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**Assessment of the Occurrence of Thyroid Cancer in
Iredell County and ZIP Codes 28115 and 28117
North Carolina**

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**Prepared by the
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Summary of the Investigation

In March 2018, the Iredell County Health Director requested North Carolina Central Cancer Registry (CCR) to assess the thyroid cancer incidence in Iredell County because the 5-year (2011-2015) age-adjusted incidence rates of thyroid cancers were statistically significantly greater than the state rates. Additional analyses were conducted by eight ZIP Codes in the county and found that most of the cases lived in the two ZIP Codes 28115 and 28117 at the time of diagnosis. Due to ongoing community concerns, a follow-up assessment was requested to determine whether the observed number of thyroid cancer cases was statistically significantly greater than expected in the specific ZIP Codes (28115 & 28117). The CCR followed the Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) 2013 guidelines¹ and CCR protocol to investigate the occurrence of thyroid cancer in the two ZIP Codes of concern.

To evaluate the occurrence of cancer in the concerned ZIP Codes, Standardized Incidence Ratios (SIRs) were calculated to compare the number of observed cancer cases to what would be expected in the two ZIP Codes, based on the cancer rates in North Carolina. The SIRs were calculated as the number of observed cases divided by the number of expected cases for the 22-year period (1995-2016) and for the five-year period (2012-2016). A 95 percent confidence interval (CI) was calculated for each SIR to determine statistical significance.

The 95 percent CI indicates that the “true” value of the SIR would be within the interval 95 percent of the time if this population was sampled 100 times. The CI is provided to illustrate how precise an estimate is; the wider the CI, the less precise the estimate and the more the estimate could vary. CI is calculated to indicate whether the SIR is statistically significant, i.e., the upper and lower bound does not include the value of one.

Based on the SIR analyses, the number of observed thyroid cancer cases in Iredell County and the two ZIP Codes were statistically significantly greater than expected. This investigation cannot be used to determine the cause of the observed cancers or identify possible associations with any risk factors. Therefore, these results are shared with the Occupational and Environmental Epidemiology Branch (OEEB) for review and to assess the feasibility of next steps.

Background

In March 2018, the Iredell County Health Director requested North Carolina Central Cancer Registry (CCR) to assess the thyroid cancer incidence in Iredell County because the 5-year (2011-2015) age-adjusted incidence rates of thyroid cancers were statistically significantly greater than the state rates. Additional analyses were conducted by eight ZIP Codes in the county and found that most of the cases were diagnosed in the two ZIP Codes 28115 and 28117. Due to ongoing community concerns, a follow-up assessment was requested to determine whether the observed number of cancer cases was statistically significantly greater than expected in the specific ZIP Codes (28115 & 28117).

The Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) define a cancer cluster as a greater than expected number of cancer cases that occurs within a group of people in a geographic area over a defined period of time¹. For the assessment described here, CCR followed the CDC and CSTE 2013 Guidelines for Investigating Suspected Cancer Clusters and Responding to Community Concerns¹ to investigate the occurrence of cancer in this community.

The CDC and CSTE guidelines include four steps¹. The first step is to collect information about the community's concerns. The second step, reported here, is to determine whether the observed number of cancer cases is statistically significantly greater than expected. It is important to note that the data and statistical analysis conducted at this step cannot determine if cancers observed in the community are associated with specific environmental, lifestyle, or other risk factors.

The guidelines also provide additional steps that can be followed when appropriate. The third step is to evaluate the feasibility of performing an epidemiologic study to examine if exposure to a specific risk factor is associated with the suspected cancer cluster, and the fourth step is to conduct an epidemiologic study, if deemed feasible in step three. Many factors are considered in making the determination to progress to steps three or four. The CDC and CSTE guidelines state, "only a small fraction of cancer cluster inquiries might meet the statistical and etiological criteria to support a cluster investigation through all the steps outlined..."¹

Methods

This document outlines the results from step two of the CDC and CSTE guidelines, and only addresses the question, "is there a statistically significant excess of cancer in the area of concern?"

Data used for this investigation were based on cases diagnosed during (1995–2016) and reported to the North Carolina CCR as of May 2018 for patients whose address at the time of diagnosis was in Iredell County, North Carolina. Cases were selected based on diagnosis codes as reflected in the pathology and medical reports reported from the hospitals and facilities. Further, cases diagnosed out of the state and country but that may be receiving treatment in facilities in North Carolina were not included as they are not required to be reported to the CCR. All cancer diagnosis and first course of treatment information from hospitals and other facilities are reported to the CCR at least six months after the diagnosis.

The reason for this is that N.C. General Statute 130A-209 requires facilities to report complete first course of treatment data and many cases have an extended period of first course of treatment. The patient may have surgery, followed by multiple courses of chemotherapy, followed by radiation therapy. In order to obtain complete and accurate data from the facilities there is a lag time of at least six months. For some cases, CCR receives multiple reports from different facilities, which are reviewed and consolidated on an ongoing basis. Hospitals and facilities continue to report cancer cases diagnosed in 2016, 2017 and prior years. Therefore, there may be cases diagnosed in 2016 that have not been reported and included in this report.

Selection Criteria

Observed cases of thyroid cancer selected for this investigation were diagnosed between 1995 and 2016 in Iredell County and specifically in ZIP codes 28115 and 28117 in North Carolina. In this investigation, the cancer cases were identified based on geocoding of the patients address at the time of diagnosis. According to the International Classification of Diseases for Oncology, 3rd edition (ICD-O3), thyroid cancer is defined as primary site C739. This study excluded histology codes 9050-9055, 9140, and 9590-9992 and included the following histology codes for the four types of thyroid cancer:

- *Papillary* – 8050, 8051, 8052, 8130, 8260, 8340, 8341, 8342, 8343, 8344, 8350, 8540.
- *Follicular* – 8290, 8330, 8331, 8332, 8335, 8337.
- *Medullary* – 8345, 8346, 8347, 8510.
- *Anaplastic* – 8020, 8021, 8032.

Estimation of Expected Thyroid Cases

To estimate the expected number of thyroid cases for Iredell County and in the ZIP codes 28115 and 28117 in North Carolina, (1995 to 2016) and (2012 to 2016) age-specific (in 10-year intervals) incidence rates for thyroid cancer were used. For Iredell County and the two ZIP codes, the denominator population of the study area was based on the U.S. 2000 and 2010 Census populations for each age group multiplied by the time-period of the study. Per CDC's recommendations, county and ZIP code level data were used to calculate Standard Incidence Ratios (SIR). To delineate the study area, E911 address points were linked to the USPS ZIP+4 database⁵ and assigned ZIP codes based on that linkage (linkage rate 97%). The distribution of these address points was compared to ZIP code area boundaries for 28115 and 28117 drawn by data vendors. For various reasons these boundaries follow closely, but not perfectly, the distribution of the address points that were assigned 28115 or 28117 by USPS. These two sources were used to delineate the study areas (28115, 28117). Census block groups³ were identified that wholly or partially intersected the study areas.

For the 22-year study, we intersected 29 Census 2000 and 44 spatially corresponding Census 2010 block groups that also were contained within or intersected by the boundaries of the study areas. For block groups that were intersected in this process, the proportion of their area within the study areas was calculated relative to their original area. The number of people living in the area over the 22-year span, for partial block groups, was estimated by applying the proportion of the block group included in the study areas to the average number of people living in the block groups as reported by the 2000 and 2010 Censuses⁴.

For block groups not intersected, whole cohorts were used to estimate expected population. Partial and whole cohorts were multiplied by 22 to generate expected population years.

For the 5-year study, we intersected 44 Census 2010 block groups that were contained within or intersected by the boundaries of the study areas, with those boundaries. For block groups that were intersected in this process, the proportion of their area within the study areas was calculated relative to their original area. The number of people living in the area over the 5-year span, for partial block groups, was estimated by applying the proportion of the block group included in the study areas to the number of people living in those block groups as reported by the 2010 Census. For block groups not intersected, whole cohorts were used to estimate expected population. Partial and whole cohorts were multiplied by 5 to generate expected population years.

Statistical Analysis

The SIRs and the 95% confidence intervals (CI) were calculated² to determine if a statistically significant excess of cancer existed in the area investigated, the number of observed cancer cases was compared to what would be expected for the area based on cancer rates in North Carolina. Characteristics such as race, sex, and age are closely related to cancer. To ensure that differences between the numbers of observed and expected cancer cases are not simply due to differences in these demographic characteristics, the expected numbers of cancer cases were calculated by multiplying the age, sex, and race-specific cancer incidence rates of North Carolina residents (reference population) by the number of people in the corresponding demographic groups in the area of investigation.

The SIR is the number of observed cases compared to (divided by) the number of expected cases for each cancer type. A SIR greater than 1.00 indicates that the observed number of cases of a specific cancer type is higher than expected and a SIR less than 1.00 indicates that the observed number of cases of a specific cancer type is lower than expected.

The 95% CI indicates that the “true” value of the SIR would be within the interval 95 percent of the time if this population was sampled 100 times. The CI is provided to illustrate how precise an estimate is; the wider the CI, the less precise the estimate and the more the estimate could vary. CI is calculated to indicate whether the SIR is statistically significant, i.e., the upper and lower bound does not include the value of one.

Rarely, communities will have the same rate as the average state rate for a similar population; most will be higher or lower. Therefore, 95 percent confidence intervals (CI) were calculated for the SIRs to determine if the observed number of cases was statistically significantly different than expected. If a 95 percent CI (range) includes 1.00, no statistically significant excess (or reduction) of cancer is indicated. If a 95 percent CI does not contain 1.00, the SIR is outside the expected range and is statistically significant. When using a 95 percent CI, 5 percent of SIR values calculated is expected to be statistically significantly higher or lower than the state average due to chance alone.

In all cases, when results are described as significant or not significant, CCR is referring only to statistical significance, with the understanding that all cases of cancer have specific

causes (most of the time the specific cause is unknown) and are significant to the individual, the family, and friends of the individuals who are affected.

Results

During 1995-2016, there were 475 cases of thyroid cancer diagnosed in Iredell county, 120 cases diagnosed in ZIP code 28115, and 140 cases diagnosed in ZIP code 28117 (Table 1.). From 2012-2016, there were 191 cases of thyroid cancer diagnosed in Iredell county, 43 cases diagnosed in ZIP code 28115, and 67 cases diagnosed in ZIP code 28117 (Table 2.). About 88% of these cases were diagnosed as papillary cancer (histology codes 8260 & 8340).

Table 1. Observed and Expected Thyroid Cancer Cases, 1995-2016				
	Observed	Expected	SIR	95% C.I.
Iredell County	475	307	1.5	(1.4-1.7)
ZIP code 28115	120	64	1.9	(1.6-2.2)
ZIP code 28117	140	60	2.3	(2.0-2.8)

Table 2. Observed and Expected Thyroid Cancer Cases, 2012-2016				
	Observed	Expected	SIR	95% C.I.
Iredell County	191	111	1.7	(1.5-2.0)
ZIP code 28115	43	23	1.9	(1.4-2.5)
ZIP code 28117	67	23	2.9	(2.3-3.7)

The SIRs for each study area and time-period was greater than one, indicating that the incidence of thyroid cancer between (1995-2016) and (2012-2016) in each study area were higher than expected. The observed number of cases for Iredell county for the 22-year period was 1.5 times the expected number of cases. The observed number of cases was 1.7 times the expected during the 5-year period. In the 28115 ZIP code, the observed number of cases were almost 2 times the number of expected cases during 1995-2016 and 2012-2016 diagnosis years. The observed number of cases in the ZIP code 28117 was more than double the number of expected cases during 1995-2016 and 3-times more during 2012-2016 diagnosis years. The confidence intervals further confirmed that the observed number of cases for thyroid cancer were significantly higher than the expected number of cases for each study area as the lower bound of each confidence interval was greater than one.

Discussion

Consistent with the second step of the CDC and CSTE guidelines for investigating suspected cancer clusters, the primary purpose of this step assessment was to determine whether the observed number of cases is statistically significantly greater than expected¹. It is not intended to determine the cause of the observed cancers or identify possible associations with any risk factors.

The assessment step in a cancer cluster investigation has several inherent limitations, and results should be interpreted with these limitations in mind. Cancer is not a single disease, but rather many different diseases. Different types of cancers vary in etiologies (causes or origins) and may not share the same predisposing factors. Cancers may be associated with a variety of factors such as genetics, lifestyle, and socioeconomic status. Because cancer is common, cases might appear to occur with alarming frequencies within a community even when the number of cases is within the expected rate for the population.

One of the major limitations of this study is that the CCR does not have individuals' histories of residential addresses or occupations. As people move, it becomes more difficult to determine whether living in the area of investigation is associated with an excess of cancers, because residential history is not tracked. Therefore, cases are not included in this investigation if the individuals had previously lived in these areas but not at the time of diagnosis. Further, latency (the time period elapsed between exposure and the onset of illness) adds to the complexity of this step in the investigation. For most adult cancers, a period of over 10 years can elapse between the beginning of an exposure to a cancer-causing agent and the development of a clinically diagnosable case of cancer. Another limitation is that all cases diagnosed in 2016 may not be included due to the lag time in reporting. These cases are included in this assessment but their relevant exposure window might have occurred before moving to the area. It is also possible that new people have moved into the area and then were diagnosed with cancer (they may already have developed cancer but not presented clinically until moving to Iredell County); these cases are included in this assessment. Lastly, the population of the study area is not available on a yearly basis. The population is based on the 2000 and 2010 Census for the 22-year study, and on the 2010 Census for the 5-year study. The estimation of expected cases is based on the assumption that the population is static over 22 years. Therefore, if the population has changed overtime, the results from this investigation should be used with caution.

Conclusions

The standard incidence ratios were estimated for thyroid cancer to investigate whether the incidence of this cancer was unusually high in each study area between (1995-2016) between (2012-2016). The result of the analysis found greater than expected numbers of thyroid cases in each study area during both time periods.

These results are shared with the North Carolina Office of Environmental and Epidemiology Branch (OEEB) for review and to assess the feasibility of next steps.

References

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