localized stage) when survival can be enhanced. This percentage is not as good as the early detection percentage, 69 percent, seen in the Denver metropolitan area during this time period. For the very earliest stage, *in situ*, where survival can be over 95 percent, only about 6 percent of cases in the census tract were detected that early, compared to 13 percent in the Denver metropolitan area.

See Soil Arsenic Concentrations section below for analysis of arsenic soil levels at homes of the 15 breast cancer cases from the 25-44 age category.

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Other Pharynx Cancer – Table 13 shows that the ratio of 2.49, resulting from 18 "other pharynx" cancers diagnosed in the entire study area during 1982-98 compared to about seven cases expected, was statistically higher than expected. The "other pharynx" category includes cancers of the tonsil, oropharynx, and hypopharynx, including the pyriform sinus. Sixteen of the 18 cases were males, and the ratios for males were elevated in all three census tracts, with the ratio of 5.18 in census tract 35.00 and the ratio of 3.14 in the entire study area being statistically high.

Table 13- Number of "Other Pharynx" Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	8	1.54	5.18**	(2.23-10.21)
Tract 36.01	3	1.53	1.96	(0.40-5.73)
Tract 36.02	5	2.02	2.48	(0.80-5.79)
Study Area	16	5.09	3.14**	(1.80-5.10)
Females				
Tract 35.00	0	0.51	0.00	NC
Tract 36.01	2	0.68	2.93	NC
Tract 36.02	0	0.94	0.00	NC
Study Area	2	2.13	0.94	NC
Both Sexes				
Tract 35.00	8	2.05	3.89**	(1.68-7.67)
Tract 36.01	5	2.21	2.26	(0.73-5.28)
Tract 36.02	5	2.96	1.69	(0.55-3.95)
Study Area	18	7.22	2.49**	(1.47-3.94)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

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Due to the statistically high ratio for "other pharynx" cancers in the study area, more detailed analysis was conducted on these cases. Smoking and alcohol consumption are considered risk factors for "other pharynx" cancers, and 15 out of 18 cases, or 83 percent, had a known history of smoking according to Cancer Registry abstracts. Limiting this calculation only to cases where smoking status was available, 15 out of 15 cases, or 100 percent, were smokers. Alcohol consumption was indicated on abstracts for eight of the 18 cases, and six of the eight cases had histories of high consumption of alcohol or alcohol abuse mentioned on the medical abstract. High consumption of alcohol was considered to be several shots per day, up to one pint per day of hard liquor, or six beers per day. A review of occupational data from Cancer Registry abstracts indicated a variety of jobs listed for those diagnosed with "other pharynx" cancers, with no particular pattern evident.

The distribution of specific types of cancer within the 18 "other pharynx" cancers in the study area was different from the distribution seen in the Denver metropolitan area. Hypopharynx cancers accounted for 61 percent of study area "other pharynx" cancers, compared to 29 percent in the Denver metropolitan area. Tonsil cancers accounted for 17 percent of study area "other pharynx" cases, compared to 32 percent in the Denver metropolitan area. Oropharynx cancers were equally represented in both datasets, with 11 percent in the study area and 10 percent in the Denver metropolitan area. The remaining types grouped together accounted for 11 percent in the study area and 29 percent in the Denver metropolitan area.

ED_002842_00000592-00030

Table 14 displays "other pharynx" cancer findings in the entire study area by race/ethnicity and age. Ratios of diagnosed-to-expected cases for white, non-Hispanics, with a ratio or 6.07, and for Hispanics, with a ratio of 2.99, were statistically high. Every age group had elevated ratios and the 55-64 age group ratio of 3.32 was statistically high. The ratios for combined age groups 35-54, with 5 cases versus 1.58 expected for a ratio of 3.16, and 35-64, with 12 cases versus 3.69 expected for a ratio of 3.25, were both statistically high, also.

Table 14 – Number of "Other Pharynx" Cancer Diagnoses by Race and by Age Compared to the Expected Number in Census Tract 35.00, 36.01, and 36.02, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	7	1.15	6.07**	(2.44-12.52
Hispanic	6	2.01	2.99*	(1.10-6.52)
Black	5	4.00	1.25	(0.40-2.92)
Age				
35-44	1	0.33	3.01	NC
45-54	4	1.25	3.20	(0.87-8.17)
55-64	7	2.11	3.32*	(1.33-6.84)
65-74	4	2.98	1.34	(0.37-3.44)
75+	2	0.46	4.39	NC
Total	18	7.22	2.49**	(1.47-3.94)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

ED_002842_00000592-00031

Larynx Cancer – Table 15 shows that the number of larynx cancers diagnosed in the study area, 15 cases compared to about 11 expected, for a ratio of 1.39, was not higher statistically than expected. In Census Tract 36.01, though, the ratio of diagnosed to expected larynx cancers was statistically high, 10 cases compared to about 3 or 4 cases expected, for a ratio of 2.92. Ratios were elevated in both males and females in this census tract.

Table 15- Number of Larynx Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	1	2.58	0.39	NC
Tract 36.01	6	2.62	2.29	(0.84-4.99)
Tract 36.02	3	3.13	0.96	(0.20-2.80)
Study Area	10	8.33	1.20	(0.58-2.21)
Females				
Tract 35.00	0	0.61	0.00	NC
Tract 36.01	4	0.80	4.99*	(1.36-12.76)
Tract 36.02	1	1.05	0.96	NC
Study Area	5	2.46	2.03	(0.66-4.75)
Both Sexes				
Tract 35.00	1	3.19	0.31	NC
Tract 36.01	10	3.42	2.92**	(1.41-5.37)
Tract 36.02	4	4.18	0.96	(0.26-2.45)
Study Area	15	10.79	1.39	(0.78-2.29)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

ED_002842_00000592-00032

Due to the statistically high ratio for larynx cancers in Census Tract 36.01, more detailed analysis was conducted on these cases. Smoking and alcohol consumption are considered risk factors for larynx cancers, and six of 10 cases, or 60 percent, had a known history of smoking, according to Cancer Registry abstracts. Limiting this calculation only to cases where smoking status was available, six of six cases, or 100 percent, were smokers. Alcohol consumption was indicated on abstracts for five of the 10 cases, and two of the five cases had histories of high consumption of alcohol, namely alcohol abuse or chronic alcoholism, mentioned on the medical abstract. A review of occupational data from Cancer Registry abstracts indicated a variety of jobs listed for those diagnosed with larynx cancers, with no particular pattern evident.

The distribution of specific anatomic sites within the 10 larynx cancers in Census Tract 36.01 was comparable to the distribution seen in the Denver metropolitan area. Cancers of the glottis and supraglottis accounted for 80 percent of the larynx cancers in the tract, and 83 percent in the Denver metropolitan area. Glottis cancers accounted for 30 percent of cases in the tract, compared to 48 percent in the Denver metropolitan area. Supraglottis cancers accounted for 50 percent of cases in the tract, compared to 35 percent in the Denver metropolitan area. All other sites accounted for 20 percent in the tract, compared to 17 percent in the Denver metropolitan area. Note that the percentages of cases by anatomic site in the census tract were based on a small number of cases, so a single case in a category represents 10 percentage points.

ED_002842_00000592-00033

Table 16 displays larynx cancer findings in census tract 36.01 by race/ethnicity and age. Ratios of diagnosed-to-expected cases for each race/ethnicity group were elevated; the ratio of 3.24 for the Black group was statistically high. Every age group had elevated ratios though within expected statistical limits. The combined 65+ age group ratio of 3.06, where there were six cases compared to about two cases expected, was statistically high.

Table 16 – Number of Larynx Cancer Diagnoses by Race and by Age Compared to the Expected Number in Census Tract 36.01, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	2	0.24	8.48	NC
Hispanic	3	0.83	3.64	(0.75-7.58)
Black	5	1.54	3.24*	(1.05-7.58)
Age				
45-54	2	0.36	5.53	NC
55-64	2	0.99	2.03	NC
65-74	4	1.35	2.97	(0.81-7.61)
75+	2	0.62	3.24	NC
Total	10	3.42	2.92**	(1.41-5.37)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

ED_002842_00000592-00034

Brain and Other Nervous System Cancer – Table 17 shows that the number of brain and other nervous system cancers diagnosed in the study area, with 16 cases compared to about 10 expected, for a ratio of 1.58, was not higher statistically than expected. Most of the cases were males, and their ratio of 1.96, resulting from 11 cases compared to about six expected, was close to being statistically high. However, most of the elevation in males was due to the higher number of male cases in census tract 36.01, where there were five cases compared to about two expected. The remaining six male cases in Census Tracts 35.00 and 36.02, compared to about four expected, resulted in a ratio of 1.53,

Table 17- Number of Brain and Other Nervous System Cancer Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	5	2.37	2.11	(0.68-4.93)
Tract 36.01	5	1.67	3.00	(0.97-7.01)
Tract 36.02	1	1.56	0.64	NC
Study Area	11	5.60	1.96	(0.98-3.51)
Females				
Tract 35.00	0	1.96	0.00	NC
Tract 36.01	4	1.32	3.03	(0.83-7.76)
Tract 36.02	1	1.27	0.79	NC
Study Area	5	4.55	1.10	(0.36-2.57)
Both Sexes				
Tract 35.00	5	4.33	1.15	(0.37-2.70)
Tract 36.01	9	2.99	3.01**	(1.38-5.72)
Tract 36.02	2	2.83	0.71	NC
Study Area	16	10.15	1.58	(0.90-2.56)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

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which was within expected statistical limits. Focusing on Census Tract 36.01, though, the ratio of diagnosed to expected brain and other nervous system cancers was statistically high for males and females combined, with nine cases compared to about three cases expected, for a ratio of 3.01. Ratios were elevated in both males and females in this census tract. Due to the statistically high ratio for brain and other nervous system cancers in Census Tract 36.01, more detailed analysis was conducted on these nine cases. Smoking and alcohol consumption are not generally considered risk factors for these cancers, and Cancer Registry abstract data revealed little information about these factors. A review of occupational data from the Cancer Registry abstracts was also not informative, because only three of the nine cases diagnosed with brain and other nervous system cancers were adults, and two of the three adults had no occupational data listed.

The distribution of histologic cell types within the nine brain and other nervous system cancers in Census Tract 36.01 was comparable to the distribution seen in the Denver metropolitan area. Gliomas accounted for 22 percent of cases in this census tract, compared to 7 percent of cases in the Denver metropolitan area. Glioblastoma percentages were 22 percent, compared to 37 percent in the Denver metropolitan area. Astrocytoma percentages were 22 percent, compared to 30 percent for the Denver metropolitan area. All other types accounted for 33 percent in this census tract and 26 percent in the Denver metropolitan area.

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Table 18 displays brain and other nervous system cancer findings in census tract 36.01 by race/ethnicity and age. Ratios of diagnosed-to-expected cases for each of the race/ethnicity groups were elevated, with the ratio of 3.79 in Blacks, resulting from

Table 18 – Number of Brain and Other Nervous System Cancer Diagnoses by Race and by Age Compared to the Expected Number in Census Tract 36.01, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	1	0.45	2.23	NC
Hispanic	4	1.46	2.74	(0.75-7.02)
Black	4	1.06	3.79*	(1.03-9.70)
Age				
0- 4	2	0.25	7.97	NC
5- 9	2	0.18	10.87	NC
10-14	0	0.07	0.00	NC
15-19	2	0.09	21.51	NC
20-24	0	0.12	0.00	NC
25-34	1	0.28	3.60	NC
35-44	1	0.25	4.05	NC
45-54	0	0.36	0.00	NC
55-64	0	0.41	0.00	NC
65-74	1	0.46	2.17	NC
75+	0	0.52	0.00	NC
Total	9	2.99	3.01*	(1.38-5.72)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
*Ratio is statistically high at p=.05 level.
**Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

ED_002842_00000592-00037

four cases, compared to about one expected, being statistically high. Three of the four Black cases were age 0-19, a combined age group where the ratio of 10.10, resulting from six cases compared to about one case expected, was statistically high. The remaining combined 20+ age group ratio of 1.25, resulting from three cases compared to about two or three cases expected, was within expected statistical limits. The ratios in each age group separately were not tested statistically due to the low case counts.

For the six brain cancers age 0-19 in Census Tract 36.01, the distribution of histologic cell types was compared to the distribution seen in the Denver metropolitan area brain cancer cases of this age. Gliomas accounted for 17 percent of cases in this census tract compared to 12 percent of cases in the Denver metropolitan area. Glioblastoma percentages were 33 percent compared to 6 percent in the Denver metropolitan area. Astrocytoma percentages were 17 percent compared to 46 percent. All other types accounted for 34 percent in this census tract and 36 percent in the Denver metropolitan area. Note that each of these six cases represents about 17 percent of the total, so a change of only one or two cases in a particular category has a major affect on this distribution comparison.

ED_002842_00000592-00038

Multiple Myeloma. Table 19 shows that the number of multiple myeloma cancers diagnosed in the study area, 21 cases compared to about 14 expected, for a ratio of 1.47, was not higher statistically than expected. In Census Tract 36.02, though, the ratio of diagnosed-to-expected multiple myelomas was statistically high, with 13 cases compared to about six cases expected, for a ratio of 2.25. This elevation was seen more in females, with a statistically high ratio of 3.27, than males, with a ratio of 1.32, which was not statistically high.

Table 19- Number of Multiple Myeloma Diagnoses Compared to the Expected Number in Census Tracts 35.00, 36.01, and 36.02 by Sex, 1982-98

	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
Males				
Tract 35.00	3	2.15	1.39	(0.29-4.08)
Tract 36.01	2	2.54	0.79	NC
Tract 36.02	4	3.03	1.32	(0.36-3.38)
Study Area	9	7.72	1.17	(0.53-2.21)
Females				
Tract 35.00	2	1.66	1.21	NC
Tract 36.01	1	2.15	0.47	NC
Tract 36.02	9	2.75	3.27**	(1.50-6.20)
Study Area	12	6.56	1.83	(0.94-3.19)
Both Sexes				
Tract 35.00	5	3.81	1.31	(0.42-3.07)
Tract 36.01	3	4.68	0.64	(0.13-1.87)
Tract 36.02	13	5.78	2.25*	(1.20-3.84)
Study Area	21	14.28	1.47	(0.91-2.25)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

ED_002842_00000592-00039

Due to the statistically high ratio for multiple myelomas in Census Tract 36.02, more detailed analysis was conducted on these 13 cases. Smoking and alcohol consumption are not generally considered risk factors for these cancers, and Cancer Registry abstract data revealed little information about these factors. Seven cases had no information; three cases were listed as nonsmokers; and three cases had a history of smoking. Of these three, two abstracts also mentioned alcohol consumption. A review of occupational data from the Cancer Registry abstracts indicated a variety of jobs listed for those diagnosed with multiple myeloma with no particular pattern evident.

Table 20 displays multiple myeloma findings in Census Tract 36.02 by race/ethnicity and age. Ratios of diagnosed to expected cases for each race/ethnicity group were elevated, but within expected statistical limits. The ratio of 4.16 for the 75+ age group, resulting from six cases compared to about one or two cases expected, was statistically high. The remaining age groups combined, from age 45 to 74, had seven cases, compared to about four cases expected, for a ratio of 1.74, which was within expected statistical limits.

Table 20 – Number of Multiple Myeloma Diagnoses by Race and by Age Compared to the Expected Number in Census Tract 36.02, 1982-98

Race	Cancers Diagnosed	Cancers Expected	Ratio of Diagnosed to Expected (SIR)	95% C.I. for Ratio
White Non-Hispanic	1	0.28	3.60	NC
Hispanic	2	0.49	4.10	NC
Black	10	4.93	2.03	(0.98-3.73)
Age				
45-54	1	0.40	2.51	NC
55-64	1	1.62	0.62	NC
65-74	5	2.01	2.49	(0.81-5.81)
75+	6	1.44	4.16**	(1.53-9.07)
Total	13	5.78	2.25*	(1.20-3.84)

Note: Diagnosed/Expected ratios that have a 95 percent confidence interval that brackets the value 1.00 are not considered statistically high or low.
* Ratio is statistically high at p=.05 level.
** Ratio is statistically high at p=.01 level.
NC = not calculated due to fewer than 3 diagnoses (see methods section for explanation).

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Table 21. Summary table of statistically significant cancer findings by geographic area (census tract) and gender.

Cancer Type	Males and Females Combined				Male				Female			
	Tract 35.00	Tract 36.01	Tract 36.02	Entire Study Area	Tract 35.00	Tract 36.01	Tract 36.02	Entire Study Area	Tract 35.00	Tract 36.01	Tract 36.02	Entire Study Area
All cancers	S			S					S			
Bladder							(nc)		(nc)	(nc)		
Lung		S		S		S		S				
Pancreas	S						(nc)		S	(nc)		S
Colorectal												S
Cervix	(na)	(na)	(na)	(na)	(na)	(na)	(na)	(na)				S
Breast	(na)	(na)	(na)	(na)	(na)	(na)	(na)	(na)	S			
"Other Pharynx"	S			S	S			S	(nc)	(nc)	(nc)	(nc)
Larynx	(nc)	S			(nc)				(nc)	S	(nc)	
Brain & other CNS		S	(nc)				(nc)		(nc)		(nc)	
Multiple Myeloma			S			(nc)			(nc)	(nc)	S	

S = Statistically elevated number of cancers reported
nc = Significance not calculated due to small number of diagnosed cases (n<3)
na = Not applicable
Blank cell indicates that the number of cancers diagnosed is within the expected statistical range.

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STATISTICAL ANALYSIS AND MULTIPLE COMPARISONS

Studies examining multiple health outcomes in several sub-populations may observe statistically elevated rates of those outcomes simply due to chance. This statistical phenomenon is commonly referred to as the "multiple comparisons" problem. If these tests are conducted at a 95 percent confidence level, about 5 percent of the tests are predicted to be statistically significant by chance alone; about 2.5 percent would be expected to be statistically higher than expected and 2.5 percent lower. To fully evaluate the issue of multiple comparisons, ratios for every type of cancer in males and females for each census tract were calculated. For the VBI70 study population, this evaluation resulted in over 160 independent comparisons, or over 320 comparisons, if census tracts and gender-specific ratios are aggregated. With the 160 independent comparisons being tested with 95 percent confidence intervals, about 2.5 percent of these comparisons, or about four ratios, would be expected to be elevated statistically simply due to chance variations. In this analysis, six ratios, or 4 percent of the independent comparisons, were statistically high. Evaluating all comparisons, with census tracts and gender-specific ratios aggregated, 22 ratios were statistically high. All statistically high ratios were investigated further to identify additional factors for individual cancer cases, such as demographic, smoking, or cancer cell type data, that might help interpret the findings.

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SOIL ARSENIC CONCENTRATIONS

Soil sampling has been completed by EPA to determine arsenic concentrations in yards of approximately 3,000 of the 4,000 residences within the VBI70 study area. An electronic file containing soil arsenic measurements by address was reviewed so that arsenic concentrations in the soil of homes where lung cancer cases were diagnosed could be evaluated in more detail. A review was also conducted of all available data for homes of residents diagnosed with bladder cancer. In addition, soil arsenic data were reviewed for two subpopulations with statistically high numbers of cancers reported in an unusually young cross-section of the population, namely women under the age of 45 diagnosed with breast cancer in Census Tract 35.00, and individuals under age 20 diagnosed with brain or other nervous system cancer in Census Tract 36.01, to determine whether a high level of arsenic in soil was a potential source of exposure in these homes.

Table 22 compares the distribution of arsenic concentrations by geographic area and for homes of residents diagnosed with specific types of cancer.

Table 22 – Distribution of arsenic concentrations in soil in residential yards

Location	Number Tested	Average soil arsenic concentration				
		< 50 mg/kg	> 100 mg/kg	> 200 mg/kg	> 300 mg/kg	> 400 mg/kg
VB-I70 Study Area	2949	78.5 %	12.2 %	5.3 %	2.8 %	1.8 %
Tract 35.00	1243	78.2 %	12.5 %	5.0 %	2.6 %	1.1 %
Tract 36.01	801	81.9 %	11. 6 %	4.4 %	2.6 %	2.2 %
Tract 36.02	905	75.6 %	12.6 %	6.5 %	3.2 %	1.5 %
Homes of Lung cancer cases (All Tracts)	84	84.5 %	8.3 %	4.8 %	3.6 %	1.2 %
Homes of Bladder cancer cases (All Tracts)	12	91.7 %	8.3 %	0	0	0
Homes of Breast cancer cases (Tract 35.00)	10	90.0 %	10.0 %	10.0 %	0	0
Homes of Brain/CNS cancers (Tract 36.01)	3	66.7%	0	0	0	0

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The data in Table 22 indicate that the distributions of arsenic concentrations in soil are similar for each individual census tract and that each tract is similar to the distribution in the entire study area. Soil arsenic data were available for 84 homes out of the total of 135 lung cancer cases diagnosed within the VBI70 area between 1982-1998. However, as shown in Table 22, the distribution of soil arsenic in yards where lung cancer cases resided appeared to be representative of the VBI70 study area as a whole. Homes of bladder cases (soil data available for 12 of 20 homes), and of breast cancer cases residing in Census Tract 35.00 and diagnosed at an early age of onset (soil data available for 10 of 15 homes), appeared to be under-represented at the high end of the distribution. For example, fewer homes had concentrations of arsenic in soil above 200 mg/kg, as demonstrated in Table 22. Among those in Census Tract 36.01 diagnosed with brain or other nervous system cancer before the age of 20, none of the homes had a soil arsenic level above 100 mg/kg, although data were available for only 3 of 6 homes.

Table 23 provides a comparison of soil arsenic concentrations for each census tract at all homes where soil arsenic testing was done (n=2949). Homes were stratified into categories of properties with average soil arsenic concentrations of less than 150 mg/kg and yards with arsenic concentrations at or above 150 mg/kg. A stratification break-point for the soil arsenic concentration of 150 mg/kg was selected to provide the highest possible soil arsenic level for which adequate data were available to allow for statistical comparison between the "high" and "low" categories. Table 23 indicates that the general distribution into "high" and "low" arsenic categories and for 95th percentile, median, and maximum soil concentrations are relatively similar for each of the three tracts. A p-value of 0.43 was calculated using a chi square test, indicating that there is not a statistically significant difference between census tract (geographic area) and the number of homes with average soil arsenic levels at or above 150 mg/kg. Any observed differences are likely a chance finding and are normal random variation from the mean.

Table 23 - Soil Arsenic Concentration Summary Statistics for Individual Census Tracts.

Census Tract	Number of yards with average soil arsenic concentration <150 mg/kg	Number of yards with average soil arsenic concentration ≥150 mg/kg	95th percentile (mg/kg)	Median Concentration (mg/kg)	Maximum Concentration (mg/kg)
35.00 (1243)[1]	1151	92 (7.4%)[2]	207	15.3	656
36.01 (801)[1]	737	64 (8.0%)[2]	184	16.9	898
36.02 (905)[1]	824	81 (9.0 %)[2]	241	14.6	1418

1 – Indicates the number of properties tested within the census tract.
2 - Percent of "high" arsenic properties (≥150 mg/kg) within the census tract

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Table 24 displays the relative risk of developing lung cancer for individuals living at "high" soil arsenic properties. For each census tract, each home where a lung cancer case was diagnosed was placed into an "exposed" or "unexposed" category based on the soil arsenic level at that home. Relative risk and a 95 percent confidence interval were calculated for each census tract. For homes in Census Tract 36.01 with a "high" soil arsenic level (≥150 mg/kg), there was approximately a 20 percent increased risk of being diagnosed with lung cancer (RR=1.23), but this finding was not statistically significant.

Table 24 – Two-by-Two Tables of Lung Cancer Case Counts Stratified by Soil Arsenic Concentration, for Individual Census Tracts.

Census Tract	Number of properties with diagnosed lung cancer case	Number of properties with no diagnosed lung cancer case	Relative Risk
35.00 [1] Soil < 150 mg/kg Soil ≥ 150 mg/kg	28 1	1123 91	0.45 (0.06, 3.25)[2]
36.01 Soil < 150 mg/kg Soil ≥ 150 mg/kg	28 3	709 61	1.23 (0.39, 3.95)[2]
36.02 Soil < 150 mg/kg Soil ≥ 150 mg/kg	22 2	802 79	1.08 (0.25, 4.52)[2]

1 Counts for Census Tract 35.00 include a small portion of Census Tract 16.00
2 95% confidence interval is shown in parentheses.

Similar statistical tests were not conducted for homes of residents diagnosed with bladder cancer or for those diagnosed with breast or brain cancer at an unusually young age of onset due to the small number of properties with a high soil arsenic concentration at those residences. Of the 20 bladder cancer cases in the study area, 12 homes had soil arsenic measurements. The mean soil Arsenic concentration was 26.5 mg/kg, with a median of 13.0 mg/kg. None of the 12 homes had a soil concentration greater than 150 mg/kg. Of the15 breast cancer cases age 25-44 in Census Tract 35.00, 10 homes had soil arsenic measurements. The mean soil arsenic concentration was 27.9 mg/kg with a median of 5.5 mg/kg. One of the 10 homes, or 10 percent, had a concentration over 150 mg/kg, which is similar to the 11 percent of high arsenic homes for the entire tract. Soil data were available for three of six homes in Census Tract 36.01, where a statistically elevated number of brain/ONS cancers were diagnosed in individuals under age 20. All homes had soil arsenic levels below 150 mg/kg, with an average concentration of 34 mg/kg.

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DISCUSSION AND CONCLUSIONS

Current epidemiological literature indicates that arsenic ingestion has consistently been recognized as a risk factor for lung, bladder, and skin cancer in large populations exposed to high doses of arsenic in Mexico and several other Asian and South American countries. Studies in smaller U.S. populations, however, have not detected similar outcomes (NRC, 1999; ATSDR, 2000). Arsenic has been associated with an increase in other internal cancers, such as kidney and liver, but the findings are not as consistent between studies (Bates, 1992; Chen, 1990). One rare occurrence of cancer, liver angiosarcoma, has been noted in workers exposed to arsenic and in individuals treated with Fowler's solution, a potassium arsenite medication. A review of Cancer Registry records for individuals in the VBI70 study area showed that the number of liver and kidney cancers diagnosed in the VBI70 study area was within the expected statistical range. In addition, no liver angiosarcomas were diagnosed in the study area during the time period being investigated. While the Cancer Registry routinely collects data on all melanoma skin cancers, nonmelanocytic basal and squamous cell carcinomas, the cell types that are associated with arsenic exposure, are only reported if the case is at an advanced stage at diagnosis, meaning cancer has already spread to the lymph nodes or another organ in the body. For the VBI70 area, only one case was reported that fit that description. Therefore, analysis of skin cancer was not possible.

The findings of this study suggest that there is a trend toward a higher than expected rate of cancer in the VBI70 community when compared to cancer outcome in the rest of the Denver metropolitan area. However, this finding must be interpreted cautiously. For cancer types with an established association with arsenic exposure-- bladder and lung cancer-- the outcome is mixed, with no elevation in bladder cancer and a moderate increase in lung cancers diagnosed in males in Census Tract 36.01 (SIR= 1.65, 95th CI = 1.14-2.31). The study does not provide evidence of an association between lung cancers and soil arsenic levels. For other types of cancer that are elevated-- pancreas, breast, cervical, colorectal, "other pharynx", larynx, brain and other nervous system, and multiple myeloma-- there is no established association with arsenic exposure. Outcomes for individual cancer types are discussed below in greater detail.

<u>Arsenic-associated cancers: Bladder and Lung Cancer</u>

The primary focus of this evaluation, in response to community concerns, was to assess the incidence of all cancers combined, bladder cancer, and lung cancer in the Vasquez Boulevard-I70 study area during 1982-98. Bladder and lung cancer are the two internal cancers most strongly associated with arsenic ingestion (NRC, 2001). Bladder cancer ratios in the study area were all within expected statistical limits. Lung cancers were statistically higher than expected in the study area, mostly due to a statistically high ratio for males, particularly in Census Tract 36.01. Because smoking is also a well-recognized risk factor for lung cancer, with roughly 85 percent of all lung cancers attributable to smoking (APHA, 1998; ACS, 1995), a review of all lung cancer case records was conducted to determine smoking status. Cancer Registry abstracts indicated that over three-fourths of all the diagnosed lung cancer cases in the study area were confirmed to have

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a reported history of smoking. Individual smoking histories were determined for 107 of the 135 lung cancer cases. Of the 107 cases for whom smoking status was available, 97 percent were smokers. All of the males diagnosed with lung cancer in Census Tract 36.01, for whom smoking status could be determined, or 25 of 34 cases, were smokers.

Inhalation of arsenic has long been recognized as a risk factor for increased incidence of lung cancer, with demonstrated synergism, or multiplicative risk, with smoking. Epidemiological evidence, similarly, indicates increased risk of lung cancer from ingestion of arsenic in drinking water. Synergism between exposure to arsenic in drinking water and tobacco smoke has been demonstrated and tends to vary in magnitude with the level of arsenic exposure (Ferreccio, 2000; Hertz-Picciotto, 1992).

Some epidemiological information is available which indicates that exposure to certain chemicals can be associated with a shift in the distribution of histology, resulting in an increased number of lung tumors of a specific cell type. For example, radon has most often been linked to an increase in small cell tumors. A histological review of all lung tumors diagnosed in this particular study area indicated a distribution of cell types that was very close to the distribution in the rest of the Denver metropolitan area, with no notable increases in any particular cell type. For arsenic, results of epidemiological studies where lung cancer histology has been examined have been mixed, with some studies reporting an increase in the proportion of adenocarcinomas, while others have reported no increases in any one particular cell type in arsenic exposed cohorts showing an increase in lung cancer (Newman, 1976; Wicks, 1981). Similar histological distributions have been reported for arsenic-exposed smokers and nonsmokers (Pershagen, 1987). Smoking, in the absence of arsenic exposure, has been associated with a higher proportion of adenocarcinomas in females but not in males (Thun, 1997; Travis, 1995).

Other known environmental risk factors for lung cancer, in addition to arsenic exposure, include exposure to asbestos, radon, and other forms of air pollution. Other air pollutants that may be carcinogenic to the lung are diesel exhaust, pitch and tar, dioxin, chromium, cadmium and nickel compounds.

The finding in this study of a higher ratio of lung cancer in men, but not in women, is an inconsistency suggesting these cancers may not have been caused by an agent in the ambient environment. A residential environmental exposure to a cancer-causing substance, such as drinking contaminated water or breathing contaminated air, typically is expected to cause a similar effect in both men and women. However, with contaminated soil, exposure can vary greatly based on individual or transient behavioral patterns, such as hand-to-mouth activity or seasonal impact on soil contact. Assumptions regarding consistency of exposure and resulting exposure dose may be less predictable.

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All Cancer Types Combined

The ratio of diagnosed to expected cases for "all cancers combined" was statistically high for males and females combined for the entire study area. Cancers overall among males and females separately were within expected statistical limits. Elevations in several types of cancer contributed to the higher ratios among males and females combined. These elevations are discussed below for each individual cancer type. Table 21 provides a summary of all statistically elevated cancers for males, females, and both genders combined for each census tract area.

Pancreatic cancer

Pancreatic cancers in males in the study area were within expected statistical limits, but in females the ratio of pancreatic cancers to expected cases was statistically high, showing almost a two-fold increase (SIR=1.70). Smoking is a known risk factor for pancreatic cancer with incidence rates twice as high for smokers as for nonsmokers, and close to half of the female pancreatic cases in the study area with known smoking histories were smokers. Other risk factors identified in the epidemiological literature include a history of chronic pancreatitis or diabetes, cirrhosis, higher fat diets, obesity, and lack of physical activity (ACS, 1995; Michaud, 2001). Work in petroleum, rubber and textile industries has also been implicated in some studies, with a weak or non-positive association found for occupational exposure to arsenic (Weiderpass, 1998 and Ojajarvi, 2000).

Colorectal Cancer

Colorectal cancer ratios for men in the study area were within expected statistical limits, but ratios for females were statistically high, with small increases in all census tract areas, races and age groups evaluated. Recent research conducted by the American Cancer Society (Chao, 2000) links long-term smoking with higher risk for colorectal cancer. Nearly half of the female cases from this study were smokers. Other risk factors for colorectal cancer reported in the epidemiological literature include family history of colorectal cancer or polyps pre-existing inflammatory bowel disease; physical inactivity; possible dietary characteristics, such as high-fat and/or low-fiber diet; and alcohol consumption (ACS, 1995). Similar to lung and pancreas cancer, the finding of a higher ratio of colorectal cancer in women but not in men, is an inconsistency suggesting that these cancers may not have been caused by an agent in the ambient environment, but are more likely related to predisposing family history or lifestyle factors such as smoking or diet.

Cervical Cancer

Cervical cancers in the study area were statistically higher than expected. Almost half of the cervical cancers in the study area were invasive, indicating a problem with late detection. Women in the 45-74 age range and white, non-Hispanic women had over twice as many cervical cancer diagnoses as expected. Smoking is a risk factor for cervical cancer, and over half of all

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patients with recorded information about smoking status had a history of smoking. Other risk factors for cervical cancer include infection with certain sexually transmitted infections, called human papillomavirus; sexual intercourse before age 18; multiple sex partners; and poor nutrition (ACS, 1995). The epidemiological literature does not suggest an association with exposure to arsenic and increased risk of developing cervical cancer.

Breast Cancer

Breast cancers in the overall study area were within expected statistical limits. The ratio of diagnosed to expected breast cancer cases in Census Tract 35.00, however, was statistically high, a finding partly attributed to a higher proportion of second breast tumors, particularly in Hispanic women. Ten of the 69 breast cancers diagnosed, or 14 percent, occurred in women with a previous diagnosis of breast cancer which would place them in a risk category that is double that of the general population (Kelsey, 1993). Mexican-Americans have been reported to have the highest rate of multiple primary breast cancers in the U.S., consistent with the finding in this study where the majority of women diagnosed with multiple primaries were Hispanic (Gilliand, 1998; Polednak, 1989). However, the proportion of multiple primaries reported for Hispanic women in this study, totaling 19 percent, was higher than reported elsewhere. Breast cancers in this census tract were also detected at later stages when survival may not be as good as that achievable with early detection.

One recognized risk factor for later stage disease at the time of diagnosis that may be of significance for this community is the disparity in the use of mammogram screening for women in lower socio-demographic groups, particularly Spanish-only speakers (Fox, 1998). Fifteen of the 69 breast cancers diagnosed in Census Tract 35 occurred in women under the age of 45, a finding that suggests the potential for genetic predisposition or family history of breast disease. Overall, genetic predisposition is believed to account for a relatively small fraction, from 5-10 percent, of all breast cancers. However, women with an inherited genetic mutation for breast cancer (i.e., BRCA1 and BRCA2 mutations) will typically develop breast cancer at a younger age and are more likely to develop bilateral breast cancers. Presence of such hereditary "susceptibility genes" is often detected by the occurrence of breast cancer in multiple family members, and may predispose an individual to other types of cancer, most notably ovarian cancer (Foulkes, 1998).

Risk to women with a family history of breast cancer is about four times that of other women (ACS, 2000). Relative risk to subsequent family members, if there is a genetic etiology involved, is greatest when breast cancer is diagnosed in other family members at a young age. There is no information currently available to determine what factors may be contributing to the finding in this study of several individuals diagnosed with breast cancer at a young age, or for the high numbers of multiple primary breast cancers diagnosed in Hispanic women. Other plausible contributing factors would include a high number of extended families with similar predisposing factors living in this same census tract, a higher proportion of individuals with a higher overall risk of developing breast cancer than is typical of the comparison population, and longer than

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average residency for people in this community, resulting in a higher likelihood of diagnosing multiple primaries while an individual resides in the same census tract.

In addition to a family history of breast cancer, other well established risk factors for breast cancer include, menstrual cycle starting early in life; biopsy-confirmed atypical hyperplasia; obesity after menopause; never having children or having a first child after age 30; and alcohol consumption of more than two drinks per day. Oral contraceptive use for more than 10 years and hormonal replacement therapy for more than 15 years are also known risk factors. In recent years, there has been high interest in the possibility of an association between breast cancer and exposure to environmental chemical exposures such as organochlorine pesticides, PCBs and other hormonally active agents, popularly known as "endocrine disruptors" or "environmental estrogens". Recent, more carefully designed case-control studies of large populations have generally failed to confirm the association of pesticide exposure and breast cancer reported in earlier descriptive studies, although even the more robust studies conducted to date have not represented a wide range of race or ethnic groups (Snedeker, 2001). Despite the large number of identified risk factors, almost half of all breast cancer is diagnosed in women without any of these identifiable risk factors.

Larynx and "Other Pharynx" Cancer

Head and neck cancers such as larynx and "other pharynx", which includes cancers of the tonsil and cancers of the oro- and hypo-pharynx and pyriform sinus, have been associated in the literature with tobacco use and heavy use of alcohol (Talamini et al, 1998; Thun, 1997), as well as poor nutrition (American Cancer Society, 2001), and human papillomavirus (McKaig et al, 1998). Tobacco use is the most important risk factor, accounting for about 85 percent of all head and neck cancers. Risks for smokers for cancer of the larynx and hypopharynx are 5-to-35 times that for non-smokers, depending on the level of use. Some studies have reported an increased risk of developing cancer of the larynx in people with diets high in meat fat or low in fruits or vegetables (De Stefani, 1995; Riboli, 1996). Occupational exposures associated with increased risk of developing laryngeal and hypopharyngeal cancer include exposure to wood dust, paint fumes and other chemicals used in the plastics, textile, petroleum and metalworking industries. Asbestos has been linked with laryngeal cancer in some studies.

Cancer of the larynx has not been associated with arsenic exposure in the majority of human epidemiological studies conducted to investigate disease outcomes from arsenic ingestion. One study did report higher serum arsenic levels in patients with laryngeal cancer, compared to patients without cancer (Rostkowska-Nadolska, 1999), and another study reported higher numbers of arsenic in tumors of the larynx, compared to adjacent non-malignant tissue (Collecchi et al., 1986). No studies were located that indicate an association between arsenic exposure and "other pharynx" cancers.

In the VBI70 neighborhoods studied, cancer of the larynx was elevated in one of the three census tracts studied (tract 36.01), with ratios being statistically higher than expected for females, but

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not for males. A more detailed analysis of the cases in Census Tract 36.01 determined that fiveof the 10 diagnosed cancers occurred in Blacks, which was statistically higher than expected. As shown in Table 16, every age group had somewhat elevated diagnosed–to-expected ratios, although all within expected statistical limits, contributing to the overall finding of a statistically elevated number of larynx cancers for Census Tract 36.01 as a whole. Smoking histories were available for six of the 10 cases diagnosed in Tract 36.01, with all of these individuals reported to be smokers. Two individuals also had a history of high alcohol consumption with alcohol abuse or chronic alcoholism mentioned on the medical abstract. As discussed above, both smoking and alcohol consumption are known risk factors for this form of cancer.

The number of "other pharynx" cancers diagnosed was found to be significantly elevated among males in Census Tract 35.00, with over five times the number of expected cases being reported over the time period studied, for a total of eight cases diagnosed compared to about two expected). Sixteen of the 18 cases diagnosed for the entire study area occurred in males. Numbers of "other pharynx" cancer were statistically high for Whites and Hispanics, but within the expected range for Blacks. All of the cases, for whom smoking history could be determined, 15 of 18 cases, were reported to be smokers. In addition, six of the cases were reported to have a history of heavy consumption of alcohol. A difference in the distribution of anatomic sites was noted, with a higher percentage of hypopharynx and lower percentage of tonsil cancers in the VBI70 cases, compared to the rest of the Denver metropolitan area. This finding would be consistent with the presence of a higher proportion of smokers among the VBI70 cases, due to the high relative risk of developing cancer of the hypopharynx that was noted above for smokers.

For individuals diagnosed with cancer of the larynx and "other pharynx", smoking and heavy alcohol consumption are likely the primary risk factors contributing to the development of disease, due to the preponderance of these high risk behaviors reported on their medical abstracts.

Brain and Other Central Nervous System Cancers

The underlying causes of tumors of the brain and nervous system are largely unknown, with a variety of genetic, viral, and environmental factors recognized by the American Cancer Society as contributors to increased risk (ACS, 2001). There is strong evidence of an association between these types of cancers and exposure to ionizing radiation, such as radiotherapy. Studies have not generally found an association with lifestyle factors such as smoking or alcohol consumption. Other reported environmental and occupational risk factors for developing brain or other nervous system tumors include occupational exposure to pesticides; residence on a farm; home pesticide use; work in the petroleum industry; exposure to nitrosamines; and ingestion of aspartame (Lenhard, 2001). There is mixed to weak evidence regarding increased risk due to occupational exposure to low-level electric and magnetic fields, or non-ionizing radiation. For children, a higher risk of developing certain types of brain tumors has been associated with parental employment in agricultural, electricity, or motor-vehicle related occupations, and for maternal employment in the textile industry (Cordier, 2001). No indication of increased mortality due to

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brain or other nervous system cancer was found in individuals exposed to arsenic at levels resulting in a 3- to 4-fold increase in urinary arsenic levels (Buchet, 1998), an exposure level far greater than would be expected from an environmental or residential exposure to arsenic in soil.

The number of brain and other nervous system tumors identified through the Colorado Central Cancer Registry was not statistically elevated for the VBI70 study area as a whole. However, the number of cases diagnosed in one geographic area, Census Tract 36.01, was statistically high. As shown in table 18, ratios of diagnosed-to-expected numbers of cancer were elevated for each race/ethnic group investigated, with a statistically high number of cases reported for Blacks. Among these Black residents, four cases were diagnosed compared to about one expected. Individuals under the age of 20 were disproportionately affected, with a 10-fold increase over the number of expected cancers, with six cases diagnosed compared to less than one case expected. Some differences were noted in the cell type distribution for these six cases, with relatively more glioblastomas and fewer astrocytomas occurring in Census Tract 36.01 than in the rest of the Denver metropolitan area. Low-grade astrocytomas are the most common histologic type of brain and central nervous system cancer diagnosed during childhood (Lenhard, 2001). Therefore, a finding of elevated numbers of glioblastomas in individuals under the age of 20 appears to be an unusual finding. This outcome may in part be an artifact of the small total number of cases diagnosed, resulting in an unstable estimate due to a large percentage change based on a difference in cell type of only one or two cases. Two genetic or familial syndromes (Li-Fraumeni syndrome and Turcot syndrome) are described in the literature as predisposing to glioblastomas. However, this risk factor would likely be attributable to a very small number of individuals (Inskip, 1995).

Multiple Myeloma

Multiple myeloma was statistically elevated in one of the three census tracts (36.02), with most of the excess cases occurring in females, particularly those 75 years of age and older. Multiple myeloma is characterized by the overgrowth and malfunction of plasma cells in the bone marrow. There are few established risk factors for multiple myeloma, with the exception of increasing age. Diagnosis of multiple myeloma is most common among persons 65 to 70 years old and is uncommon among persons less than 40 years of age (Durie, 2001). For the VBI70 area, the average age at diagnosis is about 70, which is consistent with the expected age at diagnosis for the population at large. Children and siblings of patients who have this disease have a slightly increased risk, and this disease typically affects Blacks more often than Whites and men more often than women (Brown et al., 1999). Multiple myeloma has not been associated with lifestyle factors, such as tobacco use or alcohol consumption. Few occupational exposures have been identified as risk factors, although some studies have indicated that workers in certain petroleum-related industries may have an increased risk (Stagnaro et al., 1999). Investigations of exposure to large amounts of ionizing radiation as a potential risk factor for multiple myeloma have had inconsistent outcomes and suggest this exposure would account for only a small number of cases at most (Durie, 2001;Hatcher 2001). Weak supportive data of an association between

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trichloroethylene exposure and multiple myeloma has been reported (Wartenberg et al., 2000). No association with arsenic exposure was identified in the literature.

Assessment of soil arsenic concentration data

Soil arsenic concentrations at the homes of 20 bladder cancer cases; 135 lung cancer cases; and select sub-populations with breast cancer and brain and other nervous system cancers were assessed as an indicator of the likelihood that soil may be an important arsenic exposure source contributing to an increased risk of cancer. Means, medians, and proportions of homes above selected cutoff values were calculated. For homes of residents diagnosed with lung cancer, distributions of soil arsenic concentrations were quite similar to the distribution of arsenic in soil across the site as a whole. There was no statistically significant association detected between "high" soil arsenic concentrations, defined as above 150 mg/kg, and the occurrence of lung cancer for any of the three census tracts studied. Nine of 10 homes in Census Tract 35.00, where a resident was diagnosed with breast cancer at early age of onset, less than 45 years old, had a relatively low soil arsenic concentration in yard soil, indicating that arsenic exposure is not likely to be a strong contributor to the finding of elevated numbers of breast cancer. Similarly, soil arsenic concentrations were all comparatively low at homes of individuals in Census Tract 36.01 diagnosed with early onset of brain and other nervous system cancer.

One limitation of this analysis was that soil data were not available for many of the properties where cancer was diagnosed. In addition, although analysis of arsenic soil levels was useful as an indication of the potential for an exposure source in the home, no information was available on residence history of individuals diagnosed with cancer. Therefore, no individual dose levels could be estimated. It is also important to note that ecological studies such as this may have insufficient power to attribute small to moderate increases in cancer occurrence to any one risk factor. The "high" soil arsenic concentrations at this study area are at levels that would be expected to contribute an additional 1 in 1,000 to 1 in 10,000 extra cases of cancer above the background rate of 1 in 2 to 1 in 3 people developing cancer over a lifetime. This level of increased risk is likely to be a minor contributor to the overall numbers of lung cancers when compared to effects from increased rates of smoking. For males in Census Tract 36.01, there was approximately a 65 percent increase in the number of lung cancer cases reported, compared to the expected level. Based on a review of the Cancer Registry abstracts for these cases, there was also a notably high rate of smoking reported in these individuals, with 100 percent of those for whom smoking status was available-- 25 of the 34 cases-- reported to be smokers. For the entire study area, smoking status was available for 107 of the 135 lung cancer cases. Of these 107 cases, 3 individuals diagnosed with lung cancer were non-smokers, and 104 were smokers. Therefore, smoking is likely to have had a far more significant effect on disease outcome in this group of individuals than exposure to arsenic in soil.

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Summary

Cancer incidence, when compared to a standard population using statistical testing procedures, allows the identification of sub-populations with "higher than average" rates of specified types of cancers. To interpret this information, however, other information available from the Colorado Central Cancer Registry regarding common risk factors, including occupation, smoking history, and alcohol consumption, should be considered, as well as the frequency of cancer of specific anatomical sites, and the distribution of histological cell type within those anatomical sites. An equally important source of information for interpretation of cancer incidence data is the epidemiological literature, which provides a substantial body of scientific and medial information describing the relationship between cancer, population incidence, and the known associated risk factors. The significance of this information for the cancer types of interest in the VBI70 study has been discussed in detail in previous sections of this report.

The analysis of cancer incidence data for the VBI70 area indicates that there is a trend toward a higher than expected rate of cancer within certain sub-populations of the community. Cancer incidence was statistically high for nine specific anatomical sites- lung, pancreas, colorectal, cervix, breast, "other pharynx', larynx, multiple myeloma, and brain and other central nervous system cancers. None of these cancers was elevated in both genders at a statistically significant level, and elevations tended to occur in only one of the three census tract areas for each elevated cancer type, with no evidence of generalized clustering in any one neighborhood. Of the cancer types that were statistically elevated, only one-- lung cancer-- is recognized in the epidemiological literature as having an established association with exposure to arsenic.

The finding in this study of a higher than expected number of lung cancer cases was not consistent across gender or geographic area, with elevations occurring only in men in Census Tract 36.01. The elevation in men, and not in women, tends to indicate other causal factors, such as occupational exposure or a higher rate of smoking in men. In this study, 97 percent of the individuals who were diagnosed with lung cancer, and for whom smoking status was available, were smokers. In addition, soil arsenic concentrations are generally similar for each of the three census tracts studied, while elevations in lung cancer occurred in only one tract. Therefore, the finding of an elevation of lung cancer in only one of these three census tracts is not consistent with the hypothesis that this increase is due to exposure to arsenic in soil. For individuals diagnosed with lung cancer in the VBI70 area, smoking is likely a primary cause of this finding. Other factors, such as exposure to carcinogens in an occupational setting or other chemical exposures from indoor or ambient air, may also contribute to the overall individual and population risk. For lung cancer, the possibility of some effect from exposure to arsenic in soil can not be ruled out by this analysis, but any such effect would likely be small compared to the smoking effect.

Due to the lack of an established association in the scientific literature between arsenic exposure and increased risk of developing cancers of the breast, pancreas, colon and rectum, cervix, "other pharynx", larynx, brain and other nervous system, or multiple myeloma, it is not believed that the

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elevation in these types of cancer is associated with arsenic contamination in soil. The potential for other environmental causes within the community, however, is unknown.

For several of these cancers, a higher proportion of the tumors were diagnosed at a later, more invasive stage of the disease than is typical for the Denver metropolitan area overall, possibly indicating poor access to medical care in this community. The association between smoking and increased cancer risk has been established for other organ tissues besides the lung, namely, oropharynx, esophagus, pancreas, bladder, kidney, and colorectal (Wynder, 1998; Doll, 1994). The most pronounced risk is for cancer of the lung, and larynx, and this risk may be 10-to-30 times greater than for nonsmokers (Wynder, 1998; Doll et al., 1994). Suggestive evidence has associated smoking with hepatocellular cancer, squamous cell carcinoma of the uterine cervix, and possibly, breast cancer (Morabia et al., 1996; Lash and Aschengrau, 1999). Excess consumption of alcohol is associated with cancer of the oral cavity, including the larynx, pharynx, esophagus, and liver. In this study, a history of smoking and excessive alcohol consumption are likely risk factors in the development of cancer of the larynx, "other pharynx", lung, colon and rectum and possibly pancreas, as one or both risk factors were noted in Central Cancer Registry abstracts for most cases, and this linkage has been reported in the epidemiological literature.

Two additional types of cancers-- brain/other nervous system and multiple myeloma-- were reported at statistically high levels, but have no known association with smoking or high alcohol consumption. Brain and other nervous system cancer were reported in statistically high numbers for one of the three census tract areas (Tract 36.01). Most of these cases were diagnosed in individuals under the age of 20, with a greater number of glioblastoma cell types reported compared to the typical cell type distribution in the rest of the Denver metropolitan area. The cause for this finding is not known. However, based on the absence of any reported link in the epidemiological literature, this outcome is not believed to be associated with exposure to arsenic in soil. Multiple myeloma was statistically high in Census Tract 36.02, with the majority of cases occurring in females and those over the age of 75. There have been few established risk factors other than age identified by the American Cancer Society as causative agents for multiple myeloma. Some epidemiological evidence of increased risk for farmers and workers in petroleum-related industries has been noted. There is no indication that arsenic is a risk factor for this disease.

Analysis of the breast cancer data indicates several important findings for women in Census Tract 35.00 that may deserve further attention. Namely, the data indicate: (1) an elevated incidence of breast cancer in Hispanic women, (2) occurrence of greater than expected numbers of breast cancer cases in women under the age of 45, (3) an elevated incidence of multiple primary breast tumors, particularly in Hispanic women, and (4) and later stage detection than is typically seen in the Denver metropolitan area as a whole. The data indicate that Hispanic women are at increased risk of developing breast cancer and may benefit from increased screening to enhance detection of breast cancer at the earliest, most treatable stage of the disease.

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The reason for the later stage at diagnosis in Hispanic women is not clear from this study but may be influenced by a high proportion of Spanish-only speakers in the community who may be reluctant to seek breast screening, or higher numbers of residents with poor access to medical care. This would be consistent with census data that indicate a relatively high percentage of Spanish-speaking households and households below the poverty level in the VBI70 area. In addition, occurrence of breast cancer in 15 women under the age of 45 may deserve additional investigation.

The predominant types of cancers determined to be statistically high in the VBI70 area are associated with known behavioral and pre-existing disease risk factors, such as smoking, poor dietary habits, excessive alcohol consumption, viral infections, or family predisposition. The findings of this report will be communicated to the Comprehensive Cancer Control Section at the Colorado Department of Public Health and Environment to encourage improved cancer control strategies in these Denver neighborhoods within the VBI70 study area.

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RECOMMENDATIONS

- Continued monitoring of cancer statistics through the Colorado Central Cancer Registry (CCCR) and review of lung, bladder, colorectal, pancreas, cervix, breast, "other pharynx", larynx, brain and other nervous system, and multiple myeloma cancer incidence to determine trends in the community. Update cancer incidence ratios when two or more years of additional data become available.

- Share findings of breast cancer occurrence with members of the Colorado Women's Cancer Control Initiative (CWCCI) and the Comprehensive Cancer Prevention and Control Program (CCPC) at the Department of Public Health and Environment.

- Collaborate with and facilitate efforts of the Colorado Women's Cancer Control Initiative, the Comprehensive Cancer Prevention and Control Program, and the State Tobacco Education Prevention Partnership (STEPP) to coordinate with community partners and contractors to increase education and prevention in the Vasquez Boulevard/I-70 area. These efforts will include:

  - Provide education to the community about known risk factors for cancer, primarily diet and nutrition, smoking, and level of physical activity.

  - Make special efforts to provide information to potentially under-served individuals, such as Spanish-speakers and others with poor access to health care and diagnostic testing.

  - Provide information to the community that will encourage individuals to talk with their health care provider about cancer screening to improve early detection.

  - Encourage all women to seek breast and cervical cancer screening with mammograms and pap tests at recommended intervals according to current American Cancer Society guidelines. Provide referral to appropriate programs, including the Colorado Women's Cancer Control Initiative, for uninsured women (see Attachments 1 and 2).

  - Encourage all women previously diagnosed with breast cancer to consult with a physician about recommended intervals for screening and to discuss the potential for family susceptibility.

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Attachment 1 – Colorado Women's Cancer Control Initiative (CWCCI) Eligibility Requirements

Colorado Women's Cancer Control Initiative

Eligibility Requirements for Free Breast and Cervical Cancer Screenings:

- Colorado residency; women living in a state bordering Colorado who obtain health care in Colorado are eligible.
- No health insurance to cover screening and diagnostic services; women with Medicare-Part B are not eligible.
- No mammogram or Pap test in the past 12 months.
- Women ages 40 to 64.
- Family income at or below 250 percent of the federal poverty guidelines, with appropriate verification.

2001 Income Eligibility Guidelines

Household Size	Annual Income	Monthly Income
1	$21,475.00	$1,790.00
2	$29,025.00	$2,419.00
3	$36,575.00	$3,048.00
4	$44,125.00	$3,677.00
5	$51,675.00	$4,306.00
6	$59,225.00	$4,935.00
7	$66,775.00	$5,565.00
8	$74,325.00	$6,194.00

For each additional family member, add $7,550 per year.

Available Exams for Women Over Age 50:
1. Pap Test/Pelvic Exam
2. Clinical Breast Exam
3. Mammogram

Available Exams for Women Ages 40 - 49:
1. Pap Test/Pelvic Exam
2. Clinical Breast Exam
3. Mammogram - Up to 25 percent of all women screened are eligible; priority to women with one or more risk factors:
   - Mother, sister or daughter with breast cancer prior to age 50;
   - Two or more first-degree relatives (mother, sister, daughter) with breast cancer at any age;
   - Personal history of breast cancer; and
   - Clinical breast examination symptomatic for cancer.

Call (303) 692-2600 to find out more about eligibility for free breast and cervical cancer screenings.

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Attachment 2 - American Cancer Society Guidelines for Cancer Screening

1. **Current American Cancer Society guidelines for colorectal cancer screening**

Starting at age 50, the ACS recommends choosing one of the following schedules:

FOBT annually and flexible sigmoidoscopy every five years, or
Flexible sigmoidoscopy every five years, or
FOBT annually, or
Colonoscopy every 10 years, or
Double contrast barium enema every five years.

2. **Current American Cancer Society guidelines for breast cancer screening**

American Cancer Society encourages women to begin receiving annual mammograms at age 40.

3. **Current American Cancer Society guidelines for cervical cancer screening**

The American Cancer Society recommends that all women begin yearly Pap tests at age 18 or when they become sexually active, whichever occurs earlier. If a woman has had three negative annual Pap tests in a row, this test may be done less often at the judgment of a woman's health care provider.

If a hysterectomy was done for cancer, more frequent Pap tests may be recommended. Some women believe they do not have to be examined by a health care provider once they have stopped having children. This is not correct. They should continue to follow ACS guidelines.

Source: www.cancer.org

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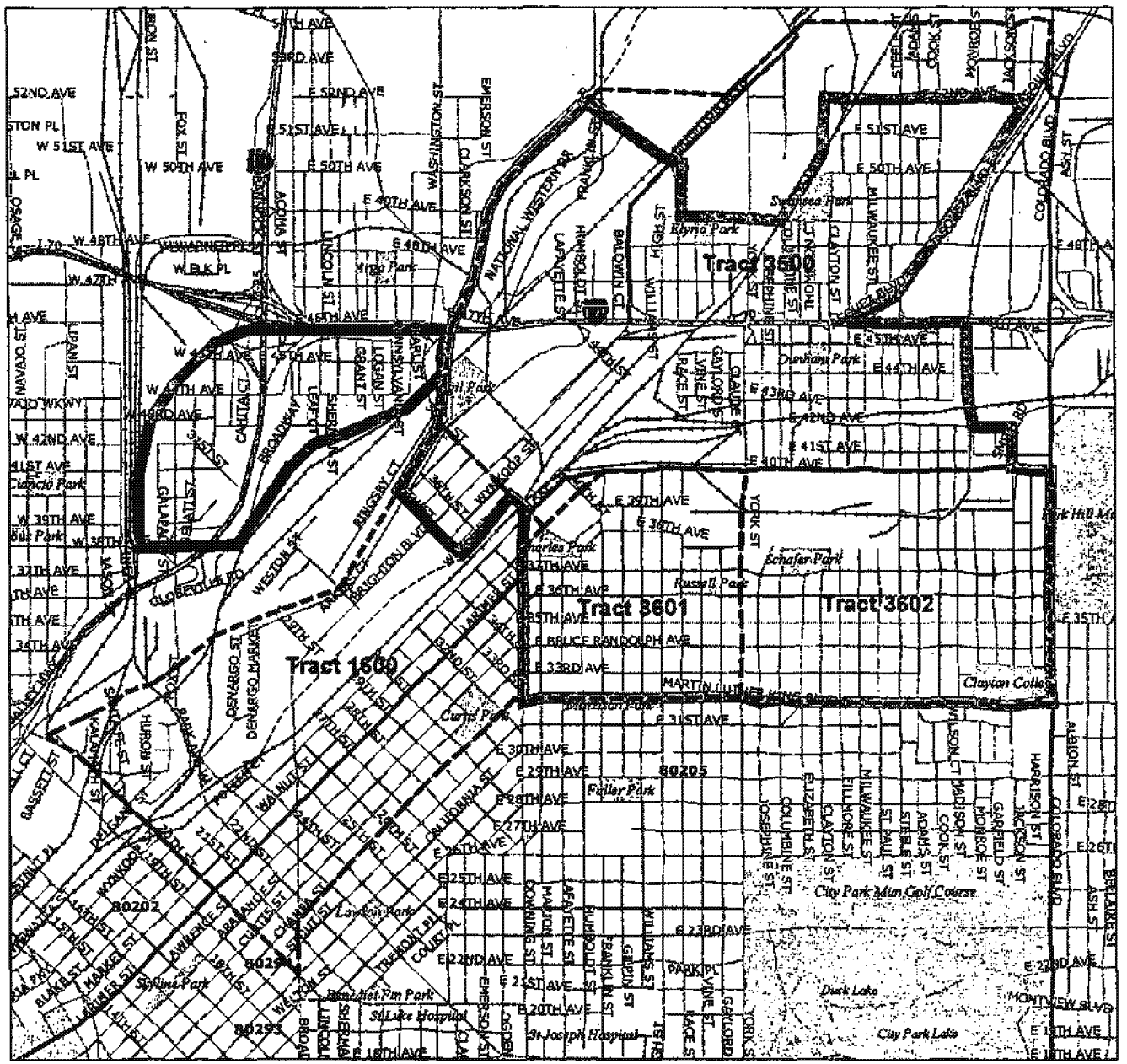
Figure 1

Vasquez Boulevard / I-70 Census Tract Boundaries



Colorado Department of Public Health and Environment