NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

ROY COOPER • Governor
MANDY COHEN, MD, MPH • Secretary
BETH LOVETTE, MPH, BSN, RN • Acting Director
Division of Public Health

January 25, 2019

MEMORANDUM

TO: Jane Hinson, Director
Iredell Department of Public Health

FROM: Zack Moore, MD, MPH, State Epidemiologist and Epidemiology Section Chief
Chandrika Rao, PhD, Director, NC Central Cancer Registry

RE: Report on Thyroid Cancer in Iredell County, 1995–2016

At the request of your department and citizens of Iredell County, staff with the NC Central Cancer Registry and the Epidemiology Section prepared the attached report on thyroid cancer in your county. The report compares the rate of new diagnoses of thyroid cancer in Iredell County from 1995–2016 to the state as a whole, and then describes which groups are being diagnosed with thyroid cancer. It also summarizes information about known and potential environmental exposures associated with thyroid cancer.

As you are aware, the rate of new thyroid cancer diagnoses in Iredell County was higher than the rate in North Carolina as a whole during 2005–2016, especially in the southeastern and southwestern regions of the county. The rate of new thyroid cancer diagnoses has also increased statewide, nationally and globally over the same time frame.

The reasons for higher rates of thyroid cancer diagnosis in southern Iredell County are not known. Many factors can contribute to local and regional differences in the rates of thyroid cancer diagnosis, such as changes in the population, changes in medical care or screening, or differences in environmental exposures. Radiation is the only environmental exposure that has been clearly linked to thyroid cancer; our review found no evidence of increased exposure to radiation based on routine monitoring of the area around the McGuire Nuclear Site during the past 40 years. Although scientific research has identified several chemicals that may have an association with thyroid cancer, only a comprehensive research study can determine whether exposure to any of these or other factors is directly linked to the rates of thyroid cancer in a specific area.

The health and well-being of all North Carolinians is the highest priority of the NC Department of Health and Human Services and the concerns raised by the citizens and leaders of Iredell County have been heard. The Department, along with other organizations, is working hard to

better understand the higher-than-expected rate of thyroid cancer diagnoses in parts of Iredell County and we will continue to partner and collaborate with you, your department, other local officials and researchers to provide accurate and useful health information.

As you prepare to share this report more broadly, we offer the following recommendations for the public:

- The signs and symptoms of thyroid cancer include a lump or swelling in the neck, trouble breathing or swallowing, pain when swallowing, hoarseness or other voice changes that do not go away, and a constant cough that is not due to a cold. If you experience these signs and symptoms, see your doctor.
- The United States Preventive Services Task Force and the American Cancer Society do not recommend thyroid cancer screening for people who do not have any signs and symptoms.
- We do not have enough information to recommend any specific actions to lower your risk of thyroid cancer. However, we do recommend that private well water owners routinely test their water according to DHHS recommendations to protect themselves and their families against other health effects: https://epi.publichealth.nc.gov/oee/wellwater/whentotest.html.

Should you or your staff have any questions about the report or need additional information, please don't hesitate to contact either of us. We also remain available to you and your staff to help in the development of any communication materials, handouts, etc.

Attachment

cc: Susan Robinson, Iredell County Deputy County Manager
Brady Freeman, Environmental Health Director, Iredell County Public Health Department
Senator Vickie Sawyer
Representative John Fraley
Representative Rena Turner

Thyroid Cancer in Iredell County, North Carolina, 1995–2016

Summary

What is the purpose of this report?
This report was created to provide additional information about thyroid cancer in Iredell County. It compares the rate of new diagnoses of thyroid cancer in Iredell County from 1995–2016 to the state as a whole and describes which groups are being diagnosed with thyroid cancer. The report also summarizes information about known and potential environmental exposures associated with thyroid cancer.

What were the key findings?
The rate of new thyroid cancer diagnoses has increased in Iredell County, statewide, nationally and globally over the past few decades. The rate of thyroid cancer diagnosis in Iredell County was significantly higher than the rate in North Carolina as a whole during 2005–2016. A higher rate was found in the southeastern and southwestern regions when compared with the rest of the county. Age at diagnosis for cases diagnosed in Iredell County was similar to age at diagnosis for cases diagnosed statewide and nationally.

Radiation is the only known environmental exposure that has been clearly linked to thyroid cancer. No evidence of increased exposure to radiation has been identified through routine monitoring of the area around the McGuire Nuclear Site during the past 40 years.

No specific chemicals have been clearly linked to thyroid cancer. However, researchers have published studies in the scientific literature identifying several chemicals with possible association with thyroid cancer, including certain flame retardants, benzene and nitrates.

What do these findings mean?
The reasons for higher rates of thyroid cancer diagnosis in southern Iredell County are not known. Many factors can contribute to local and regional differences in the rates of thyroid cancer diagnosis, such as changes in the population and changes in medical care or screening. These factors were not accounted for in this investigation.

No community-level exposures to radiation were identified. Although several chemicals have possible associations with thyroid cancer, only a comprehensive research study can determine whether exposure to these or other factors might be associated with rates of thyroid cancer diagnosis.

What are the next steps?
The North Carolina Department of Health and Human Services will continue to monitor geographic variations in the occurrence of thyroid cancer and is developing plans to specifically examine the occurrence of thyroid cancer in other areas of North Carolina with incidence rates above the state average. We will continue working with hospitals and clinicians to confirm that all cases of thyroid cancer are being reported to the North Carolina Central Cancer Registry and provide data to researchers and others working to investigate potential causes for thyroid cancer in Iredell and elsewhere in the state.

Background

In February 2018, the North Carolina Department of Health and Human Services (DHHS) Central Cancer Registry (CCR) analyzed thyroid cancer rates in specific zip codes in Iredell County following requests from residents and the local health department. The CCR reported that the number of thyroid cancers diagnosed in Iredell County was significantly higher than the number expected based on rates in the state overall. After further analysis, the CCR identified two zip codes in the county (28115 and 28117) that had higher incidence rates than the rest of the county. In March 2018, DHHS initiated an investigation to further analyze CCR data; began to compile and summarize the scientific literature about trends in thyroid cancer diagnoses and known contaminants associated with thyroid cancer; and initiated our work with partner agencies to identify potential sources of these contaminants in the area.

Methods

Epidemiologic Analysis

Using CCR data, we calculated age-adjusted thyroid cancer incidence rates and 95% confidence intervals (CI) for these rates. An incidence rate is the number of new cases diagnosed in a specified population during a specified period of time. A 95% CI means that we are 95% confident that the true rate lies between the lower bound and upper bound of the CI. CIs are provided to illustrate how precise an estimate is; the wider the CI, the less precise the estimate and the more the estimate could vary.

Incidence rates were calculated for the state of North Carolina, Iredell County, and four geographic regions within Iredell County (northern, central, southeast, and southwest). To calculate incidence rates for the four sub-county-level regions, we combined census block groups into four geographic areas with roughly similar populations (Appendix A). A census block group is a geographical unit used by the United States Census Bureau that is between the census tract and the census block. Typically, census block groups have a population of 600 to 3,000 people (www.census.gov). Incidence rates were calculated for the following time periods: 1995–1999, 2000–2004, 2005–2009, 2010–2014, and 2015–2016 (the two most recent years for which data were available). Rates were calculated using the 2000 census population estimates for 1995–2004 and using the 2010 census population estimates for 2005–2016.

Average age at diagnosis and the proportion (percentage) of thyroid cancer cases by age and sex were calculated for cases diagnosed during the most recent 10 years for which data were available (2007–2016). Age at diagnosis was compared to thyroid cancer cases in the United States using data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program. Age at diagnosis, sex and race of cases diagnosed in Iredell County were also compared with cases diagnosed statewide.

Statistical tests were performed to determine if the average age at diagnosis in Iredell County and certain regions of Iredell County were different from North Carolina and the United States. Similar tests were used to evaluate if sex and race of thyroid cancer cases diagnosed in Iredell and certain regions of Iredell County differed from cases diagnosed statewide. The percent of thyroid cancer cases by age at diagnosis, sex, and race were graphed for all of Iredell County, regions of Iredell County with higher rates than the state rate (southeast and southwest), and North Carolina overall. Statistical significance was defined using 95% confidence intervals. Additional tables and figures from the epidemiologic analysis are located in Appendix B.

We only included one type of thyroid cancer in these analyses (papillary thyroid cancer) since this type is not hereditary, accounted for 85% of diagnoses in North Carolina and 88% of diagnoses in Iredell County during 1995–2016, and has accounted for most of the increase in thyroid cancer diagnoses in recent decades.

Literature Review

We reviewed information from the scientific literature, the American Cancer Society, and the Environmental Protection Agency's Integrated Risk Information System (EPA IRIS),[1] an open source database of chemical agents, to identify national and global trends, risk factors, and exposures potentially associated with thyroid cancer. Association in this context means that a link between exposure to the environmental contaminant and thyroid cancer was found in at least one study. However, finding an association does not confirm that the exposure caused or contributed to development of cancer. DHHS and the N.C. Department of Environmental Quality (DEQ) created a summary table of the chemical agents that have been associated with thyroid cancers in at least one human (epidemiologic) study. Additional information about the literature review can be found in Appendix C.

Assessment of Environmental Exposures

To assess potential community-level exposures to radiation in Iredell County, we reviewed the DHHS Radiation Protection Section's radionuclide monitoring data for the McGuire Nuclear Site, located on Lake Norman, from 1998–2017. The Radiation Protection Section monitors radionuclides (chemical elements that emit radiation), specifically radioactive iodine in cow's milk from one dairy farm located near the McGuire Nuclear Site and radioactive iodine and tritium in surface waters around Lake Norman and the McGuire Nuclear Site. We reviewed the data for any sample results that exceeded the Radiation Protection Services investigative action limits. These limits are based on the Environmental Protection Agency's (EPA) maximum contaminant levels for these radionuclides in different types of samples. For example, surface water investigative limits differ from cow's milk investigative limits.

DHHS is also working with the North Carolina Department of Environmental Quality (DEQ) to identify the limited data available regarding the presence of chemicals in Iredell County that have that have possible associations with thyroid cancer. This included a review of historical monitoring data from 38 community and non-transient non-community (NTNC) public water systems in two zip codes in southern Iredell County (28115 and 28117) to determine whether there were chronic, or long-term, exposures to any of these chemicals at concentrations above existing regulatory levels. Thirty-one of the 38 systems are community water systems that monitor for radionuclides. The remaining 7 systems are considered NTNC. An NTNC public water system is defined as one that regularly supplies water to at least 25 of the same people at least six months per year. Some examples are schools, factories, office buildings, and hospitals which have their own water systems. NTNC public water systems are not required to monitor for radionuclides; however, they do monitor for benzene, atrazine, hexachlorobenzene, nitrate and nitrite.

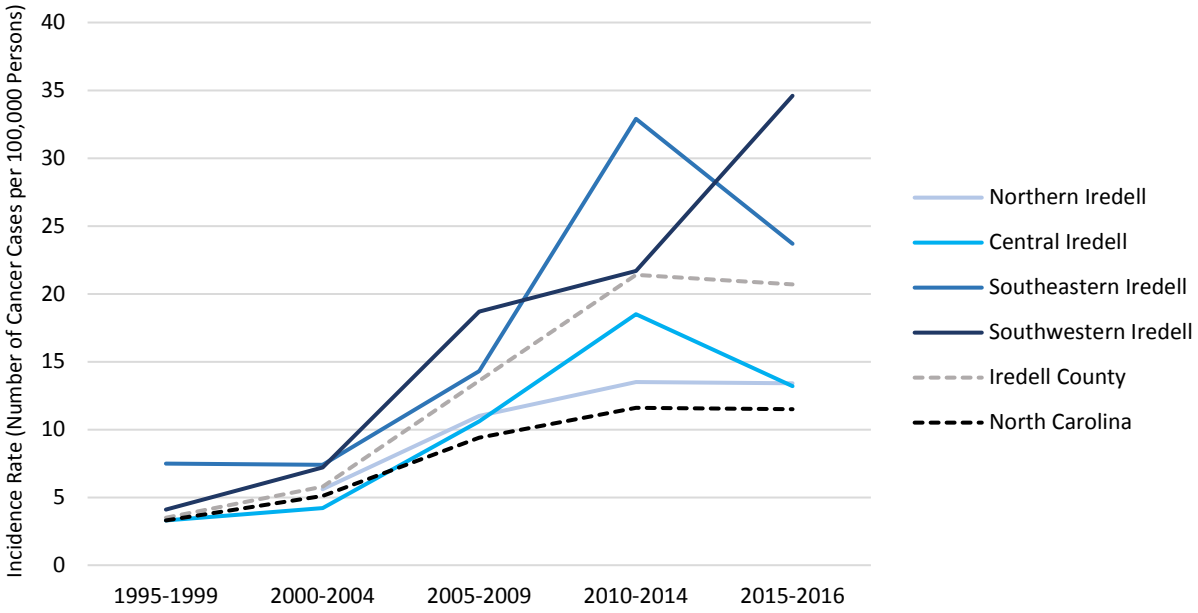
Results

Epidemiologic Analysis

In North Carolina, the age-adjusted incidence rates of papillary thyroid cancer diagnoses increased from 1995 to 2016. The rate of thyroid cancer diagnoses in Iredell County had been similar to the state rate during 1995–2004 but was significantly higher than the state rate beginning in the 2005–2009 time

period. Southeastern and southwestern Iredell had higher age-adjusted incidence rates than other parts of the county during this time period. In the most recent period for which data were available (2015–2016), southwestern Iredell had the highest age-adjusted incidence rate at 34.6 cases per 100,000 persons, meaning that 34.6 new cases of thyroid cancer were diagnosed for every 100,000 persons in the southwest Iredell during this period (Figure 1).

Figure 1. Incidence Rates of Papillary Thyroid Cancer — Iredell County, North Carolina, 1995–2016



During the most recent 5-year period for which data are available (2012–2016), the rate of papillary thyroid cancer diagnosis in North Carolina was 11.6 with a 95% confidence interval (CI) of 11.3 to 11.9 cases per 100,000 persons. The rate in Iredell County was 21.8 with a 95% CI of 18.7 to 25.2 cases per 100,000 persons. Eleven other counties in North Carolina had rates of papillary thyroid cancer diagnosis that were significantly higher than the North Carolina state rate during this time period: Brunswick, Cabarrus, Carteret, Catawba, Durham, New Hanover, Onslow, Pender, Randolph, Rowan, and Watauga.

Based on data available from CDC, the age-adjusted rate for all new thyroid cancer cases in other states ranged from 9.3–20.4 cases per 100,000 persons during a similar time period (2011–2015). The age-adjusted rate for all new thyroid cancer cases in North Carolina during this period was 12.6 cases per 100,000 with rates being higher than North Carolina's in 38 states and lower in 11.[2] Iredell County had a total thyroid cancer rate of 22.1 cases per 100,000 persons during this time period. Nationwide, 94 counties (3% of 3,142 total counties) had age-adjusted incidence rates greater than or equal to 23.0 cases per 100,000 persons during this time period, with the highest reporting a rate of 36.5 cases per 100,000 persons.[2]

The average age at thyroid cancer diagnosis in Iredell County was similar to the average age at diagnosis statewide and nationally except in southwestern Iredell where the average age at diagnosis was slightly higher (Table 1, Table 2, Figure 2, Figure 4). Southwestern Iredell also had a higher percentage of male thyroid cancer cases than the state overall (Table 1, Figure 5). Lastly, a higher percentage of thyroid cancer cases in Iredell County were among white residents compared to the state overall (Table 1,

Figure 6). However, it is important to note that, in 2016, 69% of residents in North Carolina were white, compared to 82% in Iredell County (www.census.gov). Additional epidemiologic data are presented in Appendix B.

Table 1. Characteristics of Papillary Thyroid Cancer Cases in North Carolina, 2007–2016

	Iredell County n=333	Southeast Iredell n=108	Southwest Iredell n=101	North Carolina n=11,058	United States[a]
Age at diagnosis, years					
Average	51.5	49.9	54.2	50.4	51
Sex, %					
Male	24.6	21.3	33.7	24.0	–
Female	75.4	78.7	66.3	76.0	–
Race, %					
White	88.9	85.2	93.1	80.5	–
Other race	11.1	14.8	6.9	19.5	–

Yellow shading indicates estimates that were considered different from North Carolina (statistically significant).

[a] Average age at diagnosis during 2011–2015. National estimates for sex and race were not available for comparison (–).

Literature Review

Thyroid cancer rates have been increasing statewide, nationally and globally over recent decades.[3] 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.[4] 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.[5]

The only known environmental cause of thyroid cancer is ionizing radiation,[6,7] including radiation of the head and neck,[8,9] and exposure to radioactive iodine 129 and 131[10] and radium 226 and 228.[11]

No chemicals have been clearly linked to thyroid cancer. However, limited epidemiologic and toxicological studies have reported possible associations between environmental contaminants and thyroid cancer. The following agents have been associated with thyroid cancer in at least one epidemiologic study:

- Malathion
- Atrazine
- Solvents (used in shoe manufacturing facilities)
- Benzene
- Formaldehyde
- Polybrominated diphenyl ethers (PBDE)
- Tris [2-chloroethyl] phosphate (TCEP)
- Nitrates

- Biocides
- 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)

A summary of the literature review (including a table of the measures of association used) and a list of citations are provided in Appendix C.

During this investigation, DHHS has heard concerns from the community about the possible contribution of other chemicals to rates of thyroid cancer, particularly those related to coal ash. In response to these concerns, DHHS examined the literature for possible links between coal ash and thyroid cancer. Although coal ash can contain radionuclides, there are no published studies to support an association between coal ash exposure and thyroid cancer.

Assessment of Environmental Exposures

During 1998–2017, there were no radionuclide samples (radioactive iodine in surface water and cow's milk and tritium in surface waters) that measured greater than the investigative action limits around the McGuire Nuclear Site. Furthermore, the DHHS Radiation Protection Section reported that no radionuclides have been detected in surface waters, air, and cow's milk beyond investigational limits from the McGuire Nuclear Site during the past 40 years. Historical data may be obtained by visiting the Environmental Surveillance Program's webpage at: http://ncradiation.net/nfers/nfers.htm.

Several of the chemicals identified through the literature review as having been associated with thyroid cancer in at least one epidemiologic study are monitored by DEQ in public water systems. These include atrazine, benzene, nitrate, radium-226, radium-228, and 2,3,7,8-tetrachlorodibenzo-p-dioxin. Data for 2,3,7,8-tetrachlorodibenzo-p-dioxin were only available for 4 of the 31 community water systems in the 28115 and 28117 zip codes due to rules that allow monitoring waivers. Monitoring data from the 38 public water systems (31 community water and 7 non-transient non-community (NTNC) public water systems) in the 28115 and 28117 zip codes identified only one system with an exceedance of a federal maximum contaminant level (MCL) for these chemicals; this system exceeded the MCL for the combination of radium-226 and radium-228 in 1 out of 12 samples during 2005 to 2017. Two of the 31 community public water systems exceeded the MCL for uranium; one site exceeded the MCL in 21 out of 69 samples during 2000 to 2018 and the other exceeded the MCL in 9 out of 32 samples during 2003 to 2018. Uranium has not been linked to thyroid cancer in epidemiologic studies. However, a radioactive daughter product of uranium is radium.[12]

It is important to note that only a comprehensive research study can determine if any environmental exposures are associated with thyroid cancer diagnosis rates in Iredell County.

Conclusions

This report describes increasing rates of thyroid cancer diagnosis in Iredell County. Rates of thyroid cancer diagnosis in Iredell County have been significantly higher than the overall state rate since the 2005–2009 time period, particularly in the southeastern and southwestern regions. Few differences were seen in age, sex and race of people diagnosed with thyroid cancer in Iredell County compared to people diagnosed elsewhere in the state or country.

Radiation is the only established environmental risk factor associated with thyroid cancer. Although no chemical exposures have been definitively linked to thyroid cancer, there is an emerging body of research on environmental contaminants including flame retardants, benzene, nitrates and certain pesticides that may be associated with thyroid cancer risk based on limited data. A review of available

radiation monitoring data and data from public water systems in southern Iredell County identified no radiation releases and very few community-level exposures to concentrations in excess of the relevant regulatory limit or above the level to trigger investigational action for substances potentially associated with thyroid cancer. However, only a comprehensive research study can provide information about whether exposure to these or other factors might be associated with rates of thyroid cancer diagnosis in Iredell County.

Having a higher than expected rate of thyroid cancer diagnoses does not necessarily mean that people living in the community now are at a higher risk of developing cancer. This also does not mean that there will be a common cause identified, such as something in the environment. A greater-than-expected number of cancer cases can occur within a given population without an identifiable cause and might be due to factors such as changes in the population, changes in medical care or screening, or a chance occurrence. Thyroid cancer can be attributed to many recognized and unrecognized risk factors including: a family history of thyroid cancer, certain genetic diseases, a diet low in iodine, history of benign breast disease, obesity, exposure to ionizing radiation (e.g., from medical tests or treatment), and older age at first menstruation.[5] These factors were not accounted for in this investigation and can contribute to geographic variation in the occurrence of thyroid cancer.

There are several other limitations to consider when interpreting the information in this report. Most importantly, this is not a research study. The CCR does not collect detailed information about potential environmental exposures; therefore, no conclusions can be drawn from this report about the association between any environmental contaminant and thyroid cancer. In addition, CCR data are based on the address where the patient lived at the time of diagnosis. The CCR does not collect or track patients' historical residential addresses or occupations. Many years can pass between exposure to a cancer-causing substance and diagnosis with cancer, making it difficult to determine whether residence in the area of investigation is associated with an excess of cancers.

Historically, few investigations of increased cancer rates in a local area have resulted in identification of a specific environmental cause. In a recent review of over 400 cancer cluster investigations in the United States, only three investigations identified a link to an environmental risk factor and only one of these identified a risk factor that was considered a cause of the cancer cluster.[13] Similarly, the CDC reports that, even after thorough investigation of a potential cancer cluster, typically no cause is identified.[14]

DHHS is committed to working with local, state, and university partners to facilitate further investigation. DHHS is also sharing this information with researchers who can use it to conduct studies that can help us better understand the causes of thyroid cancer in North Carolina communities. Moving forward, DHHS will continue to assess geographic variations in the occurrence of thyroid cancer throughout the state and is developing plans to specifically examine other regions of North Carolina with elevated rates of thyroid cancer compared to the state and national rates.

Where Can I Learn More?

For more information about the North Carolina Central Cancer Registry, visit https://schs.dph.ncdhhs.gov/units/ccr/. For more information on thyroid cancer visit https://www.cancer.org/cancer/thyroid-cancer.html

For frequently asked questions on thyroid cancer in Iredell County, visit (https://www.co.iredell.nc.us/DocumentCenter/View/11592/Thyroid-FAQ).

Who Can I Contact if I Have Questions?

For questions about your health, we recommend that you contact your healthcare provider.

For questions about this report, please contact the Occupational and Environmental Epidemiology Branch at (919) 707-5900.

References

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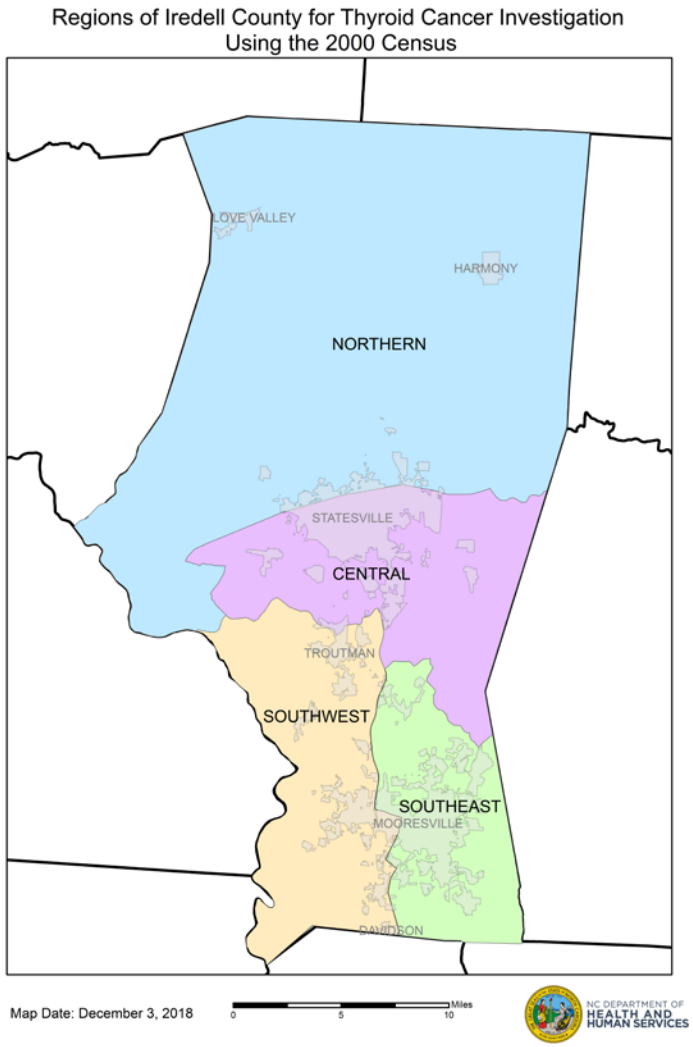
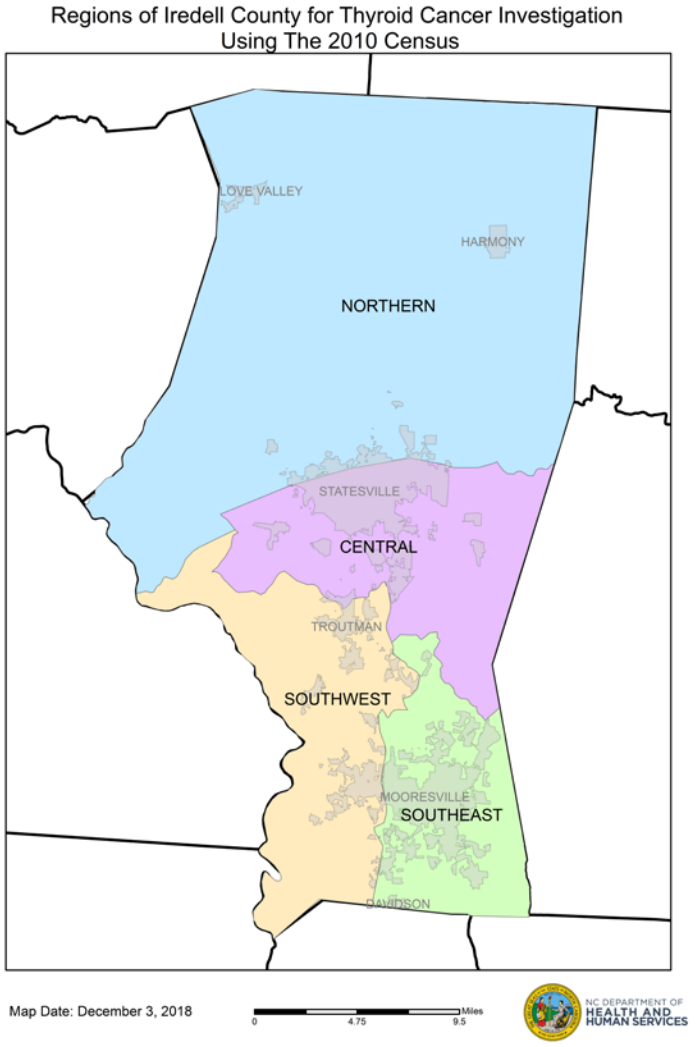
Appendix A: Regions of Iredell County Using 2000 and 2010 Census





Appendix B: Additional Epidemiologic Data

Figure 2. Percent of Papillary Thyroid Cancer Cases by Age Group — Iredell County, North Carolina, 2007–2016

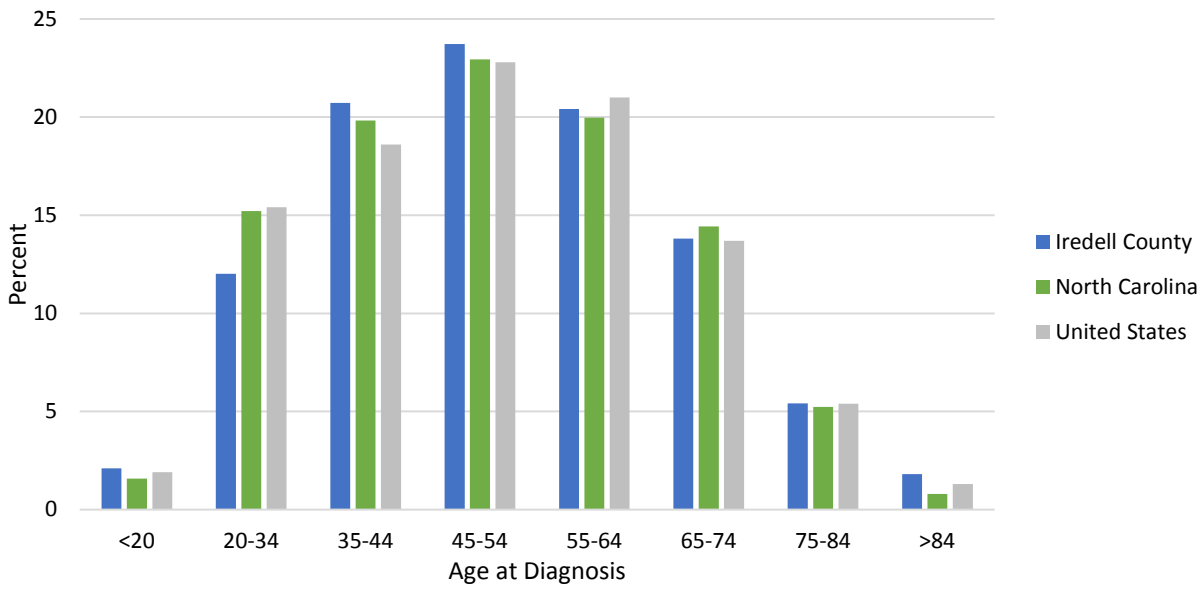


Figure 3. Percent of Papillary Thyroid Cancer Cases by Age Group — Southeastern Iredell, North Carolina, 2007–2016

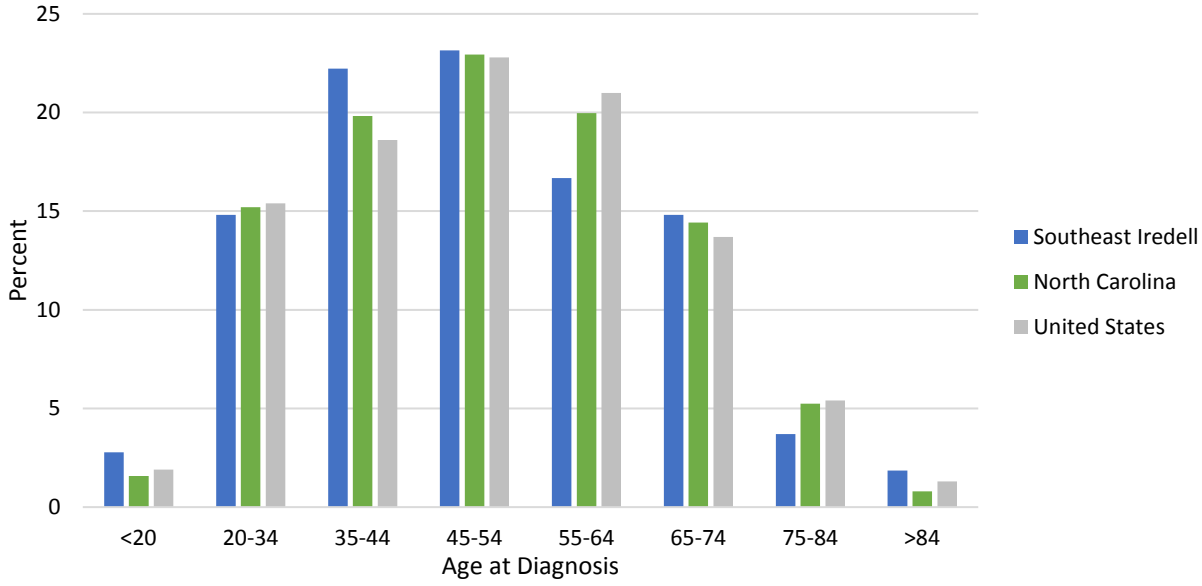


Figure 4. Percent of Papillary Thyroid Cancer Cases by Age Group — Southwestern Iredell, North Carolina, 2007–2016

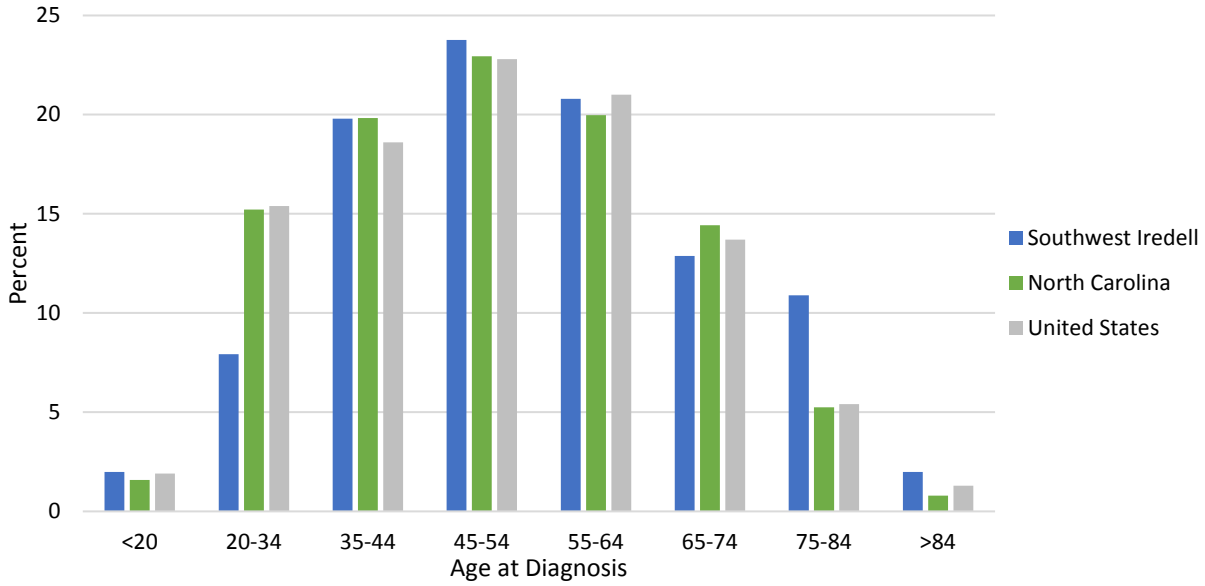


Figure 5. Percent of Papillary Thyroid Cancer Cases by Sex — Iredell County, North Carolina, 2007–2016

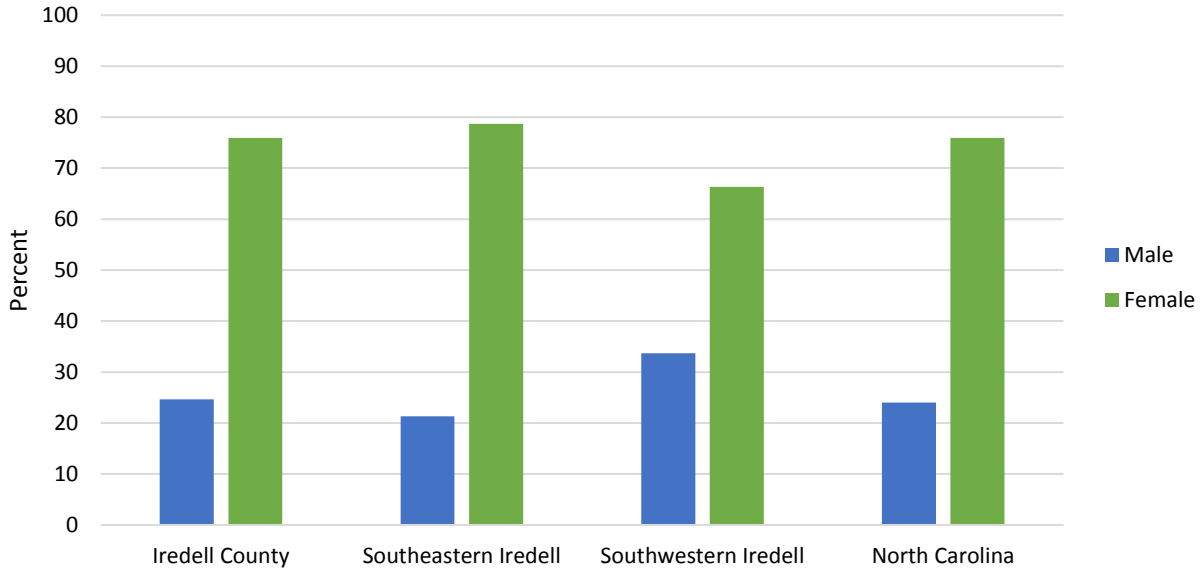


Figure 6. Percent of Papillary Thyroid Cancer Cases by Race — Iredell County, North Carolina, 2007–2016

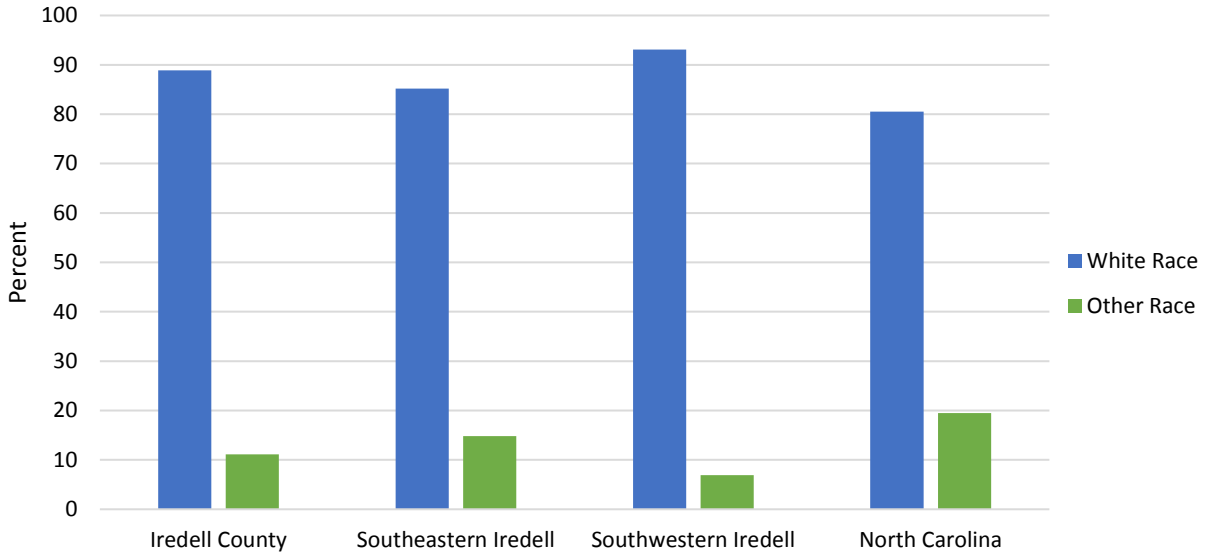


Table 3: Papillary Thyroid Cancer Incidence Rates by Region within Iredell County, 1995–2016

	Thyroid Cancer Cases	Population Estimate	Age-Adjusted Incidence Rate	95% Confidence Interval (Lower, Upper)[a]
		1995–1999[b]		
Northern Iredell	–	175,000	–	–
Central Iredell	6	190,155	3.3	(1.2, 7.0)
Southeastern Iredell	9	124,190	7.5	(3.4, 14.3)
Southwestern Iredell	5	123,955	4.1	(1.3, 10.0)
Iredell County	21	613,300	3.5	(2.1, 5.3)
North Carolina	1,353	40,393,205	3.3	(3.1, 3.5)
		2000–2004[b]		
Northern Iredell	10	175,000	5.6	(2.7, 10.5)
Central Iredell	8	190,155	4.2	(1.8, 8.2)
Southeastern Iredell	9	124,190	7.4	(3.4, 14.1)
Southwestern Iredell	10	123,955	7.2	(3.4, 13.7)
Iredell County	37	613,300	5.8	(4.1, 8.0)
North Carolina	2,094	40,393,205	5.1	(4.9, 5.4)
		2005–2009[c]		
Northern Iredell	23	197,880	11.0	(6.9, 16.7)
Central Iredell	23	200,290	10.6	(6.6, 16.1)
Southeastern Iredell	30	202,965	14.3	(9.7, 20.5)
Southwestern Iredell	36	196,050	18.7	(12.8, 26.4)
Iredell County	112	797,185	13.6	(11.2, 16.4)
North Carolina	4,622	47,677,415	9.4	(9.1, 9.7)
		2010–2014[c]		
Northern Iredell	27	197,880	13.5	(8.8, 19.8)
Central Iredell	39	200,290	18.5	(13, 25.4)
Southeastern Iredell	65	202,965	32.9	(25.3, 42.0)
Southwestern Iredell	49	196,050	21.7	(15.8, 29.1)
Iredell County	180	797,185	21.4	(18.3, 24.8)
North Carolina	5,749	47,677,415	11.6	(11.3, 11.9)
		2015–2016[c]		
Northern Iredell	12	79,152	13.4	(6.8, 24.0)
Central Iredell	11	80,116	13.2	(6.5, 23.9)
Southeastern Iredell	19	81,186	23.7	(14.2, 37.1)
Southwestern Iredell	27	78,420	34.6	(22.2, 51.5)
Iredell County	69	318,874	20.7	(16.1, 26.3)
North Carolina	2,262	19,070,966	11.5	(11.0, 11.9)

Data for number of cases less than 5 are suppressed (–)

[a] 95% confidence interval (CI) means that we are 95% confident that the true rate lies between the lower bound and upper bound of the CI. CIs are provided to illustrate how precise an estimate is; the wider the CI, the less precise the estimate and the more the estimate could vary.

[b] Rates are calculated using the 2000 census population estimates

[c] Rates are calculated using the 2010 census population estimates

Table 4. Age at Diagnosis of Papillary Thyroid Cancer Cases in North Carolina, 2007–2016

	Iredell County n=333	Southeast Iredell n=108	Southwest Iredell n=101	North Carolina n=11,058	United States
Age at diagnosis, %					
<20	2.1	–	–	1.6	1.9
20-34	12.0	14.8	7.9	15.2	15.4
35-44	20.7	22.2	19.8	19.8	18.6
45-54	23.7	23.2	23.8	22.9	22.8
55-64	20.4	16.7	20.8	20.0	21.0
65-74	13.8	14.8	12.9	14.4	13.7
75-84	5.4	–	10.9	5.2	5.4
>84	1.8	–	–	0.8	1.3

Data for counts less than 5 are suppressed (–)

Appendix C: Literature Review

A PubMed search was performed to identify factors associated with thyroid cancer, including environmental exposures. In addition, a search of the Environmental Protection Agency's Integrated Risk Information System (IRIS)[1] database was conducted to identify chemicals potentially associated with endocrine cancers. Chemicals identified in the initial IRIS search were cross-reference with PubMed to determine if any studies documented a link between exposure to these chemicals and higher rates of thyroid cancers in humans. The American Cancer Society website on thyroid cancer was searched to describe causes and risk factors for thyroid cancers.

The American Cancer Society estimates that 53,990 cases of thyroid cancer were diagnosed in the United States in 2018.[5] Thyroid cancer rates are increasing throughout the United States.[3] From 1999-2015, the age-adjusted incidence rate of thyroid cancer in the U.S. increased from 6.8 per 100,000 people to 14.5 per 100,000 people. It is unclear why thyroid cancer incidence has been increasing. One possibility is that increased screening may be detecting small thyroid nodules that might not otherwise have been detected in the past.[3] Thyroid cancer is more common among females and most cases (62%) are diagnosed between ages 35 to 64.[5] The median age at diagnosis is 51 years old.[5] Thyroid cancer is rare in children less than 10 years old.[9]

Causes of thyroid cancer are not completely understood. However, reported risk factors for thyroid cancer[5,6,10,15,16] include:

- being between 25 and 65 years old;
- being female;
- having a family history of thyroid cancer, certain genetic diseases, or having a history of goiter;
- diet low in iodine (this is not typically of concern in the United States because iodine is added to table salt);
- history of benign breast disease;
- obesity; and
- older age at first menstruation.

The only definitive known environmental cause of thyroid cancer is ionizing radiation,[1] including external radiation of the head and neck,[8,9] radioactive iodine 129 and 131,[10] and radium 226 and 228.[11] Exposure to high levels of ionizing radiation, especially during childhood, has been shown to increase the risk for thyroid cancer.[9] Sources of radiation include medical treatments using radium and radioactive iodine, and radiation fallout from power plant accidents or nuclear weapons.[6,7] Additionally, medical diagnostic procedures contribute a large proportion (approximately 50%) to the annual radiation exposure to the population.[6,7,17] In one study, uranium in drinking water was linked to non-cancerous thyroid disease.[12] However, a radioactive daughter product of uranium is radium. No studies have demonstrated an increased risk of thyroid cancers from tritium or radon exposure.[18]

No chemicals have been clearly linked to thyroid cancer. However, some epidemiologic and toxicological studies have reported possible links between environmental contaminants and thyroid cancer based on limited data.[19,20] Environmental exposures which have been associated with human thyroid cancer in one or more epidemiologic studies are shown in Table 2.

Table 2. Chemicals Associated with Thyroid Cancer in Human Studies

Chemical	Sample Size	Measure of Association[a]	Reference
Malathion	30,003	RR=2.04 (CI: 1.14, 3.63)	Lerro et al[21]
Atrazine	36,357 pesticide applicators who used atrazine	RR=4.84 (CI: 1.31, 17.93) highest intensity weighted days of use	Freeman et al[22]
Solvents	1,101,669 female workers	RR=1.91 (CI: 1.05, 3.45)	Lope et al[23]
Benzene	3,317 textile workers	HR=6.43 (CI: 1.08, 38)	Wong et al[24]
Formaldehyde	3,317 textile workers	HR=8.33 (CI: 1.16, 60)	Wong et al[24]
PBDE	140	OR =2.29 (CI: 1.03, 5.08) high vs low exposure	Hoffman et al[25]
TCEP	140	OR=2.42 (CI: 1.10, 5.33)	Hoffman et al[25]
Nitrates	21,977 women on wells or public water	RR=2.59 (CI: 1.09, 6.19) for ≥5 years	Ward et al[26]
Biocides	960	OR=1.67 (CI: 1.15, 2.43)	Zeng et al[27]
TCDD	180,639 Vietnam veterans	HR=2.88 (CI: 1.12, 7.39)	Yi et al[28]

[a]Measure of Association: RR=relative risk, HR=hazard ratio, OR=odds ratio, IR=incidence rate, CI=confidence interval

PBDE: polybrominated diphenyl ethers; TCEP: tris [2-chloroethyl] phosphate; TCDD: 2,3,7,8-Tetrachlorodibenzo-*p*-dioxon

Flame retardants known as polybrominated diphenyl ethers (PBDE) are used to prevent or delay fires in building materials, electronics, furnishings, cars and airplanes, plastics, foams and textiles. Studies in animals have shown that several classes of flame retardants can interfere with thyroid function.[29] A Duke University study found that people living in homes exposed to higher levels of two types of flame retardants, (decabromodiphenyl ether [BDE-209] and tris [2-chloroethyl] phosphate [TCEP]) in household dust were at an increased risk of papillary thyroid cancer compared to those with lower levels of these flame retardants.[25]

While pesticides have been shown to affect the thyroid gland, only a limited number of studies have detected an increase in thyroid cancer in humans associated with certain pesticides, including Malathion and Atrazine.[21,22] The Agricultural Health Study, a prospective study of pesticide exposure among applicators and their spouses in Iowa and North Carolina, found Malathion (an organophosphate) to be associated with thyroid cancer.[21] Additionally, a case-control study of thyroid cancer in Connecticut found that exposure to biocides increases risk of thyroid cancer.[27]

Several occupational epidemiological investigations examining cancer risk from chemical exposures have found elevated risk of thyroid cancer in the leather, wood, pulp or paper making industry, the shoe making industry, and working as a health care worker, janitorial worker, or a textile worker. Potential exposures to benzene, formaldehyde, solvents, and inorganic or organic gases were noted in these workers.[23,24,30,31]

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