Massachusetts
Department Of
Public Health

Evaluation of Brain Cancer Incidence in Weston and Wayland, MA

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Center for
Environmental Health,
Community Assessment
Program

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I. Introduction

In October 2004, a resident of Weston, Massachusetts contacted the Massachusetts Department of Public Health (MDPH), Center for Environmental Health (CEH) regarding concerns over a suspected increase in the incidence of brain cancer among children in Weston. Specifically, the resident reported that four school-aged children in Weston had been diagnosed with brain cancer since 2000 and expressed concerns over whether this may represent an atypical pattern or possibly be related to a common environmental factor. In addition, the resident also reported a child who had been diagnosed with brain cancer but lived in Wayland (on the Wayland-Weston border) in somewhat close proximity to the former Dow Chemical Site. In response to these concerns, the Community Assessment Program (CAP), a division within the CEH, reviewed the incidence of brain cancer in the towns of Weston and Wayland with particular attention to the incidence of this cancer type among children (i.e., ages 0-19).

II. Methods

To determine whether an atypical pattern of brain cancer exists among children in Weston and Wayland, the CAP reviewed Massachusetts Cancer Registry (MCR) data files for residents of these two towns who had been diagnosed with brain cancer during 1995-present. [Coding for this cancer type follows the International Classification of Diseases for Oncology (ICD-O) system. See Appendix A for the incidence coding definition used in this report for this cancer type.] The MCR, a division within the MDPH Center for Health Information, Statistics, Research and Evaluation, is a population-based surveillance system that has been monitoring cancer incidence in the Commonwealth since 1982. All new diagnoses of cancer among Massachusetts residents are required by law to be reported to the MCR within six months of the date of diagnosis (M.G.L. c.111. s 111b). This information is kept in a confidential database. Data are collected on a daily basis and are reviewed for accuracy and completeness on an annual basis. This process corrects misclassification of data (e.g., city/town misassignment) and deletes duplicate case reports. Once these steps are finished, the data for that year are considered "complete." At the initiation of this investigation, complete data records included diagnoses that occurred from 1/1/1982-12/31/2001. Due to the volume of information received by the MCR, the large number of reporting facilities, and the six-month period between diagnosis and required reporting, the most current registry data that are complete will inherently be a minimum of two

years prior to the current date. The 7-year period from 1995-2001 constitutes the time period for which the most recent and complete cancer incidence data were available from the MCR at the time this investigation was initiated.[1] This is an on-going surveillance system that collects reports on a daily basis, and thus, CAP staff conducted a qualitative review of case reports of diagnoses of brain cancer among residents of the towns of Weston and Wayland for more recent years (i.e., 2002-present). While this type of evaluation does not allow for the calculation of a cancer rate for 2002-present, it can provide a qualitative review of cancer patterns in a given area.

It is important to note that although some non-cancerous (i.e., benign) tumors of the brain are reported to the MCR, these cases are not included in the data summarized here. Also, only primary site (original location in the body) cancers are included in the MCR. Cancers that occur as the result of the metastasis or the spread of a primary site cancer to another location in the body are not considered separate cancers. Therefore, this analysis includes only diagnoses of invasive (i.e., malignant) primary cancers of the brain.

In order to determine whether cancer incidence in a community is occurring at a higher or lower rate than expected, a statistic called the standardized incidence ratio (SIR) is calculated using data from the MCR. More specifically, the SIR is the number of observed cancer cases in a town (or census tract) divided by the number of expected cases based upon the population of the town (or census tract) and the state's cancer rates. An SIR greater than 100 indicates that more cancer diagnoses occurred than expected; an SIR less than 100 means that fewer diagnoses occurred than expected. For example, an SIR of 150 is interpreted as 50 percent more cases than expected; an SIR of 90 indicates 10 percent fewer cases than expected. When an SIR is statistically significant, as indicated in the table by an asterisk symbol (*), there is less than a 5% chance that the observed number of diagnoses is due to chance alone. SIRs and 95% confidence intervals (CIs) are not calculated when the observed number of cases is less than five. A more detailed explanation of SIRs and 95% CIs is provided in Appendix B.

[1] The data summarized here are drawn from data entered on MCR computer files before November 22, 2005. The numbers presented may differ slightly from those published in previous or future reports, reflecting late reported cases, address corrections, or other changes based on subsequent details from reporting facilities.

Because accurate age group and gender specific population data are required to calculate SIRs, the census tract (CT) is the smallest geographic area for which cancer rates can be accurately calculated. Specifically, census tracts are small, relatively permanent geographic entities within counties (or the statistical equivalents of counties) defined by a committee of local data users following Census Bureau guidelines. CTs usually contain between 2,500 and 8,000 persons and are designed to be homogenous with respect to population characteristics. According to the U.S. Census, the town of Weston is divided into two CTs, 3671 and 3672, as is the town of Wayland (CTs 3661 and 3662) (U.S. DOC, 2000). The town boundaries and census tract locations for Weston and Wayland are illustrated in Figure 1. SIRs were calculated for brain cancer for each town as a whole and for each CT for the time period 1995-2001. As noted earlier, MCR data for the years 2002-present were not complete at the initiation of this investigation. Therefore, they were not used to calculate incidence rates; however the information was reviewed qualitatively to determine if any geographic patterns might exist.

In addition to calculating SIRs, place of residence at the time of diagnosis was mapped for each individual (e.g., adults and children) diagnosed with brain cancer in Weston and Wayland during the time period 1995-2005 using a computerized geographic information system (GIS) (ESRI, 2004). This allowed assignment of census tract location for each case as well as a qualitative evaluation of the spatial distribution of diagnoses at a smaller geographic level (i.e., neighborhoods) in order to determine the likelihood of a potential association with environmental factors (e.g. the former Dow Chemical site). The geographic pattern was determined using a qualitative evaluation of the point pattern of individuals diagnosed with cancer to assess any possible concentrations of cases. For confidentiality reasons, maps showing the location of individuals diagnosed with cancer cannot be provided. However, a summary of this evaluation with any notable findings is presented in this report.

III. Results

Five children (four from the town of Weston and one in the town of Wayland) with a reported diagnosis of brain cancer were reported in the original request to the CEH for an investigation. Information about the five children was limited and varied for each child. Full names were not

provided for any of the children; the last name of one child was listed in the letter. Address at diagnosis was listed for three children and an approximate year of diagnosis was provided for four of the five children. Following receipt of the original request, the CEH received the full names for two of the children from the resident who had made the request. Requests for additional information on children diagnosed with brain cancer were also made to three Weston school nurses that the resident listed as potential sources of information. The CEH also contacted the Weston Board of Health for reports of children with brain cancer that their office may have received. No additional information was available from the Board of Health or the Weston school nurses.

Based on the information provided by the resident, the CAP was able to confirm the diagnoses of three children in the MCR (three Weston residents). All three children were reported to the MCR with a diagnosis of brain cancer (two were diagnosed in 1995-2001 and one was diagnosed during the 2002-present period). Although MCR data were reviewed through the present time (November 2005), the CAP was unable to confirm a cancer diagnosis for two of the children reported to the CEH. One possible reason for this may be a recent diagnosis of cancer that has not yet been reported to the MCR. Another possibility is that these children were diagnosed before moving to Weston or Wayland. Finally, it is also possible that these children may have actually been diagnosed with a pre-cancerous or non-cancerous condition (e.g., aplastic anemia) which would not be included in the MCR data files, or with another primary cancer type. Information reviewed from the MCR on all brain cancers (in adults and children) diagnosed in Weston and Wayland from 1995 to the present will be discussed later in this report.

A. Brain Cancer Incidence in Weston

During the time period of 1995-2001, two children (i.e., age 0-19) were diagnosed with brain cancer town-wide, while about one child would have been expected to be diagnosed with brain cancer in Weston. Overall, the town-wide incidence of brain cancer (including children and adults) was statistically significantly elevated for the time period of 1995-2001. A total of 15 individuals were diagnosed with brain cancer while about six diagnoses would have been expected (SIR = 238, 95% CI = 133-392). This elevation was due to an increase in females in the town of Weston. Ten females were diagnosed with this cancer type while approximately

three cases were expected (SIR = 364, 95% CI = 174-670); this difference is statistically significant (see Table 1).

The town of Weston is made up of two CTs, one that covers the northern section of town (CT 3671) and the other encompasses the southern portion of town (CT 3672). Both Weston CTs border Wayland CT 3662 (See Figure 1). For the two children diagnosed during the 1995-2001 time period, their residences at the time of diagnosis, as reported to the MCR, were determined to be in different census tracts in Weston. During 1995-2001, CT 3672 experienced a statistically significant elevation in the overall (males and females combined) rate of brain cancer with 11 diagnoses observed and four diagnoses expected (SIR = 273, 95% CI = 136-489). The overall elevation was due to a statistically significant increase in the incidence of brain cancer among females in CT 3672. Seven females in this CT were diagnosed with brain cancer during this time period while approximately two cases were expected (SIR = 387, 95% CI = 155-797). Among females in CT 3671, three diagnoses of brain cancer were observed versus about one expected for this time period.

Table 1 - Brain Cancer Incidence in Weston, MA: 1995-2001

	Total				Males				Females			
	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Town total	15	6.3	238*	133-392	5	3.6	140	45-328	10	2.7	364*	174-670
CT 3671	4	2.3	NC	NC	1	1.3	NC	NC	3	0.9	NC	NC
CT 3672	11	4.0	273*	136-489	4	2.2	NC	NC	7	1.8	387*	155-797

Notes: Obs = observed; Exp = expected; 95% CI = 95% confidence interval;
NC = not calculated; * = statistical significance

B. Brain Cancer Incidence in Wayland

Among children (i.e., age 0-19) in the town of Wayland, one child was diagnosed with brain cancer during the 1995-2001 time period, which is what would have been expected based on the statewide brain cancer experience for children. Town-wide incidence of brain cancer, during this period, among males and females combined was slightly above the rate expected. A total of nine

individuals were diagnosed with brain cancer while seven cases were expected (SIR = 129, 95% CI = 59-244) (See Table 2). This elevation was not statistically significant.

The town of Wayland has two CTs, one that covers the northern section of town (CT 3662) and the other encompasses the southern portion of town (CT 3661) (See Figure 1). During 1995-2001, two residents of CT 3661 (both male) were diagnosed with brain cancer while approximately three cases were expected. For CT 3662, seven individuals were diagnosed with brain cancer while approximately four were expected. However, the elevation was not statistically significant (See Table 2).

Table 2 - Brain Cancer Incidence in Wayland, MA: 1995-2001

	Total				Males				Females			
	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Town total	9	7.0	129	59-244	5	3.9	127	41-297	4	3.1	NC	NC
CT 3661	2	2.6	NC	NC	2	1.4	NC	NC	0	1.2	NC	NC
CT 3662	7	4.4	160	64-330	3	2.5	NC	NC	4	1.8	NC	NC

Notes: Obs = observed; Exp = expected; 95% CI = 95% confidence interval;
NC = not calculated; * = statistical significance

C. Temporal Distribution of Brain Cancer in Weston and Wayland

From 1995-present, a total of 20 individuals from the town of Weston have been reported to the MCR with a diagnosis of brain cancer. This includes the 15 individuals diagnosed during 1995-2001 (including two children ages 0-19) and five individuals (including one child) diagnosed in the 2002-present time period. A total of 11 individuals from the town of Wayland have been reported to the MCR with a diagnosis of brain cancer from 1995-present. This includes nine individuals diagnosed during 1995-2001 (including one child) and two individuals diagnosed in the 2002-present time period (including one child).

Dates of diagnosis for residents of Wayland and Weston diagnosed with brain cancer were evaluated to assess any time trends that might be present since 1995. The years of diagnosis for

each individual diagnosed with brain cancer in each of the two towns generally varied throughout the time period of 1995-present, thereby not indicating unusual temporal patterns.

D. Geographic Distribution of Brain Cancer

In addition to determining census tract-specific incidence ratios for brain cancer in the towns of Weston and Wayland, a qualitative evaluation of the spatial distribution of residents of Weston and Wayland diagnosed with brain cancer from 1995-present was conducted to assess any possible geographic concentration of diagnoses in specific neighborhoods within these two communities.

Review of geographic distribution of Wayland and Weston residents diagnosed with brain cancer from 1995-present did not reveal any unusual spatial patterns or concentrations of individuals diagnosed with brain cancer within any census tract including in the area of South Wayland around the former Dow Chemical Site. That is, the residence of individuals diagnosed with brain cancer did not appear spatially concentrated or "clustered" in any one area of the town. In general, the geographic distribution of diagnoses closely matched the pattern of population density in Wayland and Weston.

E. Review of Case Information

Despite numerous scientific and medical investigations, and analyses, the causes of brain cancer are still largely unknown. However, a few risk factors have been identified. The most well-established risk factor is exposure to ionizing radiation (e.g., from radiation therapy to the head and neck) (ACS, 2004a). In addition, rare cases of brain cancer run in some families. Some types have also been associated with certain rare genetic disorders, such as neurofibromatosis type 1, von Hippel-Lindau disease, and Li-Fraumeni syndrome (ACS, 2004a). Environmental exposures, such as vinyl chloride, aspartame (a sugar substitute), and electromagnetic fields, have been suggested as risk factors for brain cancer, but the evidence to support these associations is inconsistent (ACS, 2004a). Please refer to Appendix C for further information on brain cancer.

Available case information from the MCR was evaluated for individuals diagnosed with this cancer type from 1995-present. The information reviewed included date of diagnosis, age at diagnosis, histology (cancer cell type), and previous cancer diagnoses. However, information about personal risk factors that may also influence the development of brain cancer (e.g., family history and heredity) are not collected by the MCR or any other readily accessible source, and therefore, could not be evaluated in this investigation.

1. Age at Diagnosis

After a peak in childhood (generally under 10 years of age), the risk of developing brain cancer increases with age from age 25 to age 75. Brain cancers occur with different frequencies among the various age-groups, and most brain cancer occurs more frequently in older populations (i.e., those over 50 years of age) (Ries et al, 2004). Statewide, cancers of the brain and central nervous system (CNS) are the second most common type of cancer in children.

From 1995-present, the average age at diagnosis among the 20 individuals in Weston with brain cancer was 58, with a range of 6 to 92 years of age at diagnosis. Two children (i.e., ages 0-19) from 1995-2001 and one child from 2002-present were diagnosed with brain cancer and reported to the MCR. The majority of individuals (70%, n = 14) were 50 years of age or older at the time of diagnosis. Females in Weston (who experienced a statistically significant elevation in the incidence of brain cancer during 1995-2001) had an average age of 49 at diagnosis with a range of 6 to 84 years; half of the females diagnosed from 1995-present (six of 12) were over the age of 50 at the time of diagnosis.

From 1995-present, the average age of diagnosis among the 11 individuals in Wayland diagnosed with brain cancer was 45, with a range of 3 to 77 years of age at diagnosis. During this time period, two children (i.e., ages 0-19) were diagnosed with brain cancer. Thirty-six percent (n = 4) were 50 years of age or older at the time of diagnosis.

2. Histology

The most common primary brain tumors are gliomas. Gliomas are a general classification of malignant tumors that include a variety of types, named for the cells from which they arise:

astrocytomas, oligodendrogliomas, and ependymomas. In addition to these main types, there are a number of rare brain tumors, including medulloblastomas, which develop from the primitive stem cells of the cerebellum and are most often seen in children. In adults, the most frequent types of brain tumors are astrocytic tumors (mainly astrocytomas and glioblastoma multiforme). About half of all childhood brain tumors are astrocytomas and 25% are medulloblastomas (ACS, 2004b).

Of the 20 individuals from Weston reported to the MCR with brain cancer during 1995-present, approximately 85% (n = 17) were diagnosed with a glioma, the most common type of brain cancer. Other histology types included a medulloblastoma, a germinoma, and a general neoplasm of the brain. Each of the three children in Weston diagnosed with brain cancer during this time period had a different histology which included a pilocytic astrocytoma, a medulloblastoma and a germinoma. Of the 12 females diagnosed with brain cancer in Weston during this time period, 75% (n = 9) were diagnosed with a glioma.

All of the 11 individuals in Wayland were diagnosed with a glioma. Both children in Wayland reported to the MCR with a diagnosis of brain cancer during 1995-present were diagnosed with the astrocytoma sub-type of glioma.

Our review of the various histologies, for all of the individuals diagnosed with brain cancer, revealed that for both children and adults in both communities, no unusual patterns of histology were observed.

3. Previous Cancer Diagnosis

One of the well established risk factors (and only established environmental risk factor) for brain tumors (either cancerous or non-cancerous) is high-dose exposure to ionizing radiation (i.e., x-rays and gamma rays) (Preston-Martin & Mack, 1996). Most radiation-induced brain tumors are caused by radiation to the head from the treatment of other cancers (ACS, 2004a). Review of specific patient information from the MCR for the 1995-present time period identified two individuals (both females and residents of CT 3672) in Weston and one individual (male) in Wayland diagnosed with brain cancer who had been previously diagnosed with cancer. These

three patients may have received treatment that could have contributed to their subsequent diagnosis of brain cancer. However, it is not possible to determine whether these individuals actually received radiation therapy for their cancer.

IV. Discussion and Conclusions

According to statistics from the American Cancer Society, cancer is the second leading cause of death in Massachusetts and the United States. Not only will one out of three people develop cancer in their lifetime, but cancer will affect three out of every four families. For this reason, cancers often appear to occur in "clusters," and it is understandable that someone may perceive that there are an unusually high number of cancer cases in their surrounding neighborhoods or towns. Upon close examination, many of these "clusters" are not unusual increases, as first thought, but are related to such factors as local population density, variations in reporting or chance fluctuations in occurrence. In other instances, the "cluster" in question includes a high concentration of individuals who possess related behaviors or risk factors for cancer. Some, however, are unusual; that is, they represent a true excess of cancer in a workplace, a community, or among a subgroup of people. A suspected cluster is more likely to be a true cancer cluster if it involves a large number of cases of one type of cancer diagnosed in a relatively short time period rather than several different types diagnosed over a long period of time (i.e., 20 years), a rare type of cancer rather than common types, and a large number of cases diagnosed among individuals in age groups not usually affected by that cancer. These types of clusters may warrant further public health investigation.

During the 1995-2001 period, two children (ages 0-19) were diagnosed with brain cancer in Weston while approximately one childhood diagnosis would have been expected. The two children lived in different census tracts. When reviewing data from the MCR available for 2002-present, one additional child in Weston was reported with a diagnosis of brain cancer. During the 1995-2001 time period, one child was diagnosed with brain cancer in Wayland, which is what would have been expected based on the statewide brain cancer experience for children. Also, when reviewing MCR data for 2002-present for Wayland, one additional child was reported with a diagnosis of brain cancer. A statistically significant elevation in the overall incidence of brain cancer (adults and children) was observed in the town of Weston over this

seven-year period. This elevation was due to an excess among females living in the town, with ten observed diagnoses versus approximately three diagnoses expected (SIR = 364, 95% CI = 174-670), and more specifically, among females in CT 3672 with seven observed diagnoses versus approximately two cases expected (SIR = 387, 95% CI = 155-797). As discussed, two of these individuals had a previous diagnosis of cancer and if radiation treatment occurred it may have contributed to their brain cancer diagnosis. In Wayland, the incidence of brain cancer from 1995-2001 was slightly elevated (nine diagnoses observed versus seven diagnoses expected), but the elevation was not statistically significant.

CAP reviewed available case information and the temporal and geographic patterns of diagnoses for children and adults in these two communities. Based on what is reported in the medical literature on the known or established cancer incidence patterns for brain cancer, specifically age at diagnosis and the various histologies for brain cancer, our review of available information reported to the MCR for the individuals in Weston and Wayland did not show any unusual patterns with respect to age at diagnosis or histologies. Similarly, no temporal or geographic clustering was noted among the cases.

Finally, it is important to mention conclusions reached from the previous Health Consultation released by the CAP in February 2001 entitled *Assessment of Cancer Incidence and Exposure Opportunities from the Former Dow Chemical Site in Wayland, MA 1982-1994, 1995* (Appendix D). Review of available environmental sampling information concluded that "the site posed no public health hazard to the general public" (MDPH, 2001). The evaluation of exposure pathways from contaminants present at the Dow site in that report did not indicate that significant exposures were likely to have occurred to local residents. Although the causes of brain cancer are still unknown, based on the information reviewed in this report, it does not appear that a common factor (environmental or non-environmental) played a primary role in the development of brain cancer in Weston and Wayland.

V. Recommendations

Based on the information reviewed in this report, no further evaluation of brain cancer in Weston and Wayland is recommended at this time. However, the CEH will monitor the incidence of brain cancer among females residing in Weston as new data become available through the MCR.

VI. References

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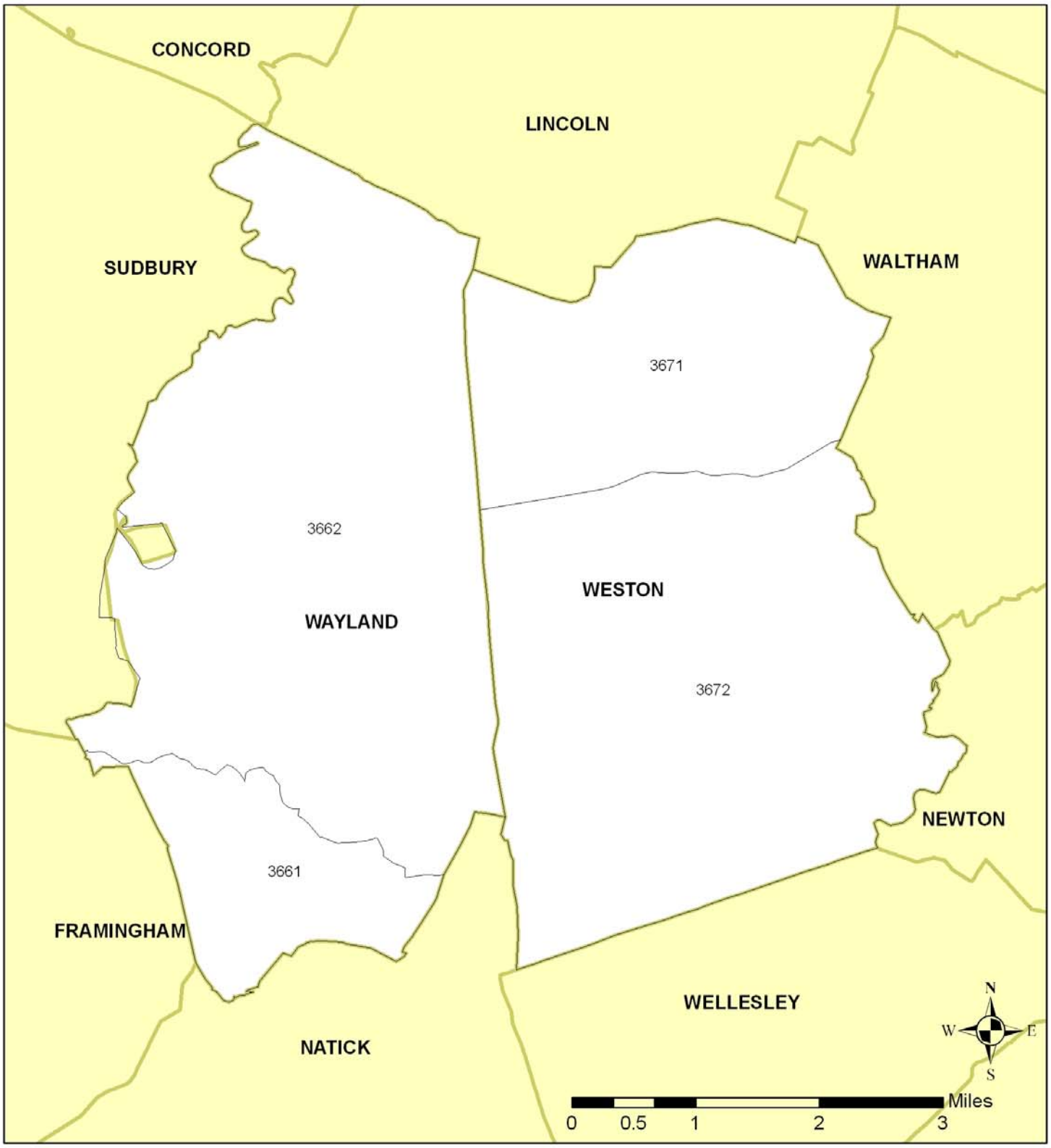
Figure 1:
Location of Census Tracts in Weston and Wayland, MA



Center for CEH Environmental Health

Geographic data supplied by:
Massachusetts Executive Office of Environmental Affairs, MassGIS;

Appendix A – Coding Definitions of Cancer Site/Type

Appendix A:
Coding Definitions of Cancer Site/Type*

Cancer Site / Type	*ICD-O-1 and Other Pre-ICD-O-2 Codes*		*ICD-O-2 Codes*		*ICD-O-3 Codes*	
	Site code	***Histology code***	***Site code***	***Histology code***	***Site code***	***Histology code***
Bladder	188.0-188.9	except 9590-9980	C67.0-C67.9	except 9590-9989	C67.0-C67.9	except 9590-9989
Brain & Central Nervous System (CNS)	191.0-192.9	See Table 1 below	C70.0-C72.9	*See ICD-O codes in Table 1 below*	C70.0-C72.9	*except 9590-9989*
Breast	174.0-174.9, 175.9	except 9590-9980	C50.0-C50.9	except 9590-9989	C50.0-C50.9	except 9590-9989
Cervix Uteri	180.0-180.9	except 9590-9980	C53.0-C53.9	except 9590-9989	C53.0-C53.9	except 9590-9989
Colon & Rectum	153.0-153.9, 154.0, 154.1, 154.9, 159.0	except 9590-9980	C18.0-C18.9, C19.9, C20.9, C26.0	except 9590-9989	C18.0-C18.9, C19.9, C20.9, C26.0	except 9590-9989
Corpus Uteri & Uterus, NOS	179.9, 182.0-182.9	except 9590-9980	C54.0-C54.9, C55.9	except 9590-9989	C54.0-C54.9, C55.9	except 9590-9989
Esophagus	150.0-150.9	except 9590-9980	C15.0-C15.9	except 9590-9989	C15.0-C15.9	except 9590-9989
Hodgkin's Disease	140.0-199.9	includes O9650-O9667, P9653-P9683, B9653-B9658	C00.00-C80.9	includes 9650-9667	C00.00-C80.9	includes 9650-9667
Kidney & Renal Pelvis	189.0, 189.1	except 9590-9980	C64.9, C65.9	except 9590-9989	C64.9, C65.9	except 9590-9989
Larynx	161.0-161.9	except 9590-9980	C32.0-C32.9	except 9590-9989	C32.0-C32.9	except 9590-9989
Leukemia	140.0-199.9	includes O9800-O9943, O9951, P9803-P9943, B9803-B9943	1. C00.0-C80.9 AND 2. C42.0, C42.1, C42.4	1. includes 9800-9822, 9824-9826, 9828-9941 2. includes 9823, 9827	1. C00.0-C80.9 AND 2. C42.0, C42.1, C42.4	1. includes 9733, 9742, 9800-9820, 9826, 9831-9948, 9963-9964 2. includes 9823, 9827
Liver	155.0	except 9590-9980	C22.0	except 9590-9989	C22.0	except 9590-9989
Lung & Bronchus	162.2-162.9	except 9050-9053, 9590-9980	C34.0-C34.9	except 9590-9989	C34.0-C34.9	except 9590-9989

Appendix A (continued)

Cancer Site / Type	*ICD-O-1 and Other Pre-ICD-O-2 Codes*		*ICD-O-2 Codes*		*ICD-O-3 Codes*	
	Site code	***Histology code***	***Site code***	***Histology code***	***Site code***	***Histology code***
Melanoma	173.0-173.9	includes O8720-O8790, B8723-B8783, P8723-P8783	C44.0-C44.9	includes 8720-8790	C44.0-C44.9	includes 8720-8790
Multiple Myeloma	140.0-199.9	includes O9730, O9731, O9732, P9733, B9733	C00.0-C80.9	includes 9731, 9732	C00.0-C80.9	includes 9731, 9732, 9734
Non-Hodgkin's Lymphoma (NHL)	140.0-199.9	includes O9590-O9642, O9670-O9710, O9750, P9593-P9643, P9693-P9713, P9753, B9593-B9643, B9703	1. C00.0-C80.9 AND 2. All sites except C42.0, C42.1, C42.4	1. includes 9590-9595, 9670-9717 2. includes 9823, 9827	1. C00.0-C80.9 AND 2. All sites except C42.0, C42.1, C42.4	1. includes 9590-9596, 9670-9729 2. includes 9823, 9827
Oral Cavity & Pharynx	140.0-149.9	except 9590-9980	C00.0-C14.8	except 9590-9989	C00.0-C14.8	except 9590-9989
Ovary	183.0	except 9590-9980	C56.9	except 9590-9989	C56.9	except 9590-9989
Pancreas	157.0-157.9	except 9590-9980	C25.0-C25.9	except 9590-9989	C25.0-C25.9	except 9590-9989
Prostate	185.0, 185.9	except 9590-9980	C61.9	except 9590-9989	C61.9	except 9590-9989
Stomach	151.0-151.9	except 9590-9980	C16.0-C16.9	except 9590-9989	C16.0-C16.9	except 9590-9989
Testis	186.0-186.9	except 9590-9980	C62.0-C62.9	except 9590-9989	C62.0-C62.9	except 9590-9989
Thyroid	193.9	except 9590-9980	C73.9	except 9590-9989	C73.9	except 9590-9989

*Note: Includes invasive tumors only, selected by excluding in situ stages J0, S0, TTISNXM0, TTANXMX, TTANXM0, TTAN0MX, TTISN0M0, TTISNXMX, TTISN0MX, TTISN0M0, TTIN0M0, TTIN0MX, TTINXM0, and TTINXMX (1982-1994 data) or by specifying behavior code (1995-present data).

Table 1: Histology codes for Brain and Central Nervous System (pre-ICD-O-3)

ICD-O O 9370, 9380, 9381, 9382, 9390, 9391, 9392, 9400, 9401, 9403, 9410, 9411, 9420, 9421, 9422, 9423, 9424, 9430, 9440, 9441, 9442, 9443, 9450, 9451, 9460, 9470, 9471, 9472, 9473, 9480, 9481, 9490, 9500, 9501, 9502, 9503, 9530, 9539, 9540, 9560, 9561.

SNOP P 9363, 9383, 9393, 9403, 9413, 9423, 9433, 9443, 9453, 9463, 9473, 9483, 9493, 9503, 9533, 9543, 9563.
HLTHSTT B 9383, 9393, 9403, 9433, 9443, 9453, 9463, 9473, 9483, 9493, 9503, 9530, 9533, 9537, 9543, 9563.

Source: Massachusetts Department of Public Health, Bureau of Environmental Health Assessment (December 1998)

Appendix B

Appendix B – Explanation of a Standardized Incidence Ratio (SIR) and 95% Confidence Interval

Appendix B

Explanation of a Standardized Incidence Ratio (SIR) And 95% Confidence Interval

In order to evaluate cancer incidence a statistic known as a standardized incidence ratio (SIR) was calculated for each cancer type. An SIR is an estimate of the occurrence of cancer in a population relative to what might be expected if the population had the same cancer experience as some larger comparison population designated as "normal" or average. Usually, the state as a whole is selected to be the comparison population. Using the state of Massachusetts as a comparison population provides a stable population base for the calculation of incidence rates. As a result of the instability of incidence rates based on small numbers of cases, SIRs were not calculated when fewer than five cases were observed.

Specifically, an SIR is the ratio of the observed number of cancer cases to the expected number of cases multiplied by 100. An SIR of 100 indicates that the number of cancer cases observed in the population evaluated is equal to the number of cancer cases expected in the comparison or "normal" population. An SIR greater than 100 indicates that more cancer cases occurred than expected and an SIR less than 100 indicates that fewer cancer cases occurred than expected. Accordingly, an SIR of 150 is interpreted as 50% more cases than the expected number; an SIR of 90 indicates 10% fewer cases than expected.

Caution should be exercised, however, when interpreting an SIR. The interpretation of an SIR depends on both the size and the stability of the SIR. Two SIRs can have the same size but not the same stability. For example, an SIR of 150 based on 4 expected cases and 6 observed cases indicates a 50% excess in cancer, but the excess is actually only two cases. Conversely, an SIR of 150 based on 400 expected cases and 600 observed cases represents the same 50% excess in cancer, but because the SIR is based upon a greater number of cases, the estimate is more stable. It is very unlikely that 200 excess cases of cancer would occur by chance alone.

To determine if the observed number of cases is significantly different from the expected number or if the difference may be due solely to chance, a 95% confidence interval (CI) was calculated for each SIR. A 95% CI assesses the magnitude and stability of an SIR. Specifically, a 95% CI is the range of estimated SIR values that has a 95% probability of including the true SIR for the population. If the 95% CI range does not include the value 100, then the study population is significantly different from the comparison or "normal" population. "Significantly different" means there is less than 5% percent chance that the observed difference is the result of random fluctuation in the number of observed cancer cases.

For example, if a confidence interval does not include 100 and the interval is above 100 (e.g., 105-130), then there is statistically significant excess in the number of cancer cases. Similarly, if the confidence interval does not include 100 and the interval is below 100 (e.g., 45-96), then the number of cancer cases is statistically significantly lower than expected. If the confidence interval range includes 100, then the true SIR may be 100, and it cannot be concluded with sufficient confidence that the observed number of cases is not the result of chance and reflects a real cancer increase or decrease. Statistical significance is not assessed when fewer than five cases are observed.

Source: Massachusetts Department of Public Health, Bureau of Environmental Health Assessment (December 1998)

Appendix B

In addition to the range of the estimates contained in the confidence interval, the width of the confidence interval also reflects the stability of the SIR estimate. For example, a narrow confidence interval (e.g., 103--115) allows a fair level of certainty that the calculated SIR is close to the true SIR for the population. A wide interval (e.g., 85--450) leaves considerable doubt about the true SIR, which could be much lower than or much higher than the calculated SIR. This would indicate an unstable statistic.

Source: Massachusetts Department of Public Health, Bureau of Environmental Health Assessment (December 1998)

Appendix C – Risk Factor Summary for Brain Cancer

Brain and central nervous system (CNS) tumors can be either malignant (cancerous) or benign (non-cancerous). Primary brain tumors (i.e., brain cancer) comprise two main types: gliomas and malignant meningiomas. Gliomas are a general classification of malignant tumors that include a variety of types, named for the cells from which they arise: astrocytomas, oligodendrogliomas, and ependymomas. Meningiomas arise from the meninges, which are tissues that surround the outer part of the spinal cord and brain. Although meningiomas are not technically brain tumors, as they occur outside of the brain, they account for about 50% of all reported primary brain and spinal cord tumors. The majority of meningiomas (about 85%) are benign and can be cured by surgery. Therefore, approximately 7.5% of brain and CNS tumors are malignant meningiomas. In addition to these main types, there are a number of rare brain tumors, including medulloblastomas, which develop from the primitive stem cells of the cerebellum and are most often seen in children. Also, the brain is a site where both primary and secondary malignant tumors can arise; secondary brain tumors generally originate elsewhere in the body and then metastasize, or spread, to the brain (ACS, 1999a). The American Cancer Society estimates that 18,500 Americans (10,620 men and 7,880 women) will be diagnosed with primary brain cancer (including cancers of the central nervous system, or spinal cord) and approximately 12,760 people (7,280 men and 5,480 women) will die from this disease in 2005 (ACS, 2005).

Brain and spinal cord cancers account for over 20% of all cancer types diagnosed among children aged 0-14 (ACS, 2005). About half of all childhood brain tumors are astrocytomas and 25% are medulloblastomas (ACS, 1999b). After a peak in childhood (generally under 10 years of age), the risk of brain cancer increases with age from age 25 to age 75. In adults, the most frequent types of brain tumors are astrocytic tumors (mainly astrocytomas and glioblastoma multiforme). Incidence rates are higher in males than in females for all types. In general, the highest rates of brain and nervous system cancer tend to occur in whites. However, this varies somewhat by type; the incidence of gliomas is lower among black men and women than whites, but for meningiomas, the reverse is true (Preston-Martin and Mack, 1996).

Despite numerous scientific and medical investigations, and analyses, the causes of brain cancer are still largely unknown. Among the possible risk factors investigated in relation to this type of cancer are ionizing radiation, electromagnetic fields, occupational exposures, exposure to N-nitroso compounds, head trauma, and genetic disorders.

The most established risk factor (and only established environmental risk factor) for brain tumors (either cancerous or non-cancerous) is high-dose exposure to ionizing radiation (i.e., x-rays and gamma rays). Most radiation-induced brain tumors are caused by radiation to the head from the treatment of other cancers (ACS, 1999a). Meningiomas are the most common type of tumors that occur from this type of exposure, but gliomas may also occur (Preston-Martin and Mack, 1996). Among adults, the risk of developing meningiomas has been associated with full-mouth dental x-rays taken decades ago when radiation doses were higher than today. Although the relationship between low-dose radiation exposure and increased risk of brain tumors has been debated in several studies, prenatal exposure from diagnostic x-rays has been related to an increase in childhood brain tumors (Preston-Martin and Mack, 1996).

In recent years, there has been increasing public concern and scientific interest regarding the relationship of electromagnetic fields (EMF) to brain cancer. However, results from recent epidemiological investigations provide little or no evidence of an association between residential EMF exposure (e.g., from power lines and home appliances) and brain tumors (Kheifets, 2001). Studies also suggest that the use of handheld cellular telephones is not associated with an increased risk of primary brain cancer (Muscat et al., 2000). However, given the relatively recent use of cellular phones, evidence is preliminary and few studies have been conducted.

Other environmental factors such as exposure to vinyl chloride (used in the manufacturing of some plastics) and aspartame (a sugar substitute) have been suggested as possible risk factors for brain cancer but no conclusive evidence exists implicating these factors (ACS, 1999a). Although some occupational studies have suggested that electrical and electric utility workers may be at a slightly increased risk of brain cancer, these studies have important limitations, such as exposure misclassifications and a lack of dose-response relationships (Kheifets, 2001). Some researchers have also reported an increased risk of brain tumors in adults among veterinarians and farmers. Exposures to farm animals and pets have been considered as possible risk factors because of their association with bacteria, pesticides, solvents, and certain animal oncogenic (cancer-related) viruses (Yeni-Komshian and Holly, 2000). However, the relationship between farm life and brain cancer remains controversial.

Recent reports have proposed a link between occupational exposure to lead and brain cancer risk, but further analytic studies are warranted to test this hypothesis (Cocco et al., 1998). In a recent case-control study, the concentrations of metal and non-metal compounds in brain biopsies from patients with primary brain tumors were compared to results from an analysis of tumor-free brain tissue. Statistically significant associations were observed between the presence of brain tumors and the concentrations of silicon, magnesium, and calcium (Hadfield et al., 1998). However, further research using a larger sample size is needed to determine whether exposure to these elements plays a role in the development of brain cancer. Other occupations that may be associated with elevated risks include workers in certain health professions (e.g., pathologists and physicians), agricultural workers, workers in the nuclear industry, and workers in the rubber industry, although specific exposures have not been established (Preston-Martin and Mack, 1996). Studies investigating the possible association between occupational exposure of parents (in particular, paper or pulp-mill, aircraft, rubber, metal, construction, and electric workers) and the onset of brain tumors in their children have provided inconsistent results (Preston-Martin and Mack, 1996).

The association between the development of brain cancer and nitrites and other N-nitroso compounds, among the most potent of carcinogens, has been heavily researched. N-nitroso compounds have been found in tobacco smoke, cosmetics, automobile interiors, and cured meats. A recent study concluded that an increased risk of pediatric brain tumor may be associated with high levels of nitrite intake from maternal cured meat consumption during pregnancy (Pogoda and Preston-Martin, 2001). However, the role of nitrites and cured meats in the development of brain cancer remains controversial (Blot et al., 1999; Bunin, 2000). Because most people have continuous, low level exposure to N-nitroso compounds throughout their lives, further studies, especially cohort studies, are needed to determine if this exposure leads to an increased risk of brain tumors (Preston-Martin, 1996).

Injury to the head has been suggested as a possible risk factor for later development of brain tumors but most researchers agree that there is no conclusive evidence for an association (ACS, 1999b). Head trauma is most strongly associated with the development of meningiomas compared with other types of brain tumor. Several studies have found an increased risk in women with histories of head trauma; in men who boxed; and in men with a previous history of head injuries. Gliomas are the most common type of childhood brain tumor and have been positively associated with trauma at birth (e.g., Cesarean section, prolonged labor, and forceps delivery). However, other studies have found no association (Preston-Martin and Mack, 1996).

In addition, rare cases of brain and spinal cord cancer run in some families. Brain tumors in some persons are associated with genetic disorders such as neurofibromatosis types I and II, Li-Fraumeni syndrome, and tuberous sclerosis. Neurofibromatosis type I (von Recklinghausen's disease) is the most common inherited cause of brain or spinal cord tumors and occurs in about one out of every 3,000 people (Preston-Martin and Mack, 1996). The disease may be associated with optic gliomas or other gliomas of the brain or spinal cord (ACS, 1999b). Of those afflicted with the disease, about 5-10% will develop a central nervous system tumor (Preston-Martin and Mack, 1996). In addition, von Hippell-Lindau disease is associated with an inherited tendency to develop blood vessel tumors of the cerebellum (ACS, 1999a). However, malignant (or cancerous) brain tumors are rare in these disorders; inherited syndromes that predispose individuals to brain tumors appear to be present in fewer than 5% of brain tumor patients (Preston-Martin and Mack, 1996).

Other possible risk factors investigated for brain cancer have included alcohol consumption, use of barbiturates, smoking and exposure to second-hand smoke, pesticides, and infectious diseases (i.e., tuberculosis and chicken pox). To date, studies on these risk factors have yielded inconclusive results. Further, the majority of individuals diagnosed with brain cancer have no known risk factors (ACS, 1999a).

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Appendix D – Assessment of Cancer Incidence and Exposure Opportunities from the Former Dow Chemical Site in Wayland, Massachusetts 1982-1994, 1995