

Linking Childhood Cancer with Potential Environmental Exposure Determinants

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ABSTRACT

Childhood chronic diseases, especially cancer, are of growing concern. Research has focused on 2 developmental periods, prenatal and postnatal. While it is hypothesized that chemical contaminants in the physical environment may play a role in the development and exacerbation of many chronic diseases, the role of environmental exposures in the etiology of these conditions remains uncertain. This can be somewhat attributed to the fact that it is very difficult to efficiently link chronic health effects with environmental exposures that are likely to have occurred temporally and spatially distant from diagnosis. This study explored the utility of linking childhood cancer cases with their birth certificate data as a method for increasing the number of geo-referenced data points available for linking health effect data with environmental monitoring data. This would begin to quantify the transiency of 1 subset of the population, and provide a basis for characterizing and estimating potentials for exposure to numerous environmental contaminants during prenatal and postnatal periods. A total of 441 unduplicated cancer diagnosis records of children who were both born and diagnosed with cancer in Wisconsin between 1995 and 2002 were linked with birth records to explore the variability between address at birth and diagnosis. The majority of records were matched to a birth record file (81.0%). Of these matched records, 86% moved <1 mile from birth to time of diagnosis. The results suggest that adminis-

trative and public health surveillance data can be used to quantify transiency. Data from the sample tested indicate that during the given time period children do not move far from their birth homes, suggesting minimal changes in exposure potential related to residence location from birth to diagnosis. This background is useful for future epidemiological investigations linking environmental factors with chronic health effects.

INTRODUCTION

Chronic diseases such as cancer, cardiovascular disease, birth defects and asthma are the leading causes of morbidity and mortality in the United States today. While it is hypothesized that chemical contaminants in the physical environment may play a role in the development and exacerbation of many chronic diseases, the role of environmental exposures in the etiology of these conditions remains uncertain. The ability to classify and quantify environmental exposures of concern occurring before and after birth is a primary source of uncertainty in tracking environmental-health relationships.

The relationship between exposure to chemical contaminants in the physical environment and childhood cancers is a priority public health concern in Wisconsin. Thus, this group was selected for initially evaluating an approach to better characterize exposure potentials. Nationally, childhood cancer is the leading cause of death among children under age 15, and approximately 270 cases of childhood cancer are diagnosed annually in Wisconsin.^{1,2} According to the National Cancer Institute (NCI), leukemia and central nervous system tumors account for at least half of the total cancers diagnosed nationally in children. Brain tumor incidence rates have increased over the past 20 years, while the rates for leukemia have remained relatively stable since 1980.¹ The environmental origins of childhood cancer and their relationship to other risk factors remain relatively uncertain; however, a number of biologically plausible environmental associations have been described in the literature. Leukemia incidence has been associated with hazardous air pollutants, pesticide use, ionizing radi-

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tion, and road traffic, and nervous systems cancers have been linked to parental pesticide exposure.² Currently, tools available to state health department practitioners for integrating data on environmental hazards and exposures and their relationship to such health concerns within the state are extremely limited.

Wisconsin clinicians frequently receive questions from their patients concerning whether a recent cancer diagnosis in a child could be related to something in their environment. Commonly these questions are forwarded to the Wisconsin Division of Public Health for response. Childhood cancers and possible geographic clustering of cases are among the most frequent concerns cited. Concerns typically focus on the here-and-now of the child's current residential area, yet research suggests that the in-utero time period may be of equal or greater concern. Analyses based solely on current residence may result in false-negative results. Linking current address with birth address could provide a more robust analytic structure. Such linkage has not been done in Wisconsin. This project assessed the feasibility of such linkage and the potential impact of transiency.

Unfortunately, no single administrative data source includes information on the location of an individual at the time of birth, where she/he moves, and address at the time of diagnosis. Data on all childhood cancer cases identified within Wisconsin are in the Wisconsin Cancer Reporting System (WCRS), which also includes residential address at the time of diagnosis. However, residential history prior to diagnosis is lacking. Thus, relying solely on WCRS data leaves public health officials, environmental health practitioners, and cancer researchers with a limited ability to explore how and when environmental exposures may have occurred during relevant developmental windows. For this project, integration of the WCRS and the birth certificate records were evaluated for their ability to increase the availability of geo-referenced data points available for their application in an enhanced surveillance system. This included an examination of the logistics for merging the datasets and quantifying the distance moved between time of birth and diagnosis in an effort to improve existing methods for linking chronic diseases and environmental exposures.

METHODS

A preliminary matching of 103 unduplicated records of children born in 1994 who had cancer diagnoses reported to the WCRS was done to develop methods for matching cancer case information with birth records. These cases were matched to the 1994 birth

file, which contains all children born in Wisconsin or to Wisconsin residents (n=69,547). Both sources had dates of birth and the name of the child. The birth records also contained the mother's birth surname and the father's surname.

Once systematic methods for matching were established, a total of 441 unduplicated records of children born between 1995-2002 and who were subsequently diagnosed with cancer during the same time period were identified from the WCRS. Cases were classified into diagnostic groups using the NCI's Surveillance Epidemiology and End Results modifications of International Classification of Childhood Cancer.³ The use of 1995 as the start date for this project was based on indications that the most accurate and reliable environmental data are those collected after 1994. Cases then were matched to their corresponding birth files, which contained information on children born in Wisconsin or born to Wisconsin residents, and geo-referenced data for birth address were added to the WCRS records. Sources of geographic information available from the birth record include responses to questions asking the mother for her state, county and minor civil division (MCD) of residence, and designated mailing address for sending birth certificate information. Where available, the mother's designated mailing address was used as the child's address at birth for geocoding purposes. Diagnosis and birth addresses were then geocoded using Centrus.

Distance moved between birth address and diagnosis address was calculated using the ArcView 3.2 Avenue script. Original distance between geographic points was computed. Distance moved was calculated and categorized based on half-mile and 1-mile intervals. Cases were further categorized into 3 age groups to explore distance traveled from birth to diagnosis by age group. Mean age within each of the distance-traveled categories was also assessed. SAS 9.1 was used for data analysis.

RESULTS

Of the preliminary set of 103 cases of cancer diagnosed in 1994, 81 (79%) completely matched on name and birth date (Table 1). Seven additional matches were made following manual review of the remaining unmatched records. Because childhood cancer diagnoses often date from 4 or more years after the birth record, some matches may not have been made because of name changes. Overall, there was an 85% (88/103) match rate for the initial matching of 1994 cases with birth records. This suggested it was possible to match a large percentage of cases with their birth certificates,

Table 1. Matching Criteria Established for Childhood Cancer Data Linkage Project, 1994

Linking Combinations	Records Matched
Birth date + child's last name + first name	81
Birth date + mother's birth name + first name	0
Birth date + father's last name + first name	0
Birth date + first name (manual review)	3
Month and year of birth + child's last name (manual review)	4
Month and year of birth + child's first name (manual review)	0
Child's last name + first name (manual review)	0
Total Records	103
Total Records Matched	88 (85%)

Table 2. Childhood Cancer Matching, 1995-2002

Birth Year	CRS Children	No. Matched to a Birth Record	% Matched
1995	98	73	74.5
1996	87	64	73.6
1997	60	48	80.0
1998	71	58	81.7
1999	49	46	93.9
2000	50	44	88.0
2001	20	19	95.0
2002	7	5	71.4
Total	441	357	81.0

CRS=cancer reporting system.

Table 3. Distance Moved from Birth Address to Diagnosis Address, 1995-2002

Distance Moved (Miles)	% of Cases (N=351)
<0	55.5
0 - .5	23.3
.5 - 1.0	6.4
1.0 - 2.0	5.0
2.0 - 3.0	4.5
3.0 - 4.0	1.7
4.0 +	3.6

Table 4. Mean Distance Moved By Age Group, 1995-2002

Age Group	No. of Cases	Mean Distance Moved in Miles (Range)	Standard Deviation
0-1	49	0.85 (0-20.8)	3.15
1-4	257	7.55 (0-191.3)	25.28
5-9	45	13.50 (0-145.9)	29.36

and that the percent of additional cases matched from the subsequent manual matching likely did not warrant the extra effort.

Once matching criteria were established, an additional 441 unduplicated records of childhood cancer cases with a diagnosis between 1995-2002 and born during the same time period were linked with birth records. A total of 357 records (81%) were matched to a birth record file based on an exact match of name and birth date (Table 2). Leukemias (35%), central nervous system tumors (14%), sympathetic nervous system tumors (12%), renal tumors (9%), soft tissue carcinomas (8%), and lymphomas (5%) were the most common diagnoses in the study sample. Approximately 20% of the cases were excluded from additional analysis because of failure to match. These children were likely born out of state or had a name change.

The 357 matched cases were then geocoded using maternal residence at the time of birth and child residence at the date of diagnosis. The majority of cases could be geocoded accurately to the address level for both diagnosis and birth address (n=314). Forty-five (14%) diagnosis addresses and 38 (12%) birth addresses could only be matched at the level of ZIP code. Such cases were assigned a geo-referenced value in the center of the ZIP code. Seven of the birth addresses had errors and could not be geocoded.

Examination of distance traveled between birth address and diagnosis address found that 86% of Wisconsin children who were both born and diagnosed with a reportable form of cancer between 1995 and 2002 moved <1 mile from birth to time of diagnosis (Table 3). Table 4 indicates that approximately 56% of childhood cancer cases did not move from time of birth to diagnosis, and 23% moved less than a half mile. The likelihood that cases had moved between birth address and time of diagnosis increased with higher age at diagnosis. The majority of childhood cancer cases diagnosed within the first year of life had diagnosis addresses within 1 mile of their birth address.

DISCUSSION

The ability to track long-term exposures to chemical contaminants and their impact on chronic diseases remains challenging. The primary goal of this study was to determine if data from 2 different administrative and public health surveillance data sets could be used to increase the amount of geographic information available for future linkages of environmental factors and health consequences. For children diagnosed with cancer, re-

sults suggest that the majority of children do not relocate in the first year of life, children who do move do not move large distances, and both the likelihood of having moved and the distance moved increases with age.

Determining when exposures to chemical contaminants in the physical environment have occurred during a person's lifespan is critical to understanding the relationship between environmental risk factors and the health effect. Some research suggests that for many of the childhood cancers that are diagnosed in the first 2 years of life, the most relevant window for exposures may be during fetal growth and development, and maternal exposures may be of primary etiological importance.⁴ The alternative hypothesis is that childhood cancers may be the result of environmental exposures that occur outside the womb during early years of rapid growth and development.⁵ For either scenario, the data suggest it is important to consider potential exposures from earliest developmental stages through time of diagnosis. The ideal method for obtaining such information is individual interviews to gather a complete history. However, this approach is not feasible for ongoing surveillance programs, where the goal is to continuously monitor and update data. In this case, it is preferable to use established administrative surveillance systems, sometimes applied in novel ways, to track environmental-health relationships. By using the birth matching approach, it was possible to explore potential differences in ambient exposures at the time of birth and at the time of diagnosis for approximately 80% of childhood cancer cases. These methods demonstrate the feasibility and utility of linking 2 administrative datasets, allowing for a more comprehensive analysis over different time periods during a child's life.

Exposure estimates will vary depending on whether or not residence at birth or residence at time of diagnosis is used for assigning exposure. The birth address would be a more representative geographic reference point for exploring potential maternal and fetal exposures, while the diagnosis address may more accurately represent what children were exposed to from the time of birth to diagnosis. Without the linkage of the WCRS to the birth certificates, exposure could only be characterized from 1 address, likely the diagnosis address. The additional geographic information expands our ability to characterize potential environmental exposures.

The results from this project also provide some clarification about the transiency of this specific population. The improved understanding for the typical distance moved also enhances our ability to link exposure to disease. There is significant temporal and spatial vari-

ability in contamination and exposure potential for different types of environmental hazards. For instance, a 1-mile move may be significant for an environmental hazard such as drinking water source, but may make little difference for estimating exposures to ambient air pollutants. A better understanding for the patterns of transiency enhances the ability to address such temporal and spatial disparities for individual contaminant types.

Different types of childhood cancers have different etiologies, based on various environmental contributors, individual genetics, and their interactions, all of which are risk factors for different types of cancers. Leukemias, the most prevalent cancers diagnosed within the study population, have been linked to both prenatal and postnatal environmental exposures such as pesticides.⁶ The prominence of agricultural practices and home pesticide use within the state suggests that environmental risk factors may play a role in the prevalence of childhood cancer in Wisconsin. Without a comprehensive surveillance system to track relevant exposures, however, this question remains difficult to answer.

Linkage of the 2 administrative datasets is an alternative approach to the more resource intensive method of individual interviews for delineating geographic information that is likely to impact the characterization of environmental exposures. Although applied research would likely require more in-depth data collection, the results indicate the linkage approach is adequate and sufficient for improving the ability to estimate exposures to ambient environmental pollutants, and for enhancing the ongoing surveillance of environmental factors and health effects.

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