Supplemental Cancer Registry Evaluation in Areas Near Terumo BCT, Lakewood, CO (2000-2019)

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Summary

Previous studies

- Since 2000, Terumo BCT has been making medical devices in Lakewood, Colorado. Like other companies that do this work, it uses ethylene oxide to sterilize medical devices.
- Breathing in ethylene oxide at certain levels over many years may increase the risk of certain types of cancers, and it can cause other health impacts.
- In 2018, a study by the Colorado Department of Public Health and Environment (CDPHE) estimated higher cancer risk based on measured and modeled levels of ethylene oxide near Terumo BCT. However, the number of cancer cases from 2000-2017 in the census tract where Terumo BCT is located was not greater than expected.
- In 2022, further analysis by the U.S. EPA predicted elevated cancer risk to community members and proposed additional actions to reduce risk surrounding facilities like Terumo BCT.

Response to community

In response to community requests, the Colorado Central Cancer Registry conducted an expanded evaluation in summer 2023. This study looked at all cancer cases and several types of cancer linked to ethylene oxide. This supplemental evaluation built on the 2018 study by including:

- Two additional census tracts located to the west and north of Terumo BCT.
- Data from two additional years by evaluating cancer cases from 2000 - 2019.

Limited findings of slightly higher number of some types of cancers

This study found slightly higher than expected numbers of some types of cancer, but it is important to note that this kind of analysis cannot determine what caused the cancers. There was variation between the different census tracts, with higher rates in one tract not found in the other two tracts. Some areas had less of certain types of cancers than would be expected. This inconsistency reduces the certainty in these findings. The small increase seen in the rate of a cancer that is both common in our population and is known to have several other risk factors also reduces the certainty. Where seen, the elevated rates found in this study are comparable to many risks found in everyday life. Cancer is not a single disease, but a group of more than 100 different diseases that share some characteristics. Not all people develop the same cancer for the same reason. Each individual has a complex genetic makeup, health history, and other risk factors that interact and can lead to the development of cancer.

Ongoing work to reduce health risks

This study provides additional, though limited, information about potential health risks in this area. Terumo BCT, working with CDPHE, has taken steps to reduce the levels of ethylene oxide in this community. We will continue to support additional reductions, including:

- Oversee measurements at Terumo BCT to verify emissions reductions from additional controls.
- Evaluate how to expand monitoring capabilities in the future to measure ethylene oxide in the community near Terumo.
- Continue to support EPA actions to reduce ethylene oxide emissions and exposures.
- Repeat this study in five years and explore opportunities to support CDC ATSDR's on-going efforts to better understand community exposures near facilities that use ethylene oxide.

View more information about Ethylene oxide and Terumo BCT.

Background

This is a follow-up to a community risk assessment of ethylene oxide near Terumo BCT done in 2018. That study found:

- The levels of ethylene oxide were higher near Terumo BCT than surrounding areas based on measurements and models.
- Predicted cancer risk was elevated near Terumo BCT.
- The number of actual cancer cases from 2000 - 2017 in the census tract where Terumo BCT is located was not greater than in surrounding areas.
- The additional controls Terumo BCT installed in 2018 reduced the levels of ethylene oxide measured in the surrounding community.

In 2022, further analysis by the U.S. EPA predicted elevated cancer risk to community members. EPA has proposed additional actions to reduce risk surrounding facilities like Terumo BCT. Terumo BCT has committed to installing additional controls to reduce ethylene oxide emissions. CDPHE will use measurements of the new controls' efficiency to better understand these impacts.

In response to community concerns, the Colorado Central Cancer Registry conducted an expanded evaluation in spring 2023. In addition to the census tract that includes Terumo (109.02), the evaluation included the tracts immediately west and north of the facility (109.01 and 158) and expanded the number of years to include data from 2000 to 2019 (Figure 1).

This type of evaluation cannot determine the cause of cancer cases. There are many limitations to these types of studies, because:

- We lack information on other risk factors for cancer.
- We don't know how long people who developed cancer lived in this area and how much ethylene oxide they have been exposed to.
- We don't have information about people who moved out of this area before developing cancer.
- It can take many years for cancer to develop.

View more information about Ethylene oxide and Terumo BCT.

Methods

The department conducts ongoing, systematic cancer surveillance across the state to look for trends over time and to find cancer patterns in regions or groups of people. This cancer incidence surveillance is possible using data collected by the Colorado Central Cancer Registry (CCCR). All cancers diagnosed in Colorado are reported to the cancer registry, with the exception of non-melanoma skin cancers, as mandated by Colorado law and Board of Health regulations. This invaluable data allows the department to effectively answer questions about cancer incidence in communities statewide. The CCCR was used to assess the incidence of cancer in the vicinity of the Terumo BCT facility.

The epidemiological study design used in this analysis of diagnosed and expected numbers of cancer cases is descriptive and ecological. The descriptive element provides a numerical summary of disease frequency, whereas the ecological component examines entire communities or populations, rather than individuals. Ecological studies have been conducted frequently in communities adjacent to potential environmental exposures, since they are efficient and can

be completed within a reasonable period of time. Ecological studies are usually viewed as exploratory and may generate hypotheses to be considered in additional studies, if appropriate.

Cancer rates from the cancer registry for men and women of comparable ages were used to calculate the expected number of cancers for the state. A cancer rate is the number of new cancer cases diagnosed per 100,000 population per year. The population in the study area, stratified by gender and age, was multiplied by the cancer rate for each gender and age group in the comparison population to produce the expected number of cancers.

Table 1. Age group specific expected cancer rate calculations and observed counts *

Age Group	Observed Colorado Cases (A)	Colorado Population (B)	Area of Interest Population (C)	Expected Cancer Cases (A / B x C = E)
Age 25-34	220	390000	8000	4.51
Age 35-44	425	375000	7500	8.50
Age 45-54	1250	344000	7500	27.25
Age 55-64	2800	268000	6500	67.91
Age 65-74	3250	163000	4500	89.72
Age 75+	2725	98000	1950	54.22
			Total Expected Cases for Area of Interest	252.12

*This table is for demonstrational purposes and does not contain actual data.

This method assures that any differences found are not due to differences in demographic composition. For example, census tracts with a higher proportion of elderly individuals would be expected to have higher cancer rates since the incidence of most cancers increases dramatically with increasing age.

A diagnosed-to-expected ratio, also referred to as a standardized incidence ratio (SIR), is then calculated by dividing the number of cancers diagnosed in the area by the number of expected cases.

$$SIR = \frac{Observed\ Cancer\ Cases\ (O)}{Expected\ Cancer\ Cases\ (E)}$$

If the ratio is greater than 1, then more cancer cases than expected were reported in the area. When this occurs, the next step is to look more closely at that relationship. It is important to know if that ratio could have been higher by chance alone, so a confidence interval is calculated for the ratio. The confidence interval has a lower number (minimum value) and a higher number (maximum value). It is common to use a 95 percent confidence interval which means that we are 95 percent sure that the true ratio is within the range between the lower and higher values. If the ratio is greater than 1 but the confidence interval includes the number 1, then the ratio is within expected statistical limits. If the confidence interval does not include the number 1, then the ratio is statistically significant. A statistically significant elevated ratio means that there were more diagnosed cases than expected and that there is less than a 5 percent chance that this greater number is due to chance alone. Statistical testing is not done on ratios with less than three diagnosed cases due to variability in small numbers.

Observed cancer cases were defined as all newly diagnosed invasive tumors occurring in individuals residing within the community at the time of diagnosis. All invasive cancers diagnosed between January 1, 2000 and December 31, 2019 were included. Population data was obtained at the census tract level by age and sex from the 2000 decennial census, the 2010 decennial census, and the 2020 American Community Survey (5-year estimates) and averaged over the 20-year study time period.

The following limitations of this ecological, incidence-based registry evaluation must be considered:

- This epidemiological study design used in this analysis of diagnosed and expected number of cancer cases is descriptive and ecological. Information on other potential causes of disease (such as lifestyle behaviors, occupation, genetic predisposition) is lacking.
- This study design does not allow conclusions to be made about causal associations between exposure and any single cancer or group of cancers. The study design and results only aid in determining whether the number of cancers are greater than or less than expected. This may help determine whether future studies would be useful and relevant.
- Population data at the census tract level may contain large margins of error and may not accurately describe the underlying population over the time period. Discrepancies in the underlying population may dramatically impact the expected number of cancer cases.
- The population under study generally is a community or part of a community, leading to a relatively small number of individuals comprising the total population (e.g., small denominator for rate calculations). Small denominators frequently yield wide confidence intervals, meaning that estimates like the SIR may be imprecise.
- The estimates of expected cancers are a central tendency (average) of expected cases for the time period 2000-2019. Actual cancer rates for specific populations, such as in smaller cities, towns or neighborhoods, may be higher or lower than the “average expected” cancer rate.
- The geographical area of residence was used as a substitute measure of exposure. This exposure estimate may raise the likelihood of exposure misclassification, reducing the ability of the study to observe a statistically significant difference between groups.
- For the majority of adult cancers, the long latency period (i.e., the time between exposure to a causal agent and the first appearance of symptoms and signs) complicates attempts to associate cancers occurring at a given time in a community with local environmental contamination. Often decades intervene between the exposures that initiate and promote the cancer process and the development of clinically detectable disease.
- Population mobility, or in and out migration from the community, can affect both the number of observed cancer cases in the area of interest, as well as the underlying population data. Community residents may move out of the area prior to a cancer diagnosis, excluding them from the analysis, or a relatively new resident’s cancer diagnosis may be included despite them not having a similar level of community exposure.

Results

Cancer is a disease common within the general population, and remains at the forefront of public health concern. In Colorado, over 25,000 new cases of cancer are registered each year. On average, Coloradoans have approximately a 1 in 3 risk of developing cancer in their lifetime. Whether an individual develops cancer during his or her lifetime depends on a variety of factors. This complex, multistage, process involves both external (e.g. chemical, radiation, and viruses) and internal factors (e.g., hormonal, immune conditions, and inherited mutations).

Given the frequency with which cancers are diagnosed, situations may arise where an unusual number of primary-site cancers (i.e., place in the body where the cancer started) are diagnosed among people in a particular location. It is possible this may be due to chance. These unusual patterns may also result from the following:

- Differential recommended cancer screening practices
- Access to health care, which may be more reflective of other social and economic factors (e.g., limited access to optimal healthcare services)
- Genetic susceptibility to a particular cancer
- Behavioral risks and social determinants of health, occupational exposures, and in some cases, exposures to environmental sources

In order to evaluate the current and historical prevalence of cancer in the community surrounding Terumo BCT, the Colorado Central Cancer Registry (CCCR) compared cancer diagnosis counts in each census tract in the area of interest (109.01, 109.02, and 158), and the three census tracts combined, to expected cancer counts in the state. This analysis examined all cancers combined, and five individual types of cancer: Hodgkin's lymphoma, non-Hodgkin's lymphoma, multiple myeloma, lymphocytic leukemia, and breast cancer (females only). These cancer types were chosen due to their possible linkage to ethylene oxide exposure. All cancers among residents of this census tract diagnosed between 2000 and 2019 were included in this count as Terumo began sterilization in the early 2000s. Statistical testing was not done on ratios with less than three diagnosed cases due to variability in small numbers.

In census tract 109.01, located west of the facility, the number of cancers diagnosed among males and females individually and combined was nearly identical to the expected number of cancers for all cancer types in this assessment. Although the ratio in certain cases was greater than one, the confidence intervals included the number 1, indicating the ratio was within the expected statistical limits. This means we are 95% sure that the true ratio is within the confidence interval range. Table 1 displays the number of diagnosed cancers in the study area by cancer type and gender for 2000-2019, compared to the number that would be expected based on the population of male and female Coloradoans by age group. Overall, none of the five individual types of cancer were statistically different in census tract 109.01 compared to the rest of Colorado.

Census tract 109.02, which contains the Terumo BCT facility, showed a slightly higher than expected number of diagnoses for select cancer sites in this assessment. Table 2 displays the number of diagnosed cancers in census tract 109.02 by cancer type and gender for 2000-2019, compared to the number that would be expected based on the population of male and female Coloradoans by age group. The number of all cancers diagnosed slightly exceeded the expected number for males, females, and for both sexes combined. Additionally, four Hodgkin's Lymphomas were diagnosed in males over this time period when fewer than one would have been expected based on the statewide rate. None of the other cancer sites and sex combinations were elevated at a statistically significant level.

In census tract 158, to the north of the facility, the number of all cancers diagnosed among males and females individually and combined was not higher than expected at a level that is statistically significant in this assessment.

However, there was a higher than expected number of breast cancers diagnosed among females over this time period; about 1 additional breast cancer diagnosis per year. Despite this higher than expected number of breast cancers diagnosed among females over this time period, the observed number of other individual cancer types and all cancers combined were close to expected numbers. Additionally, there were fewer than expected numbers of non-Hodgkin's lymphoma diagnosed among females at a statistically significant level. Table 3 displays the number of diagnosed cancers in census tract 158 by cancer type and gender for 2000-2019, compared to the number that would be expected based on the population of male and female Coloradoans by age group.

Table 4 displays the number of diagnosed cancers for the combined study area by cancer type and gender for 2000-2019, compared to the number that would be expected based on the population of male and female Coloradoans by age group. The number of observed cancer cases for the three census tracts combined were similar to the number of expected cancer cases over this time period. For males, the all cancer category was very slightly elevated at a statistically significant level. No other cancer site and sex combinations were elevated at a statistically significant level.

Discussion

Overall cancer rates in this area were similar to statewide rates. These results are consistent with predictions of ethylene oxide levels in this area. However, this kind of analysis cannot determine what caused the cancers. Cancer is not a single disease, but a group of more than 100 different diseases that share some characteristics. Not all people develop the same cancer for the same reason. Each individual has a complex genetic makeup, health history, and other risk factors. Many cancers are influenced by a combination of factors.

Where seen, the elevated rates found in this study are comparable to many risks found in everyday life. In census tract 158, ~30% increased risk of breast cancer was observed. Similar increased risks for breast cancer have been associated with moderate alcohol consumption (25%) or hormone replacement therapy (26%). Also, there are significant increases in risk associated with genetics. While there is no evidence to suggest whether or not these risk factors are more prevalent in women living in census tract 158, the fact that many factors are not accounted for in our analysis as well as the fact this is a small increase in the rate of a common disease reduces the certainty of associating these findings with ethylene oxide exposure. Similarly, for Hodgkin's lymphoma, the virus that causes mononucleosis is associated with a much greater increase in risk than the small elevated risk seen in this area (source: American Cancer Society).

There are also inconsistencies in the results that reduce the ability to make definitive conclusions. For example, while breast cancer rates were higher in census tract 158, the breast cancer rates in the other two census tracts were as expected. In the combined areas, "all cancers" were higher in males, but none of the cancer types specifically associated with ethylene oxide were elevated. With limited information on other behavioral and genetic risk factors for cancer, minimal residential history, and the fact that cancer can take many years to develop, a causal determination cannot be made.

The higher than expected number of diagnosed cancers indicates a need for future assessment. The Colorado Cancer Registry plans a follow-up analysis in five years. In the meantime, steps to reduce ethylene oxide emissions from Terumo BCT have been taken, with more reductions expected once new controls become operational.

Conclusion

This evaluation found small increases in certain types of cancer that are linked to ethylene oxide. Results were inconsistent across census tracts but included higher than expected cases of breast cancer (23 additional cases) and Hodgkin's lymphoma (3 additional cases) over the 20-year study period.

This kind of study only establishes the cancer rate and whether it is above what is expected based on cancer rates across Colorado. It does not determine that ethylene oxide caused or contributed to these cancers. The study lacks information on:

- Individuals' other risk factors for cancer.
- How long people who developed cancer lived in this area and how much ethylene oxide they were exposed to.
- People who moved out of this area before developing cancer.

Not all people develop the same cancer for the same reason. Each individual has a complex genetic makeup, health history, and other risk factors that interact and can lead to the development of cancer. As a result, no single study is likely to prove that an environmental exposure was the sole cause of a person's cancer.

The department remains committed to working with EPA and Terumo to reduce ethylene oxide emissions and risk in the community. Our plans include:

- Oversee measurements at Terumo BCT to verify emissions reductions from additional controls.
- Evaluate how to expand monitoring capabilities in the future to measure ethylene oxide in the community near Terumo.
- Continue to support EPA actions to reduce ethylene oxide emissions and exposures.
- Repeat this study in five years and explore opportunities to support CDC ATSDR's on-going efforts to better understand community exposures near facilities that use ethylene oxide.

Figures and Tables

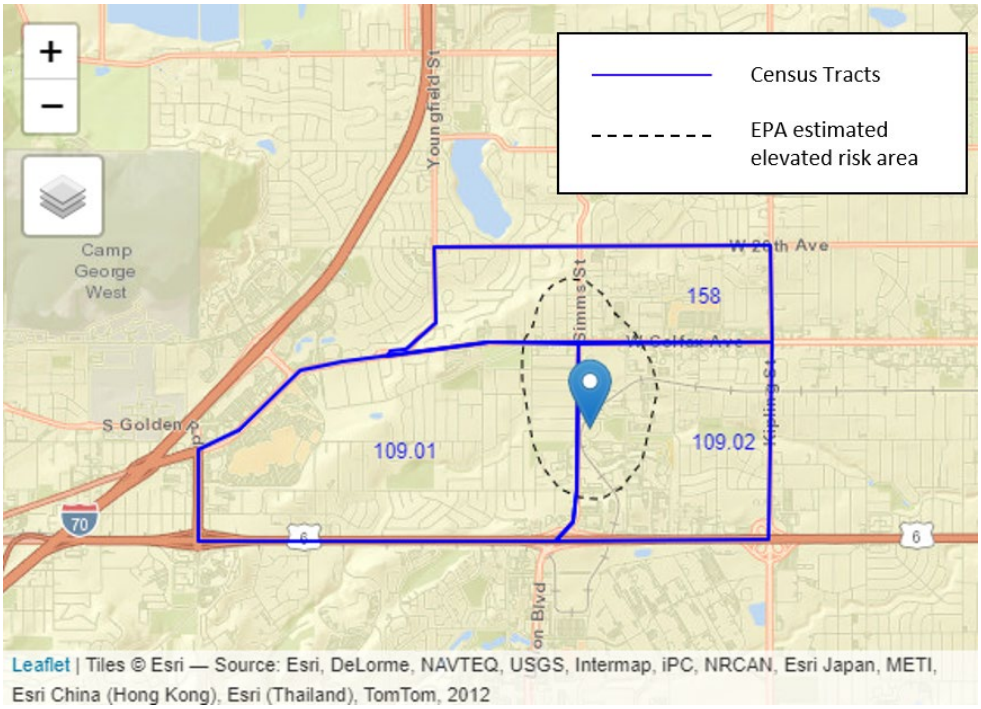

Figure 1. Map of three census tracts (outlined in solid blue line) included in this evaluation. Blue pin represents Terumo BCT. The black dotted line represents EPA's 2022 estimate of the elevated risk area after additional controls were put in place in 2018. The elevated risk area from 2000-2018 was likely larger, though there is uncertainty in the actual emissions across that time period.

Table 1. Number of new cancer diagnoses in census tract 109.01 compared to expected number (statewide) for males and females from 2000 to 2019.

Population Group	Cancer	Cancers Diagnosed	Cancers Expected	Diagnosed/ Expected	95% C.I. for Ratio
Males	All Cancers	260	257.02	1.01	(0.89-1.14)
	Hodgkin's Lymphoma	0	1.58	0.00	NC
	Non-Hodgkin's Lymphoma	11	11.36	0.97	(0.48-1.62)
	Multiple Myeloma	4	4.10	0.98	(0.25-2.17)
	Lymphocytic Leukemia	8	4.79	1.67	(0.71-3.03)
Females	All Cancers	222	228.73	0.97	(0.85-1.10)
	Breast	76	75.89	1.00	(0.79-1.24)
	Hodgkin's Lymphoma	1	1.14	0.88	NC
	Non-Hodgkin's Lymphoma	7	8.57	0.82	(0.32-1.53)
	Multiple Myeloma	5	2.66	1.88	(0.59-3.89)
	Lymphocytic Leukemia	2	2.75	0.73	NC
Females and Males	All Cancers	482	485.74	0.99	(0.91-1.08)
	Breast (females only)	76	75.89	1.00	(0.79-1.24)
	Hodgkin's Lymphoma	1	2.73	0.37	NC
	Non-Hodgkin's Lymphoma	18	19.94	0.90	(0.53-1.37)
	Multiple Myeloma	9	6.76	1.33	(0.60-2.34)
	Lymphocytic Leukemia	10	7.54	1.33	(0.63-2.28)

Note: Diagnosed/Expected ratios that have a 95% Confidence Interval that include the value 1.00 are not considered statistically high or low; NC – not calculated due to less than 3 diagnoses; Source: Colorado Central Cancer Registry, CDPHE, 5/31/23

Table 2. Number of new cancer diagnoses in census tract 109.02 compared to expected number (statewide) for males and females from 2000 to 2019.

Population Group	Cancer	Cancers Diagnosed	Cancers Expected	Diagnosed/ Expected	95% C.I. for Ratio
Males	All Cancers	114	88.13	1.29	(1.07-1.54)
	Hodgkin's Lymphoma	4	0.75	5.33	(1.39-11.83)
	Non-Hodgkin's Lymphoma	4	4.08	0.98	(0.25-2.17)
	Multiple Myeloma	1	1.37	0.73	NC
	Lymphocytic Leukemia	2	1.75	1.14	NC
Females	All Cancers	120	97.55	1.23	(1.02-1.46)
	Breast	33	31.56	1.05	(0.72-1.43)
	Hodgkin's Lymphoma	0	0.57	0.00	NC
	Non-Hodgkin's Lymphoma	6	3.68	1.63	(0.59-3.19)
	Multiple Myeloma	1	1.12	0.89	NC
	Lymphocytic Leukemia	2	1.22	1.64	NC
Females and Males	All Cancers	234	185.68	1.26	(1.10-1.43)
	Breast (females only)	33	31.56	1.05	(0.72-1.43)
	Hodgkin's Lymphoma	4	1.32	3.03	(0.79-6.72)
	Non-Hodgkin's Lymphoma	10	7.77	1.29	(0.61-2.21)
	Multiple Myeloma	2	2.49	0.80	NC
	Lymphocytic Leukemia	4	2.97	1.35	(0.35-2.99)

Note: Diagnosed/Expected ratios that have a 95% Confidence Interval that include the value 1.00 are not considered statistically high or low; NC – not calculated due to less than 3 diagnoses; Source: Colorado Central Cancer Registry, CDPHE, 5/31/23

Table 3. Number of new cancer diagnoses in census tract 158 compared to expected number (statewide) for males and females from 2000 to 2019.

Population Group	Cancer	Cancers Diagnosed	Cancers Expected	Diagnosed/ Expected	95% C.I. for Ratio
Males	All Cancers	215	194.22	1.11	(0.96-1.26)
	Hodgkin's Lymphoma	1	1.25	0.80	NC
	Non-Hodgkin's Lymphoma	12	9.00	1.33	(0.69-2.20)
	Multiple Myeloma	3	3.22	0.93	(0.18-2.29)
	Lymphocytic Leukemia	6	3.81	1.57	(0.57-3.08)
Females	All Cancers	260	254.88	1.02	(0.90-1.15)
	Breast	97	73.82	1.31	(1.07-1.59)
	Hodgkin's Lymphoma	3	1.03	2.90	(0.55-7.11)
	Non-Hodgkin's Lymphoma	3	10.55	0.28	(0.05-0.70)
	Multiple Myeloma	4	3.37	1.19	(0.31-2.64)
	Lymphocytic Leukemia	6	3.44	1.74	(0.63-3.41)
Females and Males	All Cancers	475	449.10	1.06	(0.96-1.15)
	Breast (females only)	97	73.82	1.31	(1.07-1.59)
	Hodgkin's Lymphoma	4	2.28	1.75	(0.46-3.89)
	Non-Hodgkin's Lymphoma	15	19.55	0.77	(0.43-1.20)
	Multiple Myeloma	7	6.58	1.06	(0.42-2.00)
	Lymphocytic Leukemia	12	7.26	1.65	(0.85-2.72)

Note: Diagnosed/Expected ratios that have a 95% Confidence Interval that include the value 1.00 are not considered statistically high or low; NC – not calculated due to less than 3 diagnoses; Source: Colorado Central Cancer Registry, CDPHE, 5/31/23

Table 4. Number of new cancer diagnoses in the combined area of census tracts 109.01, 109.02, and 158 compared to expected number (statewide) for males and females from 2000 to 2019.

Population Group	Cancer	Cancers Diagnosed	Cancers Expected	Diagnosed/ Expected	95% C.I. for Ratio
Males	All Cancers	589	539.36	1.09	(1.01-1.18)
	Hodgkin's Lymphoma	5	3.58	1.40	(0.44-2.89)
	Non-Hodgkin's Lymphoma	27	24.44	1.10	(0.73-1.56)
	Multiple Myeloma	8	8.68	0.92	(0.39-1.67)
	Lymphocytic Leukemia	16	10.36	1.55	(0.88-2.39)
Females	All Cancers	602	581.15	1.04	(0.95-1.12)
	Breast	206	181.27	1.14	(0.99-1.30)
	Hodgkin's Lymphoma	4	2.75	1.46	(0.38-3.23)
	Non-Hodgkin's Lymphoma	16	22.81	0.70	(0.40-1.09)
	Multiple Myeloma	10	7.14	1.40	(0.67-2.40)
	Lymphocytic Leukemia	10	7.41	1.35	(0.64-2.32)
Females and Males	All Cancers	1191	1120.52	1.06	(1.00-1.12)
	Breast (females only)	206	181.27	1.14	(0.99-1.30)
	Hodgkin's Lymphoma	9	6.33	1.42	(0.64-2.50)
	Non-Hodgkin's Lymphoma	43	47.26	0.91	(0.66-1.20)
	Multiple Myeloma	18	15.83	1.14	(0.67-1.72)
	Lymphocytic Leukemia	26	17.77	1.46	(0.95-2.08)

Note: Diagnosed/Expected ratios that have a 95% Confidence Interval that include the value 1.00 are not considered statistically high or low; NC – not calculated due to less than 3 diagnoses; Source: Colorado Central Cancer Registry, CDPHE, 5/31/23