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**Assessment of the Occurrence of Papillary Thyroid Cancer in
Southeastern and Southwestern Regions of Iredell County, North Carolina**

An Update

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**Prepared by the
North Carolina Central Cancer Registry
State Center for Health Statistics
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Summary of the Investigation

In July 2021, the Iredell County Health Director requested North Carolina Central Cancer Registry (CCR) for an updated report on papillary thyroid cancer incidence in Iredell County and the two areas of concern. This report has been updated to include papillary thyroid cancer cases reported to the NCCCR as of October 2021, in Iredell County and the two sub-county regions, Southeastern and Southwestern Iredell, which are consistent with the two 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 of interest, Standardized Incidence Ratios (SIRs) were calculated to compare the number of observed cancer cases to what would be expected in the Southeastern and Southwestern Iredell, 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 25-year period (1995-2019) and for four five-year time periods (2000-2004), (2005-2009), (2010-2014) and (2015-2019) with most recently available data. 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. For a statistically significant SIR, the upper and lower bound of the CI does not include 1.0.

Based on the SIR analyses, the number of observed thyroid cancer cases in Iredell County and in the Southeastern and Southwestern Iredell 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. Since the community has previously expressed concern about environmental hazards, these results will be shared with the Occupational and Environmental Epidemiology Branch (OEEB) for review and to advise on 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). In July 2021, the Iredell County Health Director requested that North Carolina Central Cancer Registry (CCR) provide an updated report on papillary thyroid cancer incidence in Iredell

County and the two ZIP Codes. This report has been updated to include papillary thyroid cancer cases reported to the NCCCR as of October 2021, in Iredell County and the two sub-county regions, Southeastern and Southwestern Iredell, which approximate these two 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, based on the information gathered in the first and second steps. 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 (1995–2019) and reported to the North Carolina CCR as of October 2021 for patients whose residential 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 2019, 2020, 2021 and prior years. Therefore, there may be cases diagnosed in 2019 that have not been reported and included in this report.

Selection Criteria

Observed cases of papillary thyroid cancer selected for this investigation were diagnosed between 1995 and 2019 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' residential address at the time of diagnosis, with additional address validation undertaken to maximize the number of addresses matched to street level or better. According to the International Classification of Diseases for Oncology, 3rd edition (ICD-O3), thyroid cancer is defined as primary site C739. This study only included papillary thyroid cancer with the histology codes listed below. *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 papillary thyroid cases for Iredell County and for ZIP Codes 28115 and 28117 in North Carolina, (1995 to 2019) and the four five-year time periods from (2000 to 2019), 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 create regions for sub-county analysis, Iredell County census block group³ areas (2010) were assigned to 4 regions (North, Central, Southwest, Southeast) for which the 2010 expected populations are as evenly distributed as possible among the regions. This ensures that cancer rates for each region are comparable as possible to other regions. In addition, other criteria were used to delineate the regions, including an attempt to approximate the ZIP code area boundary between 28117 and 28115 with the census block group boundaries. To achieve this objective, Iredell E911 address points were linked to the USPS ZIP+4 database⁵ and assigned ZIP codes (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 vendor boundaries follow closely, but not perfectly, the distribution of the address points that were assigned 28115 or 28117 by USPS.

For the 25-year study, Census block groups were selected by an overlay of the study area boundary. The overlay results in 29 Census 2000 block groups and 44 Census 2010 block groups completely within or intersected by the study area boundary. For block groups that were intersected in this process, the proportion of their area within the study boundary was calculated relative to their original area. The number of people living in the area over the 25-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 25 to generate expected population years.

For the (2000-2004) the estimated population was based on Census 2000 and for these time periods, (2005-2009), (2010-2014) and (2015-2019), the estimated population was based on Census 2010.

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 investigation area.

The SIR is the number of observed cases compared to (divided by) the number of expected cases for each cancer type. An 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 personally significant to the individual, the family, and friends of the individuals who are affected.

Results

During (1995-2019), there were 511 cases of papillary thyroid cancer diagnosed in Iredell County, 151 cases diagnosed in Southeastern Iredell, and 168 cases diagnosed in Southwestern Iredell (Table 1). From (2015-2019), there were 159 cases of papillary thyroid cancer diagnosed in Iredell County, 44 cases diagnosed in Southeastern Iredell, and 57 cases diagnosed in Southwestern Iredell (Table 2). From (2010-2014), there were 182 cases of papillary thyroid cancer diagnosed in Iredell County, 65 cases diagnosed in Southeastern Iredell, and 51 cases diagnosed in Southwestern Iredell (Table 3). During (2005-2009), there were 112 cases of papillary thyroid cancer diagnosed in Iredell County, 30 cases diagnosed in Southeastern Iredell, and 36 cases diagnosed in Southwestern Iredell (Table 4). From (2000-2004), there were 37 cases of papillary thyroid cancer diagnosed in Iredell County, 9 cases in Southeastern Iredell, and 10 cases diagnosed in Southwestern Iredell (Table 5).

Table 1. Observed and Expected Papillary Thyroid Cases (1995 - 2019)				
	Observed	Expected	SIR	95% C.I.
Southeastern Iredell	151	68	2.2	(1.88-2.60)
Southwestern Iredell	168	71	2.4	(2.02-2.75)
Iredell County	511	317	1.6	(1.48-1.76)

Table 2. Observed and Expected Papillary Thyroid Cases (2015 - 2019)				
	Observed	Expected	SIR	95% C.I.
Southeastern Iredell	44	23	1.9	(1.39-2.57)
Southwestern Iredell	57	23	2.5	(1.88-3.21)
Iredell County	159	93	1.7	(1.45-2.00)

Table 5. Observed and Expected Papillary Thyroid Cases (2010 - 2014)				
	Observed	Expected	SIR	95% C.I.
Southeastern Iredell	65	24	2.7	(2.09-3.45)
Southwestern Iredell	51	25	2.0	(1.52-2.68)
Iredell County	182	98	1.9	(1.60-2.15)

Table 4. Observed and Expected Papillary Thyroid Cases (2005 - 2009)				
	Observed	Expected	SIR	95% C.I.
Southeastern Iredell	30	19	1.6	(1.07-2.25)
Southwestern Iredell	36	20	1.8	(1.26-2.49)
Iredell County	112	79	1.4	(1.17-1.71)

Table 3. Observed and Expected Papillary Thyroid Cases (2000 - 2004)				
	Observed	Expected	SIR	95% C.I.
Southeastern Iredell	9	6	1.5	(0.69-2.85)
Southwestern Iredell	10	7	1.4	(0.69-2.63)
Iredell County	37	32	1.2	(0.81-1.59)

The SIRs for each study area and time-period were greater than one, indicating that the incidence of papillary thyroid cancer between (1995-2019) and in each study area and time-period were higher than expected. The observed number of cases for Iredell County for the 25-year period was 1.6 times the expected number of cases. The observed number of cases was 1.7 times the expected during the (2015-2019) time-period. For (2010-2014), the observed number of cases for Iredell County was 1.9 times the expected number of cases. For (2005-2009) and (2000-2004), the observed number of cases for Iredell County was 1.4 times and 1.2 times the expected number of cases respectively. The observed number of cases in Southeastern Iredell and Southwestern Iredell was more than double the number of expected cases during (1995-2019). For (2015-2019), the observed number of cases in Southeastern Iredell was almost 2 times the expected number of cases and in Southwestern Iredell the observed number of cases were more than double the number of expected cases. During (2010-2014), the observed number of cases in Southeastern Iredell was more than double the number of expected cases and the observed number of cases in Southwestern Iredell was two times the number of expected cases. For (2005-2009), the observed number of cases in Southeastern Iredell was 1.6 times the expected number of cases and in Southwestern Iredell, it was 1.8 times the expected number. For (2000-2004), the observed number of cases in Southeastern Iredell was 1.5 times the expected number of cases and in Southwestern Iredell, it was 1.4 times the expected number of cases. The confidence intervals confirmed that the observed number of cases for papillary 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 for all time periods except (2000-2004).

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 during the relevant exposure period for papillary thyroid cancer. 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. Thyroid cancer rates have been increasing statewide, nationally, and globally over recent decades.

During 2011–2015, thyroid cancer was the 13th most commonly diagnosed cancer in the United States and the 14th most commonly diagnosed cancer in North Carolina. According to the American Cancer Society, some of this overall increase may be attributed to more frequent use of thyroid ultrasound during thyroid cancer screenings and higher detection rates. Ultrasound screening can detect smaller thyroid nodules than other technologies have been able to in the past. Recent international studies have suggested that some of these newly found, very small thyroid cancers (known as micro-papillary thyroid cancers) may not need immediate treatment, but instead can be safely observed. Ongoing clinical trials in the US are now looking to confirm the results of these international studies. 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 2019 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 strongest limitation of this analyses is that 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 25-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 25 years. Therefore, since the population has changed over time, the results from this investigation should be used with caution.

Conclusions

The standard incidence ratios were estimated for papillary thyroid cancer to investigate whether the incidence of this cancer was unusually high in each study area between (1995-2019) and for five-year time periods between (2000-2019). The result of the analysis found greater than expected numbers of thyroid cases in Southeastern and Southwestern Iredell County during the time periods included in this report.

This report is an update of the [Iredell County thyroid cancer investigation report](#) previously published in 2019. Since the community has previously expressed concern about environmental hazards, these results will be shared with the Occupational and Environmental Epidemiology Branch (OEEB) for review and to advise on next steps.

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