CANCER INCIDENCE DATA REVIEW

Area Surrounding Viant Medical, Inc.
Grand Rapids, MI

Michigan Department of Health and Human Services
Division of Environmental Health

Contents

Cancer Incidence Report for the Area Surrounding Viant Medical, Inc.

2001-2015, Grand Rapids, MI

Summary

The Michigan Department of Health and Human Services, Division of Environmental Health has evaluated cancer incidence in the area surrounding Viant Medical Facility, Inc. (Viant) in Grand Rapids, Michigan. This was done in response to the discovery of elevated levels of ethylene oxide (EtO) in the area. Cancer registry incidence data was evaluated for female breast cancer, multiple myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, and leukemia, which have been shown in the scientific literature to be associated with EtO exposure. Standardized incidence ratios (SIRs) and their 95% confidence intervals (CI) were calculated using county and state populations as the comparison. No statistical elevations in the frequency of any of the cancer types were observed over the 15-year time period of analysis, with the exception of multiple myeloma when compared to county rates. When compared to Kent County cancer rates, multiple myeloma showed an estimated increase of 47% (SIR 1.47, CI 1.02-2.06). However, this is based on a small number of cases (count = 25) over a 15-year time period, resulting in an imprecise estimate with borderline statistical difference. Therefore, the results of the analyses presented in this report do not suggest that further investigation is needed at this time. However, MDHHS remains committed to evaluating new information as it becomes available.

Background

The Michigan Department of Health and Human Services' (MDHHS) Cancer Registry Program and Division of Environmental Health have conducted a review of cancer incidence data for diagnosis years 2001-2015, as collected by the Michigan Cancer Registry, for a geographic area comprised of 10 census tracts surrounding the Viant Medical Inc. (Viant) facility in Grand Rapids, Michigan. The Kent County Health Department with MDHHS pursued this analysis as a response to the Michigan Department of Environment, Great Lakes, and Energy (EGLE) investigation of Viant, which led to the conclusion that levels of EtO concentrations in ambient air may present an elevated cancer risk for residents in the community surrounding the Viant facility. Viant is located at 520 Watson Street SW, Grand Rapids, Michigan. The facility has been using EtO to sterilize medical equipment at this location for 30 years. In August 2018, the United States Environmental Protection Agency (USEPA) released its latest National Air Toxics Assessment which estimates health risks from various toxic air pollutants, including EtO. The NATA estimated elevated cancer risks related to EtO in the community

surrounding the Viant facility. The Michigan Department of Environment, Great Lakes, and Energy (EGLE) Air Quality Division (AQD) investigated the conditions around Viant performing ambient (outdoor) air sampling and more refined dispersion modeling, in response to the NATA estimates. Both the measured ambient air samples and the modeled data suggested elevated concentrations of EtO present near the facility. The investigation also resulted in EGLE issuing several violation notices to Viant and initiating an enforcement action.

Long-term exposure to high levels of EtO, such as that experienced by sterilization workers in an occupational setting, is associated with cancers of the lymphohematopoietic system (cells involved in the production of lymphocytes and cells of blood, bone marrow, spleen, lymph nodes, and thymus) and breast cancer in females (USEPA, 2016). A large study of sterilizer workers conducted by the National Institute for Occupational Safety and Health (NIOSH) found increased mortality from lymphoid cancers in males and females as well as increased incidence of breast cancer in females (USEPA, 2016).

The objective of this cancer incidence review is to determine if cancer incidence in the area surrounding Viant is more than expected when compared to the cancer incidence for both Kent County and the State of Michigan. According to the Centers for Disease Control and Prevention (CDC), a higher frequency of cancer than expected for a geographic area can be due to:

- Chance or coincidence
- Underestimating the expected number of cancer cases (e.g., not considering a risk factor within the population at risk)
- Higher frequency of known causes of cancer (e.g., smoking), and/or
- Higher frequency of unknown cause(s) of cancer, yet to be determined.

Methods

A cancer case is defined as a person with a newly diagnosed cancer where the cancer type is reported to be malignant and primary. The data source for cancer cases in this report is the Michigan Resident Cancer Incidence File managed by the Michigan Cancer Surveillance Program (MCSP) in the Division for Vital Records & Health Statistics (DVRHS), Michigan Department of Health & Human Services. As required by MCL 333.2619 and Administrative Rules R. 325.9050 *et seq*., all newly diagnosed cases of invasive cancer in Michigan are routinely reported to the MCSP by reporting facilities, such as hospitals and independent laboratories. This registry collects the patient's age, sex, race, cancer site and type, and residential address at the time of diagnosis. The registry does not record the cause of an individual's cancer nor does it collect sufficient

information to determine the cause. For this report, invasive cancer incidence data for select cancer types are examined from the year 2001 through 2015, which are the most recent years that cancer incidence data are available at the census tract/block level. Population data used in this report are prepared by DVRHS based on estimates released by the National Center for Health Statistics, which originate from the 2010 US Census population (MDHHS, 2017).

The geographic area of analysis is a combination of 10 census tracts that approximate the area that may have been exposed to ambient air EtO emissions from the Viant facility. These 10 tracts include the following: 26081001400, 26081001500, 26081001600, 26081001900, 26081002000, 26081002100, 26081002600, 26081002700, 26081002800, and 26081002900. Census tracts were included in the analysis if at least 50% of the census tract area overlapped the estimated exposure area. Cancer cases are allocated to a particular census tract based on the residential address of the person diagnosed with cancer as reported at the time of their diagnosis. Figure 1 overlays the census tract area with the estimated exposure area. Figure 1 also shows the area potentially exposed to ambient EtO levels associated with a cancer risk of 1 cancer in 100,000 people (0.002 $\mu g/m^3$) according to the 2017 EGLE exposure assumptions. The area that may have been exposed to ambient EtO levels associated with a cancer risk of 1 cancer in 10,000 people (0.02 $\mu g/m^3$) is also displayed. For these cancer risk estimates, EGLE assumes constant exposure over a 70-year lifetime (EPA, 2016).

For the combined census tract area, the cancer incidence that was observed during the time period 2001 through 2015 was compared with what would be expected based on the cancer incidence for Kent County and the State of Michigan, for the following cancer types: Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, leukemia, and female breast. For this comparison, Standardized Incidence Ratios (SIRs) were calculated. The SIR is calculated by dividing the number of cases of cancer that occurred among residents of the combined census tract area (called observed cases) by the number of cases that would be expected if the area had the same cancer rate as Kent County or the State of Michigan.

- When the **SIR equals 1.00**, it means that the number of cases of cancer observed in the combined census tract area **is the same** as would be expected if that area has the same cancer rate as the comparison population (county or state).
- When the **SIR is less than 1.00**, it means that the combined census tract area **has fewer** cancer cases than expected based on the county or state rates.
- When the **SIR is greater than 1.00**, it means that the combined census tract area **has more** cancer cases observed than would be expected based on the county or state rates. For example, an SIR of 1.5

would mean that the number of cases in the area was 50 percent higher than would be expected if the area had the same cancer rate as the comparison population.

- The degree to which the SIR is different than 1.0 (further away from 1.0 in either direction) indicates the strength of evidence for a difference between the expected and observed number of cases, i.e. that the combined census tract area has higher or lower cancer incidence than the comparison population (county or state). As the SIR approaches 1.0, the evidence for higher or lower cancer incidence in the combined census tract area (versus the comparison population) gets weaker. The SIR is interpreted using the following framework (Monson, R. 1990).

SIR Value	**Strength of Evidence that the Combined Census Tract Area has Higher or Lower Cancer Incidence than the Comparison Population**
Less than 0.4	Strong evidence of decreased cancer incidence
0.4 to less than 0.7	Moderate evidence of decreased cancer incidence
0.7 to less than 0.9	Weak evidence of decreased cancer incidence
0.9 to less than 1.2	No evidence of a difference in cancer incidence
1.2 to less than 1.5	Weak evidence of increased cancer incidence
1.5 to less than 3.0	Moderate evidence of increased cancer incidence
3.0 or greater	Strong evidence of increased cancer incidence

Populations often differ in their distribution of age or sex, which may in turn affect the overall rate of cancer cases in that population. For example, if one population has a larger number of elderly adults than another, it could demonstrate a higher cancer incidence rate simply due to its age structure. Therefore, when comparing cancer incidence between populations of different age or sex distributions, it is important to account for those differences. In this report, SIR calculations account for both differences in the age structure and the sex distribution between the combined census tract area and Kent County or State of Michigan populations using indirect standardization methodology. Table 1 contains demographic information for the geographic area of analysis (10 combined census tracts) and the two comparison populations (Kent County and the State of Michigan).

Table 1: Demographic Information for the Populations of the Geographic Area of Analysis (10 Census Tracts) and the Two Comparison Populations - Kent County and the State of Michigan[1]

Demographic Characteristic		**Combined Census Tract Area N (%)**	**Kent County N (%)**	**State of Michigan N (%)**
Total		31,429	636,376	9,925,568
Sex	Male	16,347 (52.0%)	313,134 (49.2%)	4,880,579 (49.2%)
	Female	15,082 (48.0%)	323,242 (50.8%)	5,044,989 (50.8%)
Age Group	0-9 years	4,033 (12.8%)	88,749 (13.9%)	1,173,600 (11.8%)
	10 to 19 years	3,533 (11.2%)	86,342 (13.6%)	1,308,816 (13.2%)
	20 to 44 years	15,999 (50.9%)	221,178 (34.8%)	3,119,539 (31.4%)
	45 to 69 years	6,549 (20.8%)	187,033 (29.4%)	3,277,016 (33.0%)
	70 years and over	1,315 (4.2%)	53,074 (8.3%)	1,046,597 (10.5%)
Race	White alone	21,951 (69.8%)	511,125 (80.3%)	7,813,199 (78.7%)
	Black or African American alone	4,390 (14.0%)	61,686 (9.7%)	1,374,515 (13.8%)
	American Indian and Alaska Native alone	286 (0.9%)	2,581 (0.4%)	51,804 (0.5%)
	Asian alone	551 (1.8%)	18,154 (2.9%)	289,082 (2.9%)
	Native Hawaiian and Other Pacific Islander alone	7 (0.02%)	144 (0.02%)	2,808 (0.03%)
	Some other race alone	2,392 (7.6%)	19,399 (3.0%)	115,258 (1.2%)
	Two or more races	1,852 (5.9%)	23,287 (3.7%)	278,902 (2.8%)
Ethnicity	Not Hispanic or Latino	23,926 (76.1%)	570,942 (89.7%)	9,441,000 (95.1%)
	Hispanic or Latino	7,503 (23.9%)	65,434 (10.3%)	484,568 (4.9%)
Household Income[2]	<$10,000-$14,999	3,134 (24.3%)	23,692 (10.0%)	478,303 (12.3%)
	$15,000 to $34,999	3,192 (24.7%)	46,437 (19.6%)	816,615 (21.0%)
	$35,000 to $74,999	3,952 (30.6%)	80,318 (33.9%)	1,267,698 (32.6%)
	$75,000 to $149,999	1,870 (14.5%)	64,444 (27.2%)	976,049 (25.1%)
	>$150,000	767 (5.9%)	22,270 (9.4%)	349,977 (9.0%)

[1]U.S. Census Bureau, 2013-2017 American Community Survey 5-Year Estimates

[2]Percent based on number of households reporting income: 10 census tract region: 12,915, Kent County: 236,929, and state of Michigan: 3,888,646

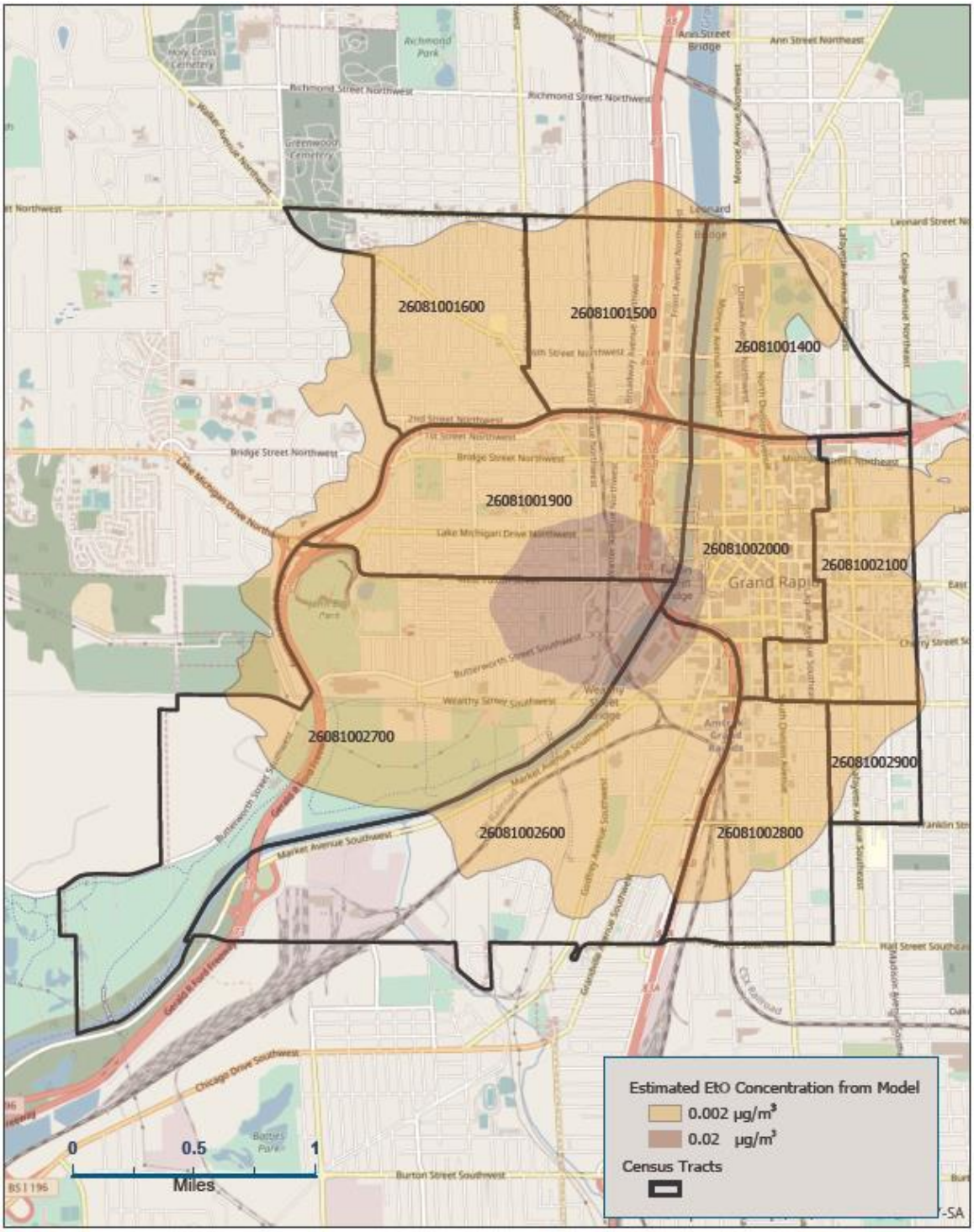
SIRs were tested for evidence of a statistical difference in cancer rates by calculating 95% confidence intervals for each SIR. The 95% confidence interval represents the range in which we would expect the SIR to fall 95% of the time. When the 95% confidence interval is wide for an SIR, it indicates that the SIR is imprecise; SIRs that are based on small numbers of cancer cases will have wide confidence intervals. If the SIR's 95% confidence interval does not include the value 1.0 in its range, then the SIR is evidence of a statistical difference in cancer rates. It is important to note that when the number of cancer cases is small, such as for rare cancer types or in smaller areas, the report of only a few extra cancer cases can result in large SIRs, making interpretation of the confidence intervals particularly important; as long as the value 1.00 is contained within the SIR's 95% confidence interval, the SIR is within the range of expected values and is not evidence of a statistical difference in cancer incidence.

Limitations

- Results of this investigation are based on surveillance data and not an epidemiologic research study of the relationship between risk factors and cancer incidence. Therefore, these results cannot indicate whether any cancer occurrence is related to or caused by environmental contaminant exposures, including EtO. Michigan Central Cancer Registry records do not include the data necessary to make such an evaluation. If a statistical increase (or decrease) is observed among the results of these analyses, it does not necessarily mean that the difference is due to an environmental exposure.
- This review cannot determine which individuals (with or without cancer) residing within the geographic area have been exposed to EtO.
- The latency period is the time that passes between being exposed to something that can cause cancer (such as an environmental contaminant) and having symptoms or being diagnosed. Latency periods vary by cancer type. Cancer observed during a specific period could be related to an exposure that occurred a long time ago.
- Migration of people into and out of an area of analysis limits the interpretation. The Michigan Cancer Surveillance Program records a person's address at time of cancer diagnosis, which may not reflect where they spent the majority of their life or the period of time when exposure to a cancer-causing agent occurred. For example, cancer cases included in the analysis of the investigation period could be related to exposures they had when they lived in another state.
- Multiple cancer data years have been combined due to the small number of cancer cases for the selected geographic area.
- The U.S. census tract boundaries serve as the geographic scope of this analysis, but do not exactly align with the estimated EtO exposure area determined by the Michigan Department of Environment, Great Lakes, and Energy (EGLE) using computer models.
- The air sample data available for verification of the computer model of EtO exposure levels were collected from a limited area around the facility. Therefore, there is uncertainty regarding the modeled EtO concentrations which are used to evaluate residential exposures.
- The available air sample data are insufficient to accurately assess historical EtO levels in the community. It is unknown how past facility emissions compare to emissions during the recent period for which data are available. It is also unknown how seasonal fluctuations in temperature, barometric pressure, wind speed, and wind direction may affect the levels of EtO in the surrounding community.
- The levels of EtO from the models suggest an increase in cancer cases is possible, however, given the low levels of exposure and the small population size, a statistical difference would most likely not be

detectable. Furthermore, the type of cancer surveillance data used in this review cannot relate cancer incidence to environmental exposures.

Figure 1: The Geographic Area of Analysis Defined by Combined Census Tracts[1] and the Area Estimated to have EtO Concentrations[2] Greater Than or Equal to 0.002 µg/m^3 and Greater than or Equal to 0.02 µg/m^3



[1]Census Tracts 26081001400, 26081001500, 26081001600, 26081001900, 26081002000, 26081002100, 26081002600, 26081002700, 26081002800, and 26081002900

[2]As determined by computer models conducted by EGLE

Results

Results for age and sex-adjusted Standardized Incidence Ratios (SIRs) and 95% confidence intervals did not show any statistical differences from expected values for non-Hodgkin lymphoma, Hodgkin lymphoma, or leukemia. The SIR for multiple myeloma showed statistically increased incidence when compared to Kent County but not when compared to the state. Female breast cancer showed statistically less incidence when compared to both the county and the state. However, for each of these, the value of the SIR would indicate that there is no (or very weak) evidence of a difference between the observed and expected number of cases. Results are presented below. Table 2 shows the observed and expected numbers of cancer diagnoses in the analysis area as well as the SIR and 95% confidence interval of the SIR. Figure 2 shows the SIRs and 95% confidence intervals represented graphically.

Table 2: Standardized Incidence Ratio (SIR)[1] for Invasive Cancers by Cancer Type, Comparing the Geographic Area of Analysis (10 Census Tracts) to Kent County and the State of Michigan, Adjusted for Age and Sex, 2001 – 2015[2]

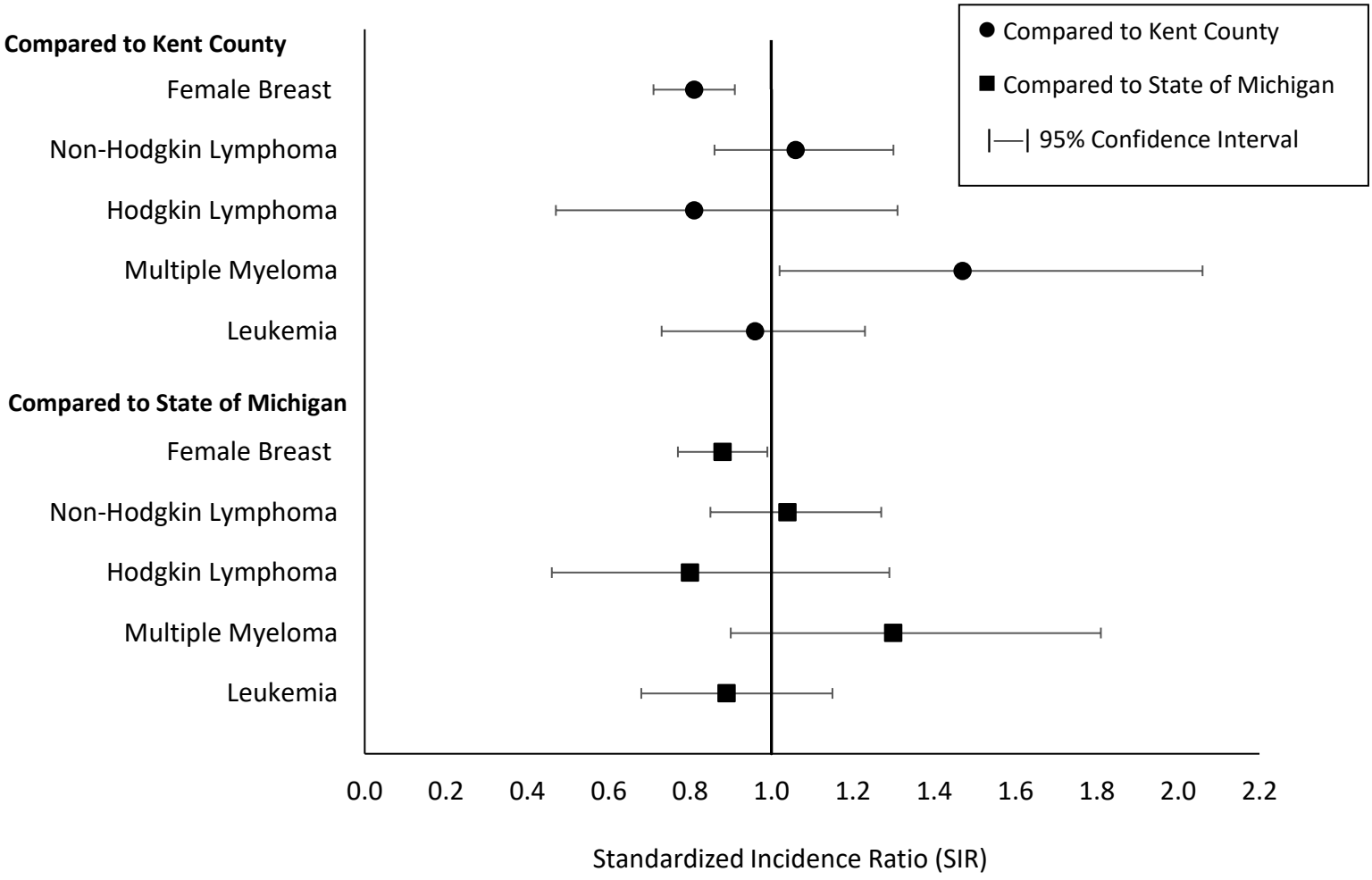
		Kent County Comparison		**State of Michigan Comparison**	
Cancer Type	Observed Number of Cases in 10-Census Tract Area	Expected Number[1] of Cases	SIR (95% Confidence interval)	Expected Number[1] of Cases	SIR (95% Confidence interval)
Female Breast	177	219.48	0.81 (0.71, 0.91)	202.23	0.88 (0.77, 0.99)
Non-Hodgkin Lymphoma	71	66.76	1.06 (0.86, 1.30)	68.19	1.04 (0.85, 1.27)
Hodgkin Lymphoma	12	14.85	0.81 (0.47, 1.31)	15.07	0.80 (0.46, 1.29)
Multiple Myeloma	25	16.96	1.47 (1.02, 2.06)	19.28	1.30 (0.90, 1.81)
Leukemia	43	44.91	0.96 (0.73, 1.23)	48.06	0.89 (0.68, 1.15)

[1]SIR is the ratio of observed to expected cases, where expected cases are calculated by multiplying the age-sex specific cancer incidence rates for the comparison population (Kent County or State of Michigan) to population estimates for the 10-census tract region surrounding Viant (2010 US Census).

[2]Source of Michigan Cancer Cases: Michigan Resident Cancer Incidence File, 2001-2015, includes cases processed through November 30, 2018. Division for Vital Records & Health Statistics, Michigan Department of Health and Human Services. Cancer cases were defined by new malignant cancer diagnoses where the listed cancer site was the primary site.

Shading indicates that the SIR was statistically higher or lower than 1.00 (95% confidence interval does not include the value 1.0)

Figure 2: Standardized Incidence Ratio (SIR)[1] for Invasive Cancers by Type, Comparing the Geographic Area of Analysis (10 Census Tracts) to Kent County and the State of Michigan, Adjusted for Age and Sex, 2001 – 2015[2]



[1]SIR is the ratio of observed to expected cases, where expected cases are calculated by multiplying the age-sex specific cancer incidence rates for the comparison population (Kent County or State of Michigan) to population estimates for the 10-census tract region surrounding Viant. Where the horizontal bar (95% Confidence Interval) touches or crosses the vertical bar at 1.0, the SIR indicates that the cancer incidence in the combined census area is not statistically different from the comparison population.
[2]Source of Michigan Cancer Cases: Michigan Resident Cancer Incidence File, 2001-2015, includes cases processed through November 30, 2018. Division for Vital Records & Health Statistics, Michigan Department of Health and Human Services. Cancer cases were defined by new malignant cancer diagnoses where the listed cancer site was the primary site.

- When compared to Kent County, the 10-census tract area had a statistically elevated number of multiple myeloma cancer cases. The number of multiple myeloma cancer cases was estimated at 47% higher than what would be expected based on Kent County incidence (95% CI = 2%-106%). The value of the SIR (1.47) would indicate, however, that the difference between the expected and observed number of cases is not substantial. When compared to the State of Michigan, no statistical increase in multiple myeloma cases is observed.

- When compared to Kent County or the State of Michigan, the 10-census tract area had a statistically lower number of female breast cancer cases. The value of the SIRs (0.81 and 0.88) would indicate, however, that the difference between the expected and observed number of cases is not substantial.

Conclusions

The results of this investigation indicate that there was a statistical increase in multiple myeloma cancer incidence in the 10-census tract region surrounding Viant when compared to Kent County, but not when compared to the State of Michigan. There were statistically less cases of female breast cancer in the 10-census tract region surrounding Viant compared to both Kent County and the State of Michigan. However, the values of the SIRs would indicate that there is no (or very weak) evidence of a difference between the observed and expected number of cases for multiple myeloma and breast cancer. Hodgkin lymphoma, non-Hodgkin lymphoma, and Leukemia were all within range of expected values. It should be noted that many of these comparisons are based off a relatively small number of cases over a long period of time, which increases the uncertainty of the estimate and makes interpretation of the confidence intervals particularly important. Note that the confidence interval for the SIR reflecting the elevated multiple myeloma cancer incidence is wide (indicating statistical imprecision) and is very nearly crossing the value 1.0 which would render the SIR not statistically different. It is also important to consider the aforementioned limitations of the analysis and the registry-based cancer surveillance data (see above). Limitations that are particularly important are that (1) data from the Michigan Central Cancer Registry does not contain the information necessary to determine that cancer incidence is related to any environmental contamination, (2) given the long period of investigation, it is possible that the migration of people into and out of the analysis area is a mitigating factor in interpreting the findings, and (3) given the low levels of exposure estimated from modeling and the small population of the area, a statistical increase in cancer incidence from EtO would most likely not be detectable. This investigation should be considered a descriptive review of cancer incidence in the area surrounding Viant Medical Facility and not as evidence that potential exposure to EtO (or any other environmental exposure) has resulted in higher or lower cancer risk. The results of the analyses presented in this report do not suggest that further investigation is needed at this time. However, MDHHS remains committed to evaluating new information as it becomes available.

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