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Association between hospital discharge rate for female breast cancer and residence in a zip code containing hazardous waste sites

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ABSTRACT

Background: Exposure to chemicals plays a role in risk of breast cancer. However, possible associations between risk of breast cancer and residential proximity to hazardous waste sites (HWSs) have not been reported.
Methods: We determined rates of hospital discharge with a diagnosis of female breast cancer in relation to residence in a zip code containing HWSs in New York State (NYS) after adjustment for ethnicity, age, income and urbanicity. Waste exposure was assessed by both the number of waste sites and the type of contaminants. Negative binomial regression was used to test the associations.
Results: After controlling for confounders, the hospital discharge rate of breast cancer for women living in zip codes having four or more HWSs or in zip codes having one HWS increased significantly (at the 0.05 level) by 9.1% and 6.4%, as compared to those living in a zip code with no HWS. The association for women living in zip codes having two or three HWSs was not significant. This indicates that the extent of exposure cannot be assessed solely by the number of waste sites. The discharge rate for women living in zip codes containing at least one volatile organic compound (VOC) waste site was significantly increased 5.6% as compared to those living in a zip code without any HWS, while the increases were not significant for women living in zip codes containing waste sites with persistent organic pollutants (POPs) or other contaminants. The significant associations were stronger for African American than Caucasian women and stronger in more urbanized than in rural areas.
Conclusions: Residence within a geographic area (defined by zip codes) that includes a hazardous waste site with VOCs is significantly associated with an increased rate of hospitalization for breast cancer, and the association is stronger for African American than Caucasian women and stronger in more urbanized than in rural areas after adjustment for the confounders.

1. Introduction

Breast cancer is the most common invasive cancer in women worldwide and the leading cause of mid-life cancer death in women (Brody et al., 2007). In a study of twins, Lichtenstein et al. (2000) concluded that 27% of breast cancer was due to heritable factors and suggested that the rest were due to "environmental factors". There is increasing evidence that exposure to chemicals plays a role in developing breast cancer (Aschengrau et al., 2003; Zhang et al., 2004; Bonner et al., 2005; Engel et al., 2005). More than 200 chemicals have been identified as potential mammary carcinogens in animals (Rudel et al., 2007). The proliferation of estrogen-sensitive breast cancer cells is stimulated by exogenous estrogen, and in vitro assays have identified about 250 chemicals that have estrogenic activity (Brody et al., 2007; Soto et al., 1995). Since estrogen has long been implicated in both the development and growth of breast cancer (Clemons and Goss, 2001), chemicals with estrogenic activity as well as with mutagenic activity might be expected to increase risk of development of the disease (Brophy et al., 2012).

Residence near to hazardous waste sites (HWSs) has been reported to result in an increased risk of congenital malformations and chromosomal abnormalities in offspring (Elliott et al., 2001; Orr et al., 2002; Brender et al., 2008), but studies focused on cancer rates

Abbreviations: NYS, New York State; HWSs, hazardous waste sites; POPs, Persistent Organic Pollutants; SPARCS, New York Statewide Planning and Research Cooperative System; ICD-9-CM, International Classification of Disease, 9th Revision, Clinical Modification; MHI, median household income; SES, social economic status; DEC, Department of Environmental Conservation; UR, urbanicity; PCB, polychlorinated biphenyls; PAHs, polycyclic aromatic hydrocarbons; VOCs, volatile organic compounds; BTEX, benzene, toluene, ethyl benzene and xylene; RR, rate ratio; CI, confidential interval; SEER, Surveillance Epidemiology and End Results; IARC, International Agency for Research on Cancer

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have not given consistent or conclusive results (Russi et al., 2008). Griffith et al. identified some HWSs in U.S. counties with analytical evidence of contaminated ground drinking water. They found significant associations (p value <0.002) between HWS counties and excess deaths for cancers of the lung, bladder, esophagus, stomach, large intestine, and rectum for white males and for cancers of the lung, breast, bladder, stomach, large intestine, and rectum for white females when compared to the non-HWS counties (Griffith et al., 1989). Porta et al. (2009) reviewed epidemiological studies on health effects associated with management of solid waste such as landfills and incinerators, and they found limited evidence of an increased risk of cancer, with an estimated excess risk of 3.5% for populations living within 3 km of old incinerators. The confidence in the evaluation and in the estimated excess risk was higher for specific cancers, such as non-Hodgkin's lymphoma and soft tissue sarcoma, than for other cancers (Porta et al., 2009).

The hypothesis of this study is that living near to certain HWSs increases the risk of development of breast cancer. In an earlier study we have reported a significant elevation in rates of hospitalization for hematologic cancers among individuals living near to HWSs containing benzene (Boberg et al., 2011). This study was designed to determine if there is an association between hospital discharge rate of female breast cancer and residential proximity to HWSs, and if so under which circumstances is the association most significant.

2. Material and methods

2.1. Study population

The New York Statewide Planning and Research Cooperative System (SPARCS) data was used to obtain data on the rates of diagnosis of breast cancer among inpatients upon hospital discharge from the years 1993 to 2008. All hospitals regulated by and located in NYS are required to report every diagnosis (up to 15) for each inpatient upon discharge to the NYS Department of Health, based on the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM). The SPARCS data available for this study does not include personal identifiers but does include patient age, gender, ethnicity and zip code of current residence. New York City maintains a separate data set and therefore was not included in this study. ICD codes used for diagnosis of female breast cancer were 174.0, 174.1, 174.2, 174.3, 174.4, 174.5, 174.6, 174.8 and 174.9. The ethnic distribution was 84.6% Caucasian, 6.3% African American, 0.2% Native American, 1.1% Asian American, 3.5% other ethnicities and 4.8% unknown. Since Caucasian and African American comprised over 90% of the patients, only these two ethnic groups were considered in this study. The percentage for patients with age below 30 was only 0.5% and therefore people under the age of 30 were also not included in this study.

Information for other important confounders not contained in the SPARCS dataset was obtained from other sources. Median household income (MHI) by zip code was obtained from Claritas, Inc. (San Diego, CA) for the years 1993–2008. MHI was used as a proxy for socioeconomic status (SES). Previous studies have shown that extremes of SES, as measured by MHI, have different health service access behaviors (Ma et al., 2007). Therefore, we restricted the analysis to zip codes with MHI ranging from $26,151 (the 10th percentile of MHI) to $58,673 (the 90th percentile of MHI) based on the mean values over 16 years. This MHI range was further divided into four levels by quartile: first quartile (1st Q) $26,151–32,853, second quartile (2nd Q) $32,853–39,047, third quartile (3rd Q) $39,047–51,909, fourth quartile (4th Q) $51,909–58,673. To control for urbanicity (UR), we applied the US Census Bureau definition of an "urban" area being more than 1,000 persons per square mile (Ma et al., 2007). We used Census data from 2000 to divide the population into three groups: UR1, UR2 and UR3. Zip codes with less than 25% of the population living in urbanized areas were classified into UR1 group. Zip codes with 25–75% of the population living in urbanized areas were classified into UR2 group. Zip codes with more than 75% of the population living in urbanized areas were classified into UR3 group. The hazardous waste site information was obtained from the NYS Department of Environmental Conservation (NYSDEC) in 2008. This information gave the location and listed the major contaminants found at each site.

We obtained the number of people living in each zip code by ethnicity, gender and age for each year between 1993 and 2008 from Claritas, Inc. (San Diego, CA). Since the United States Postal Service regularly changes zip codes, we collected the total population and the number of discharges with each subpopulation for each year separately and added them together to create the person-years variable, which then allowed determination of the hospital discharge rates in the final data set.

This is a study where the unit of analysis is a subpopulation living in a zip code, not an individual person with or without breast cancer. The outcome variable is the number of hospital discharge diagnoses in each unit of analysis, thus the incidence of breast cancer as either a primary or secondary diagnosis upon discharge. The outcome is a counting variable in each unit of analysis, and the measure of effect is the risk ratio that compares rate of diagnosis in zip codes with HWSs to those without HWSs. While this is an ecological study its goal is to estimate unit level parameters. Consequently an ecological fallacy is not possible here.

2.2. Exposure assessment

The NYSDEC has identified 818 HWSs in the state that pose a potential threat to human health. The HWSs were distributed in 416 zip codes. The contaminants in the HWSs included persistent organic pollutants (POPs) (dioxins, polychlorinated biphenyls, polycyclic aromatic hydrocarbons and chlorinated pesticides), volatile organic compounds (VOCs) (chloroethenes, chloroethanes, chloromethanes, chlorobenzenes, benzene, toluene, ethyl benzene, xylene, etc.), and other forms of waste (metals, acids, phthalates, waste oils, radioactivity, etc.). Since all 200 miles of the Hudson River from Hudson Falls to Manhattan are a National Priority List HWS determined by the U.S. Environmental Protection Agency due to high contamination of polychlorinated biphenyls in these waters, the 47 zip codes abutting the Hudson River were regarded as zip codes containing HWSs (Sergeev and Carpenter, 2005).

The waste exposure was assessed by residence in zip codes containing HWSs. First, we classified zip codes into four groups by the number of waste sites. A total of 957 zip codes that did not contain any identified waste site were classified as "Clean" zip codes. A total of 299 zip codes that each had one waste site were classified as "One" zip codes. There were 113 zip codes that each had two or three waste sites, and were classified as "Two or Three" zip codes. A total of 51 zip codes each had four or more waste sites, and were classified as "Four or more" zip codes. The distributions of the number of waste sites in the various zip codes are shown in Fig. S1 in Supplementary materials.

Alternatively, we classified zip codes into four groups by type of contaminant. There were a total of 195 zip codes that each had at least a waste site containing POPs, and these were classified as "POPs" zip codes (even though many of these sites also contained other contaminants). A total of 228 zip codes that each had at least a waste site containing VOCs (without POPs) were classified as "VOCs" zip codes. There were 40 zip codes that each had one or more waste sites containing contaminants, but none containing POPs or VOCs, and these were classified as "Other" zip codes. The 957 zip codes that did not contain any identified waste sites were classified as "Clean" zip codes. Fig. S2 in Supplementary materials shows the groups of zip codes based on type of contaminants.

2.3. Ethics statement

The authors have permission to use SPARCS data and have obtained review by the University at Albany Institutional Review Board, who declared use of the SPARCS data in this fashion is exempt from review because it contains no identifiable data. Because there are no unique identifiers in the data base, no patient consent was needed.

2.4. Statistical analysis

The breast cancer hospital discharge rate per 100,000 was calculated as the number of discharge diagnosis of breast cancer divided by the total population with the same gender, ethnicity and age group, residing in the same zip code category (defined by waste exposure), MHI and urbanicity. All statistical analyses were performed with SAS software (version 9.3; SAS Institute Inc., Cary, NC). Initially Poisson regression was used as the appropriate model with the rate ratio (RR) as the measure of effect. Since the variables were categorical, there were a fixed and finite number of covariate patterns. Extra Poisson variation was observed, and consequently the negative binomial regression model was applied and found to fit well for the analysis. The equation of the model is presented in Supplementary materials.

The modeling process began with the creation of main effects only model to adjust for potential confounding. Thereafter, the main effects model was examined for effect modifiers in the exposure vs. outcome association by considering the interactions of exposure with age, ethnicity, MHI and urbanicity.

3. Results

The population studied in relation to waste exposure, ethnicity, age, MHI and urbanicity is shown in Table 1. Nearly half (46%) of the study persons lived in zip codes without a HWS. The hospital discharge rate of breast cancer was greater among Caucasians than African Americans and increased with age up to 79. The age-adjusted discharge rates of female breast cancer were similar to the incidence rates in the Surveillance Epidemiology and End