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Groundwater uranium and cancer incidence in South Carolina

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Abstract

Objective—This ecologic study tested the hypothesis that census tracts with elevated groundwater uranium and more frequent groundwater use have increased cancer incidence.

Methods—Data sources included: incident total, leukemia, prostate, breast, colorectal, lung, kidney, and bladder cancers (1996–2005, SC Central Cancer Registry); demographic and groundwater use (1990 US Census); and groundwater uranium concentrations ($n = 4,600$, from existing federal and state databases). Kriging was used to predict average uranium concentrations within tracts. The relationship between uranium and standardized cancer incidence ratios was modeled among tracts with substantial groundwater use via linear or semiparametric regression, with and without stratification by the proportion of African Americans in each area.

Results—A total of 134,685 cancer cases were evaluated. Tracts with ≥50% groundwater use and uranium concentrations in the upper quartile had increased risks for colorectal, breast, kidney, prostate, and total cancer compared to referent tracts. Some of these relationships were more likely to be observed among tracts populated primarily by African Americans.

Conclusion—SC regions with elevated groundwater uranium and more groundwater use may have an increased incidence of certain cancers, although additional research is needed since the design precluded adjustment for race or other predictive factors at the individual level.

Keywords

Cancer; GIS; Uranium; Groundwater; Disparities

Introduction

Uranium is a naturally occurring alpha-emitting radionuclide and plausible human carcinogen [1]. Natural uranium is comprised of three isotopes, with uranium-238 (U-238, 99.27%) being the most abundant (U-235: 0.72%; U-234: 0.01%). In terms of specific activity, 48.9% can be attributed to U-238, 2.2% to U-235, and 48.9% to U-234 [1]. Upon ingestion, uranium is distributed primarily to bone, liver, kidneys, and soft tissue. The normal adult uranium body burden is about 90 μg, with 66% in bone, 16% in liver, 8% in kidneys, and 10% in other soft tissue [1]. Alpha particles emitted by uranium are readily absorbed by the human body and can damage DNA, resulting in genetic mutations, chromosomal aberrations, or altered apoptotic processes that result in abnormal mitotic activity and cellular proliferation, all of which can facilitate carcinogenesis [1, 2]. Links between ionizing radiation and cancer are well established among atomic bomb survivors and occupational cohorts. However, few studies have examined potential cancer risks associated with naturally occurring uranium in drinking water. In addition to its radiological effects, uranium's chemical properties can induce renal toxicity and elicit estrogenic effects [3]. In certain isotopic combinations, chemical and radiological uranium toxicity can exert additive effects that may be indistinguishable [1].

A relationship between elevated groundwater uranium or its decay products and cancers of the blood [4-6], bone [7], lung [8, 9], bladder [8], breast [8], or reproductive system [9] has been suggested. However, the few case-cohort studies that have addressed this issue have not supported such an association, possibly due to limited statistical power, low levels of exposure, or other factors [10-12]. These discrepancies emphasize the need to evaluate cancer risks in populations exposed to elevated groundwater uranium from natural geologic sources. Spatial methods offer unique advantages in evaluating potential environmental carcinogens, although no previous studies have applied such methods to groundwater uranium exposure.

South Carolina (SC) is an important location to study this relationship. Forty percent of the population in this state is rural, approximately twice that of the US [13]. Additionally, African-American (AA) residents (approximately 29% of the total SC population) [13] are disproportionately affected by many adverse health outcomes, including elevated incidence and increased virulence of most solid tumors (e.g., prostate, lung and bronchus, colorectal, oral and pharyngeal, laryngeal, squamous cell esophageal) [14-17].

Rural areas rely heavily on groundwater sources. Approximately 40% of SC residents regularly use ground-water as their primary drinking water source [18]. Certain areas have drinking water wells with elevated uranium concentrations exceeding the US National Primary Drinking Water Standard (maximum contaminant level or MCL) of 30 μg/L [19] by more than 50 times [20]. This study applied groundwater modeling of robust uranium data and spatial analytical techniques to test the hypothesis that SC census tracts with more frequent groundwater use and elevated groundwater uranium concentrations have higher standardized cancer incidence ratios (SIRs) than tracts with lower groundwater uranium concentrations. We also evaluated this relationship among census tracts with different proportions of AAs to assess exposure to groundwater uranium as a potential risk factor underlying racial cancer disparities in SC.

Methods

A geographic information system (GIS, ArcMAP® software version 9.2, ESRI, Redlands, CA) was used to combine incident cancer cases from the South Carolina Central Cancer Registry (SCCCR) (1996–2005) (http://www.scdhec.gov/co/phsis/biostatistics/SCCCR/SCCCRmain.htm); demographic and groundwater consumption information from the US Census Bureau (1990) (http://www.census.gov/); and groundwater uranium concentrations from the National Uranium Resource Evaluation (NURE) program database (1976–1979) (http://tin.er.usgs.gov/nure/water/), the SC Department of Health and Environmental Control (DHEC) (2001–2008) (http://www.scdhec.gov/environment/water/), and the US Geological Survey (USGS) National Water-Quality Assessment (NAWQA) program (1997–2007) (http://water.usgs.gov/nawqa/). The age distribution, proportion of AAs, median household income, and proportion of individuals using groundwater as their main water source were obtained, by census tract, from 1990 Census data. Use of the 1990 Census for residential water use provided for a latency of 6–15 years prior to assessment of the relationship between groundwater uranium use and cancer incidence. Water source was ascertained from responses to the following census question: “Do you get water from a public water system (such as a city water department or private company), individual drilled well, individual dug well, or some other source such as a spring, creek, river, or cistern, etc.?” (an individual well was defined as one providing water for less than or equal to four houses, apartments, or mobile homes). The proportion of individuals using groundwater was calculated as the sum of individuals in each tract using a drilled well, dug well, or other source divided by the census tract population. Census tracts were included in separate analyses if ≥25, ≥50, or ≥75% of the population used groundwater as their drinking water source. ‘Some other source’ constituted 1.8% of tracts classified as using groundwater. Public water systems, including those using groundwater sources, were not considered in this analysis, since those systems are required to comply with the Safe Drinking Water Act standards for uranium.

Study population

The SCCCR, initiated in 1996, has consistently received the highest rating for completeness (99.7%), accuracy, and timeliness from the North American Association of Central Cancer Registries. Cancer cases in SC diagnosed between 1 January 1996 and 31 December 2005 were identified and registered with the SCCCR according to standardized procedures [21].

Cancer types were selected a priori based on the pharmacokinetics of uranium, an oral exposure route, or a previously published cancer association. Incidence data were obtained from the SCCCR for total cancers, prostate, colorectal, lung and bronchus, female breast, kidney and renal pelvis, urinary bladder, and leukemia (all retained in final analyses). Leukemia subtypes were not evaluated due to limited number of cases. Cancers of the stomach and small intestine, esophagus, bone and joints were excluded from these analyses due to small sample sizes and sparse geographic density. Lung cancer was investigated because radon, a lung carcinogen, is a decay product of uranium, is soluble in water, and aerosolizes during activities such as showering and cooking [22]. Seventy-five percent of available cases were successfully geocoded to a 1990 SC census tract ($n = 854$ tracts), and un-matched cases were excluded. A greater percentage of geocode matches were European American (EA) (78%) when compared to non-matches (70%), and a greater percentage of matches had a current vital status of ‘alive’ (54%) compared to non-matches (49%). Six percent ($n = 36$) of census tracts had no cancer cases, which arose primarily from Census Bureau corrections of discrepancies created by discontiguous or duplicate census blocks. Primary in situ or malignant cancers (i.e., single primary or the first of two or more primaries) were included in the analysis if cases were present in ≥80% of census tracts. Cases with benign tumors (0.5%) or with other or unknown race or unknown gender (1%) were excluded.

Age and population adjustment of cancer incidence was conducted via the indirect method [23] using statewide age-specific cancer incidence rates, and the age-specific population distribution within each census tract. SIRs were calculated as the observed cases divided by the expected cases for each census tract, and the SIR was used as the outcome in regression models.

Uranium

Concentrations of total groundwater uranium for SC were obtained from the NURE (92%), SC DHEC (4%), and NAWQA (4%) databases. Sampling for the NURE database was based on the 1 degree-by-2 degree National Topographic Map Series quadrangle grid. Groundwater samples were analyzed at the Savannah River Lab via delayed neutron counting. Observations below detection were converted to a value of one half the detection limit. Spatial interpolation with geocoded data points ($n = 4{,}600$) was used to characterize the statewide distribution of groundwater uranium. Predicted groundwater uranium concentrations were obtained via ordinary kriging [24]. Goodness-of-fit statistics for model variations were compared and cross-validated to determine the optimal kriging model. Based on the predicted surface values, the ‘zonal statistics’ function in Spatial Analyst (a GIS ArcMAP® extension) was used to calculate mean uranium concentrations in each census tract ($n = 854$) based on the value raster (i.e., predicted groundwater uranium concentration surface generated by kriging) contained within each census tract polygon boundary. The predicted average census tract uranium concentration was used as the exposure variable in subsequent regression analyses among census tracts with ≥25% ($n = 297$), ≥50% ($n = 169$), or ≥75% ($n = 99$) groundwater use.

Statistical analysis

Linear and bivariate semiparametric regression were used to evaluate the relationship between groundwater uranium concentrations and cancer SIRs. The analysis was performed using R software version 2.8.1® (The R Foundation for Statistical Computing, Vienna, Austria). Linear regression was conducted to assess the relationship between cancer and groundwater uranium without modeling spatial variation. Semiparametric regression was used to evaluate both parametric (uranium and covariate effects) and nonparametric (spatial) components [25]. Semiparametric regression was applied because it models the underlying spatial trend nonparametrically and because surface estimation was not a primary inferential objective. These analyses were performed using the "SemiPar" package (spm function with a Gaussian family) in R software® [26]. Semiparametric models included the latitude and longitude of the census tract centroids to account for spatial variation. Regression coefficients (betas) represented the estimated change in cancer SIR for an incremental increase in estimated uranium exposure from the referent (quartile 1) to the upper quartiles of uranium exposure (quartiles 2, 3, or 4), after adjusting for median census tract household income, proportion of AAs, and the residual spatial variation of other unmeasured factors. We also performed a test for linear trend on the regression coefficients across the four quartiles of uranium exposure for each cancer site.

The overall goodness of fit of the linear and semiparametric regression models was assessed by calculating and comparing R^2 statistics. For semiparametric models, likelihood ratio tests were used to determine whether parametric and nonparametric components of the regression coefficient were significantly different from zero. The nonparametric component was tested by taking the boundary constraint into account [27]. When the nonparametric component did not make a significant contribution to the effect estimate, linear regression was selected as the more parsimonious analytical approach. Alternatively, if the nonparametric component of the analysis was significant, then the semiparametric model was used.

To limit data to those potentially more exposed to uranium, primary analyses considered only census tracts with ≥50% groundwater use. Sensitivity analyses were then performed with groundwater use cut-points of ≥25 and ≥75%. Regression coefficients and 95% confidence intervals (CI) for the relationship between uranium and cancer SIRs were calculated and compared for each groundwater use cut-point. An interaction term between the percent of AAs living within each census tract and the predicted groundwater uranium concentration also was tested, and subsequent regression analyses were performed with stratification by the percentage of AAs within tracts of interest. Census tracts with a high or low percentage of AAs were defined as those above or below the average proportion of AAs in each groundwater use dataset (~38%, respectively).

Results

There were 4,600 groundwater data points with measured uranium concentrations used in this analysis. The statewide average (±standard deviation) groundwater uranium concentration from the original data set was 27 ± 360 μg/L (median: 0.03 μg/L). Approximately 10% ($n = 441$) of data points were below the detection limit. The maximum concentration was 10,100 μg/L, and 84 data points (~2%) exceeded the MCL (30 μg/L).

The final kriging model, ordinary kriging with an exponential semivariogram model, was cross-validated and had a mean error = 0.25; root-mean-square error = 62.4; average standard error = 15.5; and root-mean-square standardized error = 4.9. There were 169 (20% of SC tracts) census tracts with ≥50% groundwater use (99 with ≥75% groundwater use, 297 with ≥25% use). Average groundwater uranium concentrations among census tracts used in the regression analyses are presented in Fig. 1. The predicted average uranium concentration among all census tracts ($n = 854$) ranged from 0.000025 to 228 μg/L with an average of 1.26 μg/L. When census tracts were grouped into quartiles of predicted mean uranium concentrations, the corresponding median concentrations were 0.03 μg/L ($n = 42$ tracts), 0.08 μg/L ($n = 42$), 0.19 μg/L ($n = 42$), 0.84 μg/L ($n = 43$) for quartiles 1–4, respectively (based on ≥50% groundwater use, $n = 169$ tracts).

There were 134,685 eligible cases from all cancer sites identified for analysis from 1996 to 2005. Twenty-nine percent of cases had tumors that were moderately differentiated, and

41% had a localized tumor stage. AAs comprised 22% of total cancer cases (supplemental Tables S.1, S.2). The average proportion of AAs was 33, 46, 42, and 33% in quartiles 1–4, respectively (based on ≥50% groundwater use).

Likelihood ratio tests indicated that a semiparametric model performed better when evaluating prostate, colorectal, bladder, lung, and total cancers (all $p < 0.001$), whereas linear regression models were more appropriate for breast cancer ($p = 0.50$), kidney cancer ($p = 0.43$), and leukemia ($p = 0.50$). After adjustment for census-tract median household income and percent AA, SC census tracts in the highest quartile of groundwater uranium concentrations (0.39–64.03 μg/L) had elevated total ($\beta = 0.25$, 95% CI = 0.05, 0.45), breast ($\beta = 0.32$, 95% CI = 0.02, 0.61), kidney ($\beta = 0.35$, 95% CI = 0.09, 0.61), and colorectal cancer risks ($\beta = 0.27$, 95% CI = 0.06, 0.47) compared to those in the lowest exposure quartile (not detected to 0.05 μg/L; Table 1). Tests for trend also indicated that as uranium exposure quartiles increased, there was a corresponding increase in SIRs for total ($\beta = 0.07$, $p = 0.03$), breast ($\beta = 0.09$, $p = 0.05$), kidney ($\beta = 0.10$, $p = 0.02$), and colorectal ($\beta = 0.09$, $p = 0.01$) cancer (Table 1). A tendency towards increased leukemia incidence ($\beta = 0.28$, 95% CI = −0.01, 0.57) also was observed among tracts with elevated groundwater uranium.

Among census tracts populated primarily by AAs, elevated groundwater uranium concentrations were associated with elevated SIRs for breast, lung, and kidney cancer, and trend tests exhibited an increase in SIRs across increasing quartiles of uranium exposure for breast ($\beta = 0.13$, $p = 0.03$) and colorectal ($\beta = 0.09$, $p = 0.06$) cancer (Table 1). For census tracts populated primarily by EAs, the highest quartile of uranium was associated with an increased risk of prostate ($\beta = 0.33$, 95% CI = 0.02, 0.65; trend test $\beta = 0.12$, $p = 0.03$; Table 1) and total cancer ($\beta = 0.25$, 95% CI = 0.02, 0.47; trend test $\beta = 0.09$, $p = 0.02$; Table 1) compared to tracts in the lowest uranium quartile.

Sensitivity analyses were applied to specific cancer sites (total, colorectal, breast, kidney, prostate, leukemia) if the main analyses suggested a relationship between predicted uranium levels and the change in cancer SIR by applying different groundwater use cut-points (i.e., by restricting data to census tracts with ≥25% or ≥75% groundwater use rather than ≥50%), after adjustment for percent AA and median income. Results presented in Fig. 2 indicate that the relationship between elevated groundwater uranium concentrations and cancer incidence tended to increase as the groundwater use cut-point increased. We performed ancillary analyses by calculating point estimates of the relationship between uranium levels and SIRs (i.e., beta) in the low (referent) and high uranium exposure quartiles among census tracts with 25, 50, or 75% per capita groundwater use, after adjusting for median income and proportion of AAs in each tract. Point estimates for either quartile were positive as analyses progressed from 25 to 75% groundwater use (data not shown). These analyses were performed for leukemia and breast cancer after excluding census tracts without observed or expected cases or with extreme SIRs (>3), and the effect of uranium persisted for breast cancer but was diminished for leukemia. To evaluate whether the exclusion of cases due to inaccurate geocoding may have impacted the results, regressions were repeated after removing census tracts with higher proportions of excluded cases (≥7%). The results from these analyses did not alter the interpretation of the findings presented above (supplemental Table S.3).

Discussion

Few studies have examined the relationship between groundwater uranium and cancer. This study used spatial analytical techniques to evaluate the relationship between population level groundwater use, predicted groundwater uranium, and cancer incidence in SC. Census tracts with elevated groundwater uranium concentrations and more frequent groundwater use had elevated SIRs for colorectal, breast, kidney, and total cancer. Additionally, the tendency towards an increased SIR for leukemia was consistent with previous investigations [4-6]. When sensitivity analyses were performed, the relationship between groundwater uranium and cancer incidence increased with increasing per capita groundwater use.

Evidence among atomic bomb survivors and uranium workers suggests that colorectal cancer may be induced by ionizing radiation exposure [28]. However, to our knowledge, results from this study provide the first suggestion of a relationship between groundwater uranium ingestion and increased colorectal cancer risk. Furthermore, only one previous study assessed the relationship between kidney cancer and uranium or its byproducts in drinking water, and no strong association was identified [12]. Statistical power may have been limited in that investigation due to the relatively small number of cases ($n = 110$). The kidneys are a common site of human uranium sequestration following ingestion, and results from this investigation suggest that additional research is needed to examine this relationship.

Although breast cancer is the most frequently diagnosed malignancy among women, approximately 40% of cases cannot be ascribed to a known cause [29]. Breast tissue is generally radiosensitive, although only one other study examined the relationship between breast cancer incidence and drinking water radioactivity, and a positive association was observed [8]. Elevated circulating estrogen or its metabolites are associated with increased breast cancer risk [30]. Uranium can exert estrogenic effects in rats at levels below the drinking water standard [3]. Consistent with a potential estrogenic effect of uranium, our results suggest a relationship between elevated groundwater uranium concentrations and increased breast cancer risk, particularly among AA women. These findings may help explain racial disparities in breast cancer incidence and mortality that have been identified in SC, although more detailed investigations are required to examine this possibility [15, 17].

Even though prostate cancer is the most commonly diagnosed cancer among men [31], there are unfortunately few risk factors that lend themselves to prevention or intervention. The racial disparity in prostate cancer incidence in SC exceeds the national differential, and prostate cancer mortality rates among SC AAs are among the highest in the world [32]. Results for prostate cancer in this study were inconsistent, suggesting an association with groundwater uranium among EA but not AA men. The reasons for this are unclear but may be due to the distribution of unexamined or unknown risk factors among EA and AA men in urban and rural settings. We reported a similar unexpected trend when examining the biologically based hypothesis that low soil zinc content is associated with elevated prostate cancer incidence among AA men in SC; areas with low zinc levels had elevated prostate cancer rates but the effect was not amplified among AAs [32]. Clarification of these issues must await further screening of other environmental, behavioral, or sociological risk factors, which can be efficiently accomplished using the methods presented in this study.

Results of this study are subject to limitations in the ecologic design, which precludes adjustment for race or other predictive factors at the individual level, and introduces other issues as described below and in previous discussions [32-34]. For example, information was not directly available on duration of residence at the time of cancer diagnosis, and we were unable to account for population migration during the study period. However, the rural SC counties used in this analysis had stable residential populations during the study period (Fig. 3). Potential problems associated with geocoding, such as positional inaccuracies [35], were minimized through the use of geocoding matches meeting stringent criteria. Minor differences were noted in characteristics of excluded cases compared to those included in the analysis. However, the geographic pattern of excluded cases was unrelated to the distribution of groundwater uranium concentrations (supplemental Figure S.2), and regression results did not change after census tracts with higher proportions of geo-coding exclusions were eliminated from the analysis (supplemental Table S.3).

Different methods of spatial interpolation were evaluated to generate representative groundwater uranium exposure estimates. Kriging was chosen, because model performance was optimized and the output was similar to a semiparametric smoothing method that was evaluated using different covariance structures [25]. The use of spatial modeling and categorical exposure variables helped reduce the impact of extreme values, and the tracts with elevated uranium tended to be consistent among the modeling approaches that were evaluated. Additionally, uranium concentrations predicted by the final kriging model were correlated with the average of original measurements at the census tract level (Spearman correlation coefficient = 0.40, $p < 0.0001$). A bias may have been introduced in this study because of edge effects in areas bordering other states [33]. Future studies that expand the geographical area, examining regional cancer incidence in conjunction with groundwater uranium, are needed to address this uncertainty.

There was reasonably dense coverage of groundwater uranium data in this study (supplemental Figure S.1), and it is likely that concentrations remained relatively stationary over time because underlying geology serves as the source. However, the concentrations used for these analyses may not have accurately represented individual uranium intakes due to local geochemical and hydrological variation, differences in well depth, inability to account for alternate water sources (e.g., bottled water), potential exposures via showering or gardening, or other radionuclides present in SC aquifers. Nationally, bottled water consumption is approximately 10–20% of total daily water intake [36]. It is unknown what proportion of rural SC residents ingest bottled water, although one might not expect significant supplementation since most rural residents have lower incomes compared to national rates [37]. In addition, only 1.8% of SC census tracts in this study reported using a water source other than a well. There were ten other radionuclides present in the NURE database at much lower concentrations than uranium; and most were uncorrelated with uranium except for radium-226 or −228 (Spearman correlation coefficients: $\rho = 0.31$ and $\rho = 0.14$, respectively). Thus, the potential involvement of these uranium decay by-products in the observed relationships cannot be excluded. It was also not possible to distinguish between the chemical and radiological effects of uranium, or a combination of such effects, with this study design. Assuming groundwater ingestion is the primary exposure pathway, the estimated annual radiological dose was 0.38 μSv in quartile 4 for an adult ingesting the median uranium concentration (0.84 μg/L), assuming an average drinking water intake of 1.11 L/day [38], and a dose coefficient of 4.5×10^{-8} Sv/Bq [39]. Making these same assumptions, the estimated annual radiological dose was 103 μSv for an adult ingesting the maximum predicted uranium concentration (228 μg/L), which is similar to the World Health Organization's recommended annual reference dose level (RDL) of 100 μSv for drinking water consumption [40]. While these data likely provided reasonably good contrasts among census tracts grouped according to relatively lower or higher exposure quartiles, explicit doses among individuals or target organs should await more focused individual-level studies.

In general, the association between predicted ground-water uranium concentrations and increased risks for colorectal, breast, lung, and kidney cancer was stronger for census tracts with a higher proportion of AAs. For many anatomic sites, racial disparities in cancer incidence in SC are profound [14, 16, 17]. AAs may be more vulnerable to the biological effects of uranium, although no literature on racial differences in uranium disposition was identified. There is evidence that AAs differ from EAs in their metabolism of metals (e.g., zinc) [41]. Additionally, there may be racial differences in the amount of groundwater consumption, physical activity, or the biological processing of uranium. However, the relative distribution of water consumption or physical activity among rural AA or EA residents in South Carolina is not known. If confirmed, increased cancer risks observed among primarily AA populations may have important implications for the development of environmental interventions to reduce racial cancer disparities in SC.

In summary, this study took advantage of existing databases, including the high-quality SCCCR, and innovative spatial methods to test cancer-related hypotheses associated with groundwater uranium. Despite its biological plausibility, uranium has traditionally not been considered a potent human carcinogen, primarily because of its relatively low specific activity. However, only a few studies have carefully examined its carcinogenicity in human populations and the results have been mixed. The environmental distribution of uranium is widespread, and areas with elevated groundwater concentrations can be found in South Carolina and across the globe. Results from this ecologic investigation suggest that colorectal, breast, kidney, and total cancer incidence may be elevated in areas with frequent groundwater use and elevated groundwater uranium. We speculate that AAs may be more susceptible to the effects of uranium than are EAs for cancers of the lung, kidneys, breast, and colon. Additional studies, preferably among individuals with direct uranium exposure, are needed to address the limitations inherent in this study design and more fully characterize the potential carcinogenicity of this ubiquitous radionuclide.

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Abbreviations

AA	African American
CI	Confidence interval
DHEC	Department of Health and Environmental Control
EA	European American
GIS	Geographic information system
MCL	Maximum contaminant level
NAWQA	National Water-Quality Assessment
NURE	National Uranium Resource Evaluation
RDL	Reference dose level
SC	South Carolina
SCCCR	South Carolina Central Cancer Registry
SIR	Standardized incidence ratio
USGS	United States Geological Survey

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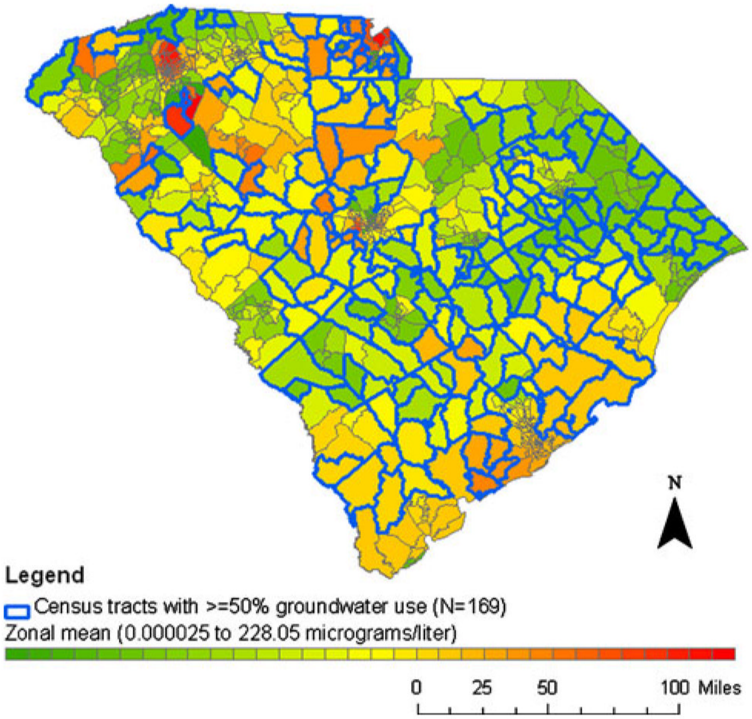

Fig. 1.

Mean census tract groundwater uranium concentration. Mean based on interpolated surface

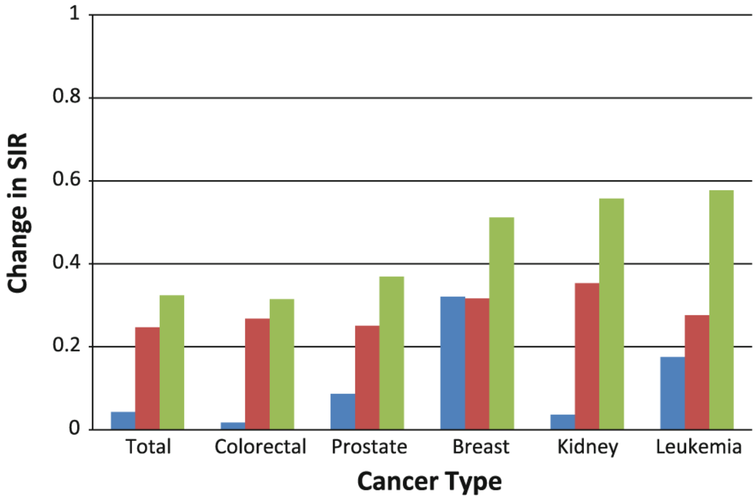

Fig. 2.

Change in cancer standardized incidence ratio (SIR) between upper and lower (referent) quartile of uranium concentration, by groundwater use and cancer type. The difference between the beta in the high quartile and the beta in the low quartiles of predicted groundwater uranium concentration, adjusted for census tract median household income and percent of African Americans. Lowest exposure quartile (*n* = 42); highest exposure quartile (*n* = 43). *Blue*: census tracts with ≥25% groundwater use; red: census tracts with ≥50% groundwater use; *green*: census tracts with ≥75% groundwater use

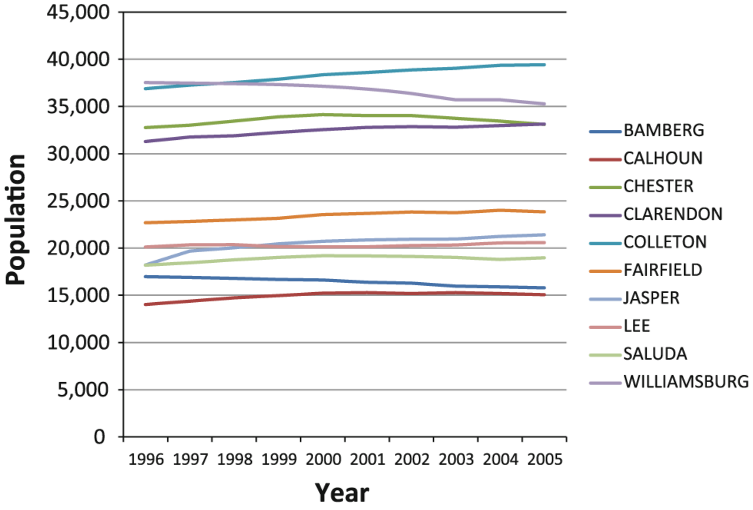

Fig. 3.

Population over time for South Carolina counties with ≥50% groundwater use

Table 1

Relationship of cancer standardized incidence ratios among quartiles of groundwater uranium concentration by cancer type, South Carolina, 1996–2005

Cancer type Uranium quartile	Unadjusted	Adjusted	Stratified	
	β (95% CI)	*β* (95% CI)	Low % AA *β* (95% CI)	High % AA *β* (95% CI)
Total [b]				
1 (*n* = 4,009)[a]	Referent	Referent	Referent	Referent
2 (*n* = 4,994)	0.14 (−0.04,0.32)	0.15 (−0.02,0.32)	0.00 (−0.21,0.21)	0.25 (−0.03,0.54)
3 (*n* = 5,367)	0.10 (−0.10,0.30)	0.15 (−0.04,0.34)	0.13 (−0.10,0.37)	0.16 (−0.15,0.47)
4 (*n* = 7,416)	0.30 (0.09,0.51)	0.25 (0.05,0.45)	0.25 (0.02,0.47)	0.27 (−0.10,0.63)
Trend *β* (*p*-value)	0.09 (0.01)	0.07 (0.03)	0.09 (0.02)	0.06 (0.33)
Prostate[b]				
1 (*n* = 608)	Referent	Referent	Referent	Referent
2 (*n* = 843)	0.20 (−0.03,0.44)	0.16 (−0.07,0.38)	0.01 (−0.29,0.32)	0.29 (−0.09,0.66)
3 (*n* = 901)	0.17 (−0.09,0.43)	0.15 (−0.09,0.40)	0.21 (−0.11,0.54)	0.17 (−0.24,0.58)
4 (*n* = 1,218)	0.37 (0.09,0.64)	0.25 (−0.01,0.51)	0.33 (0.02,0.65)	0.35 (−0.13,0.83)
Trend *β* (*p*-value)	0.11 (0.02)	0.07 (0.09)	0.12 (0.03)	0.07 (0.33)
Colorectal[b]				
1 (*n* = 423)	Referent	Referent	Referent	Referent
2 (*n* = 568)	0.12 (−0.05,0.30)	0.15 (−0.03,0.32)	0.00 (−0.29,0.29)	0.30 (0.06,0.53)
3 (*n* = 632)	0.18 (−0.02,0.37)	0.22 (0.03,0.41)	0.18 (−0.14,0.51)	0.28 (0.02,0.55)
4 (*n* = 779)	0.29 (0.08,0.50)	0.27 (0.06,0.47)	0.22 (−0.08,0.53)	0.36 (0.05,0.67)
Trend β (*p*-value)	0.09 (0.01)	0.09 (0.01)	0.08 (0.13)	0.09 (0.06)
Female breast[c]				
1 (*n* = 572)	Referent	Referent	Referent	Referent
2 (*n* = 744)	0.07 (−0.22,0.37)	−0.01 (−0.29,0.27)	−0.15 (-0.62,0.32)	0.10 (−0.23,0.43)
3 (*n* = 794)	0.12 (−0.18,0.42)	0.01 (−0.27,0.28)	−0.02 (−0.43,0.38)	0.09 (−0.27,0.45)
4 (*n* = 1,180)	0.69 (0.40,0.98)	0.32 (0.02,0.61)	0.19 (−0.27,0.66)	0.43 (0.06,0.80)
Trend *β* (*p*-value)	0.21 (<0.001)	0.09 (0.05)	0.06 (0.46)	0.13 (0.03)
Kidney & renal pelvic[c]				
1 (*n* = 103)	Referent	Referent	Referent	Referent
2 (*n* = 131)	0.09 (−0.15,0.34)	0.16 (−0.08,0.41)	−0.15 (−0.51,0.20)	0.27 (−0.07,0.62)
3 (*n* = 151)	0.11 (−0.14,0.36)	0.14 (−0.10,0.38)	0.06 (−0.25,0.37)	0.16 (−0.21,0.52)
4 (*n* = 183)	0.45 (0.20,0.69)	0.35 (0.09,0.61)	0.23 (−0.13,0.58)	0.40 (0.02,0.78)
Trend *β* (*p*-value)	0.14 (0.001)	0.10 (0.02)	0.08 (0.19)	0.10 (0.10)
Bladder[b]				
1 (*n* = 155)	Referent	Referent	Referent	Referent
2 (*n* = 137)	0.05 (−0.22,0.32)	0.12 (−0.13,0.37)	−0.09 (−0.54,0.36)	0.22 (−0.06,0.51)
3 (*n* = 189)	0.00 (−0.29,0.30)	0.12 (−0.14,0.39)	0.03 (−0.44,0.51)	0.11 (−0.19,0.42)
4 (*n* = 242)	0.28 (−0.03,0.59)	0.22 (−0.06,0.50)	0.24 (−0.21,0.70)	0.17 (−0.19,0.53)

Cancer type **Uranium quartile**	**Unadjusted**	**Adjusted**	**Stratified**	
	β (95% CI)	**β (95% CI)**	**Low % AA** **β (95% CI)**	**High % AA** **β (95% CI)**
Trend β (p-value)	0.08 (0.11)	0.07 (0.15)	0.09 (0.26)	0.03 (0.65)
Leukemia[c]				
1 (n = 98)	Referent	Referent	Referent	Referent
2 (n = 106)	−0.06 (−0.34,0.22)	−0.04 (−0.31,0.23)	−0.16 (−0.54,0.22)	0.00 (−0.40,0.41)
3 (n = 130)	0.01 (−0.27,0.28)	−0.01 (-0.28,0.26)	0.00 (−0.33,0.33)	0.21 (−0.22,0.64)
4 (n = 173)	0.48 (0.20,0.75)	0.28 (−0.01,0.57)	0.22 (−0.16,0.60)	0.31 (−0.14,0.76)
Trend β (p-value)	0.15 (0.001)	0.08 (0.07)	0.07 (0.27)	0.09 (0.22)
Lung & bronchus[b]				
1 (n = 663)	Referent	Referent	Referent	Referent
2 (n = 765)	0.06 (−0.12,0.25)	0.12 (−0.06,0.30)	−0.13 (−0.43,0.18)	0.27 (0.05,0.50)
3 (n = 761)	0.01 (−0.19,0.22)	0.09 (−0.11,0.29)	0.02 (−0.32,0.37)	0.14 (−0.10,0.39)
4 (n = 1,041)	0.12 (−0.10,0.35)	0.14 (−0.07,0.35)	0.09 (−0.23,0.42)	0.21 (−0.08,0.50)
Trend β (p-value)	0.03 (0.35)	0.04 (0.28)	0.04 (0.49)	0.03 (0.47)

Census tracts with ≥50% groundwater use only. Models adjusted for census tract median household income and percent AA. For stratified models: low % AA (<38%) and high % AA (>38%)

Grouped into quartiles of average census tract concentration (µg/L). Quartile 1 (n = 42); quartile 2 (n = 42); quartile 3 (n = 42); quartile 4 (n = 43)

AA African American, *CI* confidence interval, β the estimated change in cancer standardized incidence ratio for an incremental increase in estimated uranium exposure from the referent (quartile 1) to the upper quartiles of uranium exposure (quartiles 2, 3, or 4)

[a] Number of cancer cases in each exposure quartile

[b] Results obtained using semiparametric regression

[c] Results obtained using linear regression