

## Cancer Incidence in Andover, New Hampshire: Analysis of Potential Cancer Cluster

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#### SUMMARY:

On August 1, 2012, The NH State Cancer Registry received a concern from residents of Andover, New Hampshire (NH) regarding perceived elevated cancer incidence in Andover Village. The residents were concerned about exposure to contaminants in the community water system. At the time the concern was reported, residents had identified eight known cancer cases in an area of 20 single family residence homes. The cases were of varying types of cancer and were not associated with a specific age or gender group. The concerned citizens requested information on the number of cancer cases in the past 10 years in Andover Village Water District and for an evaluation of potential environmental exposures.

Cancer is now becoming a highly visible disease as it is the cause of approximately 23% of all deaths in United States and nearly 25% of all deaths in New Hampshire. As you might expect, the common occurrence of a disease increases the potential for cases to appear to cluster in a neighborhood. The Centers for Disease Control and Prevention (CDC) definition for a cancer cluster is a greater than expected number of cancer cases occurring within a group of people, in a geographic area, or over a period of time. According to the National Cancer Institute, a suspected cancer cluster is more likely to be a true cluster, rather than a coincidence, if it involves:

1) A large number of cases of a similar type of cancer, rather than several different types;

2) A rare type of cancer, rather than common types; and

3) An increased number of cases of a certain type of cancer in an age group that is not usually affected by that type of cancer.

After discussion with the individuals reporting the concern it was determined that the concern did not meet the base criteria to initiate a cancer cluster investigation and no specific environmental exposures could be identified (though general concern regarding the community water system was expressed), therefore a formal detailed cancer cluster investigation was not initiated. Regardless of the formal protocol, the NH State Cancer Registry followed through with an analysis of available data in acknowledgement of the concern just to be sure no specific problem could be identified. Though residents perceived high levels of cancer in the community a statistical analysis using the NH Cancer Registry data indicated that rates in Andover were not significantly different from what would be expected in a population with Andover's demographic characteristics. Additionally, after review of the water quality data, we found no evidence of regulatory violations in the community water system serving Andover Village.

Cancer is a very real and difficult group of diseases for individuals to understand and know how to protect themselves and their families from. This report does not rule out the possibility of environmental exposures in Andover or Andover Village. However, the absence of significant findings suggests there is no widespread environmental concern impacting the entire community.

There are still a wide range of preventative actions for individuals to consider if they want to reduce their overall risk of developing cancer. Therefore, in follow up to the concerns a dialogue between the community and the NH Department of Health and Human Services was opened and two community meetings were planned. The first, an educational training program on cancer prevention and early detection was held at a Town Hall meeting at Andover on June 6, 2014. The second, a discussion of the data and this report, was held on October 22<sup>nd</sup>.

An initial statistical analysis was carried out based on current Andover data recorded in the NH State Cancer Registry for the time period of 2005-2011 to investigate this concern. The contents of this report detail the findings of this analysis.

## **BACKGROUND**:

Cancer is now becoming more and more visible as people are living longer. According to the American Cancer Society, one out of three people will be diagnosed with cancer during their lifetime, making this a very common disease. Since 2005, cancer has been the #1 leading cause of death in NH overtaking heart disease and it is the cause of approximately 25% of all deaths in NH. This increases the potential for cancer cases to appear to cluster in a neighborhood.

The American Cancer Society estimates that there will be 1,665,540 new cases of invasive cancer in 2014 with an estimated 585,720 deaths in the United States. In NH, it is estimated that there will be 8,450 new cases and 2,670 deaths in 2014.<sup>1</sup> It has been further estimated that there are approximately 72,000 persons living in NH (2014) with cancer.<sup>2</sup> Overall in NH, cancer incidence and mortality has been decreasing over the last several years.

It's important to know that cancer is not just one disease; it is at least 100 different but related diseases, each associated with a specific set of causal factors. In addition, a latency period of twenty years or more is often encountered between the time of exposure to a cancer-causing substance and the diagnosis of cancer. This latency period may further obscure factors that may be involved in the disease, and in some cases historical information about exposure to cancer-causing substances is simply not available. These factors make it difficult, if not impossible, to pinpoint underlying causal factors for a variety of cancers.

The Centers for Disease Control and Prevention (CDC) defines a cancer cluster as "a greater than expected number of cancer cases occurring within a group of people, in a geographic area, or over a period of time". According to the National Cancer Institute (NCI), a suspected cancer cluster is more likely to be a true cluster, rather than a coincidence, if it involves:

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- 2) A rare type of cancer, rather than common types; and

3) An increased number of cases of a certain type of cancer in an age group that is not usually affected by that type of cancer.

The number of cases included in a cluster—and calculation of the expected number of cases will depend on how we define the time period over which the cases occurred. The selection of a time period may "create" or "obscure" a cancer cluster. If the time period is too wide, we may

<sup>&</sup>lt;sup>1</sup> American Cancer Society (2014). Cancer Facts & Figures - 2000. U.S. Department of Health and Human Services. Atlanta, GA. 2014

<sup>&</sup>lt;sup>2</sup> National Cancer Institute and CDC. State Cancer Profiles. Quick profiles for states. http://statecancerprofiles.cancer.gov/

obscure a cluster by "diluting" the cases over time. Conversely, if the time period is too narrow, we may artificially "create" a cluster.

The objective of this analysis was to determine if the rates of cancers in Andover were in excess of what would be expected for that community using data for the state of NH as a comparison.

## **METHODS**:

Data source: We analyzed data collected by the NH State Cancer Registry (NHSCR), which are certified as being of high quality, and are collected through rigorous quality checking from various NH hospitals, clinics, and physicians' offices. The NHSCR also receives cancer information from neighboring states through a data exchange agreement. The NHSCR maintains statistics on incident cancer cases among all NH residents.

Geographic area and population: As we did not have a way to determine whether people in the NHSCR were within the Andover Village Water District, we decided to analyze data for the entire town of Andover. As per the 2010 census, Andover's population was 2,371 with a median age of  $48.6 \pm 2.6$  years which was significantly higher than the NH population  $41.1 \pm 0.1$  years. Of the total Andover population, 96.5% of residents are white, which is a little higher than NH (white=94%).<sup>3</sup>

Time period: As Andover has a small population, we decided to include cases from a 7 year time period (2005-2011) because more cases provide greater statistical stability. We had reliable and complete NHSCR records through 2011. (The NHSCR generally waits 2 years from the end of a diagnosis year before publishing any cancer incidence data. 2012 data will be available by the end of 2014 or early 2015.)

Case definition: For this analysis, we included only 'invasive' cancer cases, following a standard practice used by CDC and National Program for Cancer Registry (NPCR). It included all localized, regional and distant stage cases and only in-situ urinary bladder cancer cases.

Statistical analysis: We calculated the Standardized Incidence Ratio (SIR), which is a statistical measure that examines whether the observed number of cancer cases in Andover exceeded the expected number of cases. In this way, SIR compared the cancer rate in Andover with that of the entire state of NH, taking into account differences in age in the different communities. As an aid to interpretation, an SIR of 1 means the rate of cancer in the community is the same as the state of NH. An SIR greater than 1 suggests a higher risk of cancer, and an SIR less than 1 suggests a lower risk.

The 95% confidence interval (CI) shows the variability associated with the measure; when the range between the lower and upper confidence intervals includes 1.0, then the result is not statistically significant, i.e. the most likely explanation is random chance rather than a true difference between the two populations being compared. For example, if the confidence interval

<sup>&</sup>lt;sup>3</sup> US Department of Commerce. US Census 2010, American Fact Finders

ranges from 0.06 to 26.64; the rate includes 1.0 so it is not significantly different than expected. A detailed discussion of this technique is available in Appendix A.

Each type of cancer was analyzed according to 19 age-groups (<1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, and 85+ years). This process allowed for a comparison between the observed number of cancer cases in Andover, per cancer type, to the expected number of cases derived using the comparison NH population.

## **RESULTS:**

The findings from our analyses are illustrated in Table 1. From 1/2005 to 12/2011, we found a total of 96 registered cancer cases in all of Andover town. The expected number for a town of this size and age distribution in NH is 97, which is very similar. However, this does not mean that specific cancer types are all within the expected range. We found six specific cancer types with 5 or more cases in Andover during this time period. SIR was not calculated for the cancer types with fewer than 5 cases between 2005 and 2011. We found that Andover had a slightly higher number of observed lung, colorectal, melanoma and uterus cancer cases than expected, and a slightly lower number of observed prostate and female breast cancer cases than expected, but these numbers were not outside the range of random chance (i.e., the differences were not statistically significant because the CI included 1.0).

**Table 1:** Standardized Incidence Ratios for different cancer types in Andover town for males and females, 2005-2011

Cancer Type	Gender	Expected*	Observed **	SIR	Lower CI	Upper CI
All Cancer	Male	54.8	62	1.13	0.87	1.45
	Female	43.5	34	0.78	0.54	1.09
	Both	96.7	96	0.99	0.80	1.21
Lung	Both	13.3	15	1.13	0.63	1.86
Prostate	Male	15.8	13	0.82	0.44	1.41
Colorectal	Both	8.0	13	1.38	0.69	2.47
Female Breast	Female	13.1	12	0.91	0.47	1.60
Melanoma	Both	5.1	6	1.17	0.43	2.55
Uterus	Female	3.2	5	1.57	0.51	3.67

\* 2005-2011 NHSCR data for the whole state are used to derive expected cases in Andover town

\*\* 2005-2011 cancer cases in Andover that were identified through NHSCR

SIR= Standardized Incidence Rate Ratio. CI = 95% Confidence Intervals.

#### **DISCUSSION:**

From the above analyses, our results suggest that cancer rates (overall and 6 types of cancer) were within the range of what is expected in comparable populations in NH. Statistical estimates are not exact, but these numbers do not look outside of the normal range of variability we see for any particular town. These results are reassuring, as they suggest that the most likely explanation for the observations is random chance. These analyses do not prove absolutely that there is no issue in the community, but the information does not lead us to believe there is a specific environmental factor or concern causing cancer in Andover. A further in-depth cluster investigation is not warranted at this time.

DHHS relies on the quality of the NHSCR data to conduct descriptive epidemiological analyses for the SIR calculations and we believe the quality of NH cancer data is very high. It should be noted that the SIR analyses performed were descriptive in nature and were not an in-depth epidemiological study involving personal interviews about cancer risk factors. While SIR approach has limitations, it is a satisfactory public health assessment in that it can determine whether a further epidemiological investigation (in depth cancer cluster investigation) is warranted.

There are few contaminants present in NH water that have the potential to cause cancer. People can learn about their water quality and level of contamination by requesting the consumer report from the Andover Village Water District. This is a standard annual report for all people receiving water from the system. Arsenic, radio-active substances, and a few other chemicals involved with by-products of disinfection processes are key contaminants to look at on the report. We found that since 1989, the Drinking Water & Groundwater Bureau of the NH Department of Environmental Services had not issued any violations for any Safe Drinking Water Act chemical maximum contaminant level (MCL) exceedance to the Andover Village Water District.

The ability of water contaminants to cause cancer is dependent on the types, amounts and nature of the chemicals present and their relationship to an exposed individual's cells. The degree of cancer hazard, as defined in a toxicological sense, is dependent on the concentration of a contaminant, the intensity and the duration of the exposure that a person receives. These factors are important issues in the etiology of cancer. Environmental factors are often implicated as the primary or contributing cause of cancer, however very few have been proven to be the cause of cancer. In fact only 1% to 4% of all cancer mortality can be attributed to environmental factors or pollution, while approximately 75% can be accounted for by personal behavior or lifestyle choices.<sup>4</sup> Current scientific research does not provide an absolute means of separating the effects of factors such as: heredity, gender, hormonal influences, natural occurring carcinogens in plants and animals, synthetic carcinogens, sexual habits and reproductive systems, personal lifestyle,

<sup>&</sup>lt;sup>4</sup> McKinnell Robert et al. <u>The Biological Basis of Cancer</u>. Cambridge University Press 1998. pgs. 79-114.

and a whole host of other factors associated with human cancers; from each other in order to pinpoint one cause of cancer.

It is unfortunate when any adult or child develops cancer, regardless of data and statistics, and we appreciate when this concern is brought to our attention.

## **RECOMMENDATIONS:**

The State of NH Department of Health and Human Services will disseminate the results of this analysis to the concerned citizens of Andover. We will offer consultation regarding any potential surveillance activities and act as a clearinghouse for health education information to the citizens of Andover. It is our recommendation that the citizens of Andover continue to try to reduce their chances of developing cancer by following the main prevention guidelines issued by the American Cancer Society. In general, those guidelines include:

Cessation of tobacco use. Reduction of excessive alcohol use. Limited or protected exposure to sunlight. Increasing physical activities. Practicing good nutritional habits. Preventing infection from sexually transmitted diseases. Self-examinations for cancers of the breast and skin.

For more information on cancer or prevention recommendations discussed in this section please contact the following organizations:

National Cancer Institute http://www.cancer.gov/

American Cancer Society http://www.cancer.org/

CDC: Centers for Disease Control and Prevention http://www.cdc.gov/cancer

Cancer Cluster information:

http://www.cancer.gov/cancertopics/factsheet/Risk/clusters

#### Breast Cancer Rates, Andover Town

At the Andover community meeting on October 22, 2014, the data were presented from DHHS inquiries, which showed no evidence of an increased risk of cancer overall, or of invasive breast cancer during 2005-11. Despite the data, there remained some concern among attendees at the meeting who reported knowing many Andover residents who had been diagnosed with breast cancer. Among the discussion, two specific questions arose.

## 1. Why were data restricted to 2005-2011?

The data were initially restricted to a limited, recent time period in order to identify any recent cluster associated with some change in environmental exposure. We have now also considered conducting our analyses for the earlier period for which we have cancer registry data (1995-2004), but we were not able to obtain reliable town population data by age group. Therefore our analyses are necessarily restricted to 2005 forward. We also recognize that women diagnosed before 2005 may be doing well with treatment, and so the numbers of women living with breast cancer in Andover ("prevalent cases") may contribute to an impression of a substantial burden of breast cancer in the community.

## 2. Why were in situ breast cancers excluded from the analysis?

By convention, "in situ" breast cancers are excluded from these types of analyses and from cancer incidence reports because they are not invasive cancers, and there is controversy over their meaning. Many in situ lesions never progress to breast cancer, but they cause a lot of anxiety and may be treated with lumpectomy/radiation. About 80% of ductal carcinoma in situ (DCIS) cases are diagnosed through mammography because there is usually no lump or pain that would lead to diagnosis at that stage without a mammogram. A corollary of this may be that in a health-conscious community, which values screening mammography, we could expect higher rates of in situ cases.

	Expected	Observed	SIR	Lower CL	Upper CL
Invasive	13	12	0.91	0.47	1.60
In situ	4	7	1.88	0.75	3.88
All breast cancer	17	19	1.13	0.68	1.76

Breast cancer, 2005-2011

Interpretation:

- a) Andover's rate of invasive breast cancers was 9% lower than expected (SIR=0.91) but the SIR was not statistically significant.
- b) Andover's rate of in situ breast cancers was 88% higher than expected, but again the SIR was not statistically significant and there is a wide confidence interval.

Although it is possible that an environmental exposure could specifically increase only the in situ cancers, it seems more likely that such an exposure would increase all stages of breast cancer, and we do not see such an increase. Our interpretation is that the most likely explanations for these SIR results are random variation ("chance"), and/or a high use of mammography leading to more "in situ" diagnoses.

#### 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) is 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 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. An SIR of 1 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 1 indicates that more cancer cases occurred than expected and an SIR less than 1 indicates that fewer cancer cases occurred than expected. Accordingly, an SIR of 1.50 is interpreted as 50% more cases than the expected number; an SIR of 0.90 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 1.5 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 1.5 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 1, 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 1 and the interval is above 1 (e.g., 1.05-1.30), then there is statistically significant excess in the number of cancer cases. Similarly, if the confidence interval does not include 1 and the interval is below 1 (e.g., 0.45-0.96), then the number of cancer cases is statistically significantly lower than expected. If the confidence interval range includes 1, then the true SIR may be 1, 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.

<u>Statistical significance is not assessed when fewer than five cases are observed.</u> 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., 1.03-1.15) allows a fair level of certainty that the calculated SIR is close to the true SIR for the population. A wide interval (e.g., 0.55-4.50) 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.

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Source: Massachusetts Department of Public Health, Bureau of Environmental Health Assessment (2008)