Division of Chronic Disease, Primary Care, and Rural Health

5/15/2023

a

Findings of a Cancer Inquiry Investigation
Johnson County, Indiana 2015-2017

Indiana
Department
of
Health

Originally Released December 2017
Revised December 2018
2nd Revision May 2023

EXECUTIVE SUMMARY

On November 17, 2015, the Indiana Department of Health (IDOH) opened an investigation into childhood cancers in Johnson County at the request of the Johnson County Health Officer. Local health officials received reports from citizens and the media that, since 2010, their community experienced a higher than normal number of cancers among children and expressed concerns regarding water contamination from the Webb Wellfield, a pumping station that served the city of Franklin municipal water supply.

The Centers for Disease Control and Prevention (CDC), the National Cancer Institute, and other public health institutions 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 time." Using recommended CDC investigative protocol, IDOH analyzed cancer cases occurring among children aged 0-19 years in Johnson County between 1999 and 2013. Due to the specific concerns cancers were analyzed in two groups, including all cancer types combined, and a smaller subset of the most commonly diagnosed childhood cancers, including leukemia, brain and other central nervous system tumors, neuroblastoma, Wilms tumor, lymphoma (Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma and bone cancer (including osteosarcoma and Ewing sarcoma).

Investigators calculated standardized incidence ratios (SIRs) to evaluate whether a greater than expected number of childhood cancers occurred in Johnson County. To calculate the SIRs, investigators divided the actual number of cancer cases diagnosed among children aged 0-19 years in Johnson County from 1999 to 2013 by the expected number of cases, which was based on the

incidence of cancer among children aged 0-19 years throughout Indiana during the same period of time. For all cancer types combined, the number of cases was similar to what was expected (111 cases observed, 107 cases expected, SIR = 1.04, 95% confidence interval = 0.84-1.23). The results were similar for the subset of the most common childhood cancers (79 cases observed, 77 cases expected, SIR = 1.03, 95% confidence interval = 0.80-1.26). Neither SIR indicated a statistically significant difference between the number of cases observed and the number expected. At the time of the investigation, data were not complete for 2014 and 2015, and did not become publicly available until June 2017. These data are included in the first addendum of this report.

After analyzing available data, reviewing information gathered during interviews, and comparing findings to cancer cluster criteria, this investigation indicated that the criteria for defining a cancer cluster were not met. At that time the investigation was closed. Due to the time lag that occurs with cancer registries, new analysis on all cancer cluster investigations is done every year new data becomes available to ensure no new results are found. A second addendum has been added to reflect the most recent data available. At this time in 2023, the SIR analysis still shows no signs of cancer cluster.

INTRODUCTION

On November 17, 2015, the Indiana Department of Health (IDOH) opened an investigation into childhood cancer in Johnson County at the request of the Johnson County Health Officer. Local health officials received reports from citizens and the media that, since 2010, their community experienced a higher-than-normal number of cancers among children and expressed concerns regarding water contamination from the Webb Wellfield, a pumping station that served the city of Franklin municipal water supply.

The types of cancers that occur most often in children are different from those seen in adults. According to the American Cancer Society (ACS), the most frequently diagnosed cancer types among children are leukemia, brain and central nervous system tumors, neuroblastoma, Wilms tumor, lymphoma (including both Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma and bone cancer (including osteosarcoma and Ewing sarcoma). Breast, prostate, lung, and colon cancers are most common among adults.

Little is known about the causes and risk factors for most childhood cancers. According to the [National Cancer Institute](#) (NCI), a small percent (approximately 5%) of cancers in children arise from inherited mutations (genetic mutations that can be passed from parents to their children). Identifying potential environmental causes of childhood cancer has been difficult for numerous reasons. Cancer in children is rare, which makes it difficult to study. It is also difficult to determine what exposures children might have had early in their development, as well as the frequency and duration of exposure. Exposure to ionizing radiation is associated with increased risk for childhood brain and central nervous system tumors. Although chronic exposure to benzene is associated with acute leukemia in adults, evidence linking benzene exposure with leukemia in children is lacking. Viruses thought to increase risk for certain childhood cancers include the human lymphotropic viruses I and II and the Epstein-Barr virus.

METHODS OF INVESTIGATION

DEFINITION OF A CANCER CLUSTER

The official definition of a cancer cluster used by the Centers for Disease Control and Prevention (CDC), the NCI, and other public health institutions is as follows:

> *A cancer cluster is defined 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 time.*

According to the CDC, to be classified as a cancer cluster, a group of cancer cases must meet all of the following criteria:[1]

- ***A greater than expected number:*** *A greater than expected number is when the observed number of cases is higher than what would typically be seen in a similar setting (i.e. in a group with similar population, age, race, or sex). This may involve comparing rates for groups of people over a much larger area, such as an entire state or a county.*
- ***Of cancer cases:*** *All of the cases must involve the same type of cancer, or types of cancer scientifically proven to have the same cause.*
- ***That occurs within a group of people:*** *The population in which the cancers are occurring is carefully defined by factors such as race/ethnicity, age or gender for purposes of calculating cancer rates.*

4

- *In a geographic area:* Both the number of cancer cases included in the cluster and calculation of the expected number of cases can depend on the geographic area where the cluster occurred is defined. The boundaries must be defined carefully. It is possible to "create" or "obscure" a cluster by selection of a specific area.
- *Over a defined period of time:* The number of cases included in the cluster – and calculation of the expected number of cases – will depend on how the time period over which the cases occurred is defined.

As part of the investigation, the traits of the suspected cancer cluster in Johnson County were compared to the criteria listed above.

RESULTS
Study Population

Based on the above criteria, it was necessary to identify the number of cancer cases of interest, the relevant geographic area, and a defined period of time. The addresses of those children mentioned in media reports were plotted on a map and used initially to establish the geographic area for this investigation. The next step was to identify the number of children aged 0-19 years diagnosed with cancer in the reported geographic area during a specific, relevant period. At the time of this investigation, cancer diagnosis data collected by the Indiana State Cancer Registry were verified and considered complete through December 2013. Newly diagnosed cases from 2014 and 2015 had either not yet been reported to the registry or had not yet been verified, so these two years were excluded from the initial analysis. The final study population for this investigation included 111 children aged 0-19 years diagnosed with cancer in Johnson County between 1999 and 2013. A 15-year cohort timeframe is a standard lookback period for rare cancer incidence. Standard practice for determining cancer incidence is typically done over multiple years, due to random fluctuation of cancer cases from year to year.

To determine whether Johnson County was experiencing a greater than expected number of childhood cancer diagnoses, investigators calculated a standardized incidence ratio (SIR). The SIR compares the actual number of cancers diagnosed in the study population to the number of cases that would have been expected to occur if the incidence for the study population was equal to the

incidence for a similar comparison population. For this investigation, the study population was Johnson County and the comparison population was the state of Indiana.

A SIR higher than 1 indicates a greater than expected number of cases, a SIR close to 1 indicates that the number of cases is similar to what would be expected, and a SIR lower than 1 indicates that the number of cases diagnosed was less than expected. Because there is always random error associated with statistical estimation, it is standard practice to calculate a 95% confidence interval around the SIR. A confidence interval describes the interval within which the true value may fall. In other words, the SIR may be as low as the lower confidence limit, or as high as the upper limit. If the bounds of the 95% confidence interval contain 1 than the results do not show a statistically significant difference between observed and expected.

Description of Cases

The majority of children diagnosed with cancer in Johnson County between 1999 and 2013 were white and non-Hispanic. Table 1 shows a breakdown by gender for all cancer types as well as for the subset of the most common childhood cancers.

Table 1. Distribution of cancers (number and percent of total) by gender, children aged 0-19 years, Johnson County compared to Indiana, 1999 to 2013.

	Johnson County			Indiana		
	Males	**Females**	**Total**	**Males**	**Females**	**Total**
All cancer types	59 (53%)	52 (47%)	111	2,620 (52%)	2,444 (48%)	5,065
Common childhood cancers[1]	45 (57%)	34 (43%)	79	1,952 (54%)	1,658 (46%)	3,610

[1] Common childhood cancers include leukemia, brain and other central nervous system tumors, neuroblastoma, Wilms tumor, lymphoma (Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma and bone cancer (including osteosarcoma and Ewing sarcoma).

Rates of Childhood Cancer and SIRs

The incidence rate for all cancers among children aged 0-19 years in Johnson County was 5.4 cases per 100,000 children (Table 2). The incidence rate for Indiana during the same time period was similar: 5.6 cases per 100,000 children. Restricting the analysis to the subset of the most commonly diagnosed childhood cancers, the incidence rate for Johnson County was 4.0 cases per 100,000 children while the incidence rate for Indiana was 3.9 cases per 100,000 children.

Table 2. SIRs for all cancer types and common childhood cancers, children aged 0-19 years, Johnson County compared to Indiana, 1999 to 2013.

| | Age-adjusted Incidence Rate[1] | | Observed/Expected Cases[2] (#) | SIR | 95% Confidence Interval | | p-value |
	Johnson County	Indiana			Lower Limit	Upper Limit	
All cancer types	5.4	5.6	111/107	1.04	0.84	1.23	0.71
Common childhood cancers[3]	4.0	3.9	79/77	1.03	0.80	1.26	0.80

[1] Age-adjusted incidence rates are number of cases per 100,000 children and age-adjusted to the 2000 U.S. Standard Population. This is done to account for differences in the age distribution of the populations of Johnson County and Indiana, which is necessary to make these two rates directly comparable. These rates are not directly comparable to the observed or expected counts.

[2] Expected cases equals the number of cancers that would have been expected to occur if age-specific cancer incidence in Johnson County was equal to age-specific cancer incidence throughout the state of Indiana.

[3] Common childhood cancers include leukemia, brain and other central nervous system tumors, neuroblastoma, Wilms tumor, lymphoma (Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma and bone cancer (including osteosarcoma and Ewing sarcoma).

For all cancer types, the actual number of cases diagnosed between 1999 and 2013 was similar to what was expected (111 cases observed, 107 cases expected, SIR = 1.04, 95% confidence interval = 0.84-1.23). The results were similar for the subset of the most common childhood cancers (79 cases observed, 77 cases expected, SIR = 1.03, 95% confidence interval = 0.80-1.26). Neither SIR indicated a statistically significant difference between the number of cases observed and the number expected. Statistical significance refers to the likelihood that an event has not occurred solely by random chance, and refers only to the process and results of the statistical calculations. It in no way implies any judgment about the importance or significance of cancer (see Technical Notes for more information).

Webb Wellfield

Chemical contamination of the Webb Wellfield was first reported to the Indiana Department of Environmental Management (IDEM) in 1988 during routine compliance sampling for IDEM's Public Water Supply Program of the Office of Water Quality. Cis-1,2-dichloroethene (cis-1,2-DCE) and trans-1,2-dichloroethene (trans-1,2-DCE), both industrial solvents, were detected in two of three supply wells comprising the Webb Wellfield. These compounds are often associated with natural breakdown of more commonly used industrial solvents tetrachloroethene (PCE) or trichloroethene (TCE). Although these contaminants were found in the raw water of the Webb Wellfield, after

processing, the city's drinking water remained safe to drink based on required testing conducted by the Indiana American Water Company in compliance with the Safe Drinking Water Act (§42 U.S.C. 300f et seq.). At no time did the public water supply for the City of Franklin exceed safe drinking water levels established by the United States Environmental Protection Agency (US EPA).

In 2009, the US EPA investigated the Webb Wellfield under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (§42 USC 9601 et seq.) to determine whether conditions qualified it for placement on the National Priorities List (NPL). As part of the evaluation of the site, a CERCLA Preliminary Assessment was conducted in 2010 followed by a CERCLA Site Investigation in 2011, and a CERCLA Expanded Site Inspection in 2012. The culmination of these investigations identified a source of contamination directly east of the former Houghland Tomato Factory, which lies approximately one-half mile southwest of the wellfield. The site was given an Other Cleanup Activity (OCA) designation by the US EPA in 2014, turning authority for the cleanup of the site over to IDEM. The US EPA monitors progress of OCA sites until no further action is required at the state or federal level.

The Houghland Tomato Factory site was assigned to the IDEM State Cleanup Program in March, 2013 and investigations have been on-going since then. The process to determine the depth of ground water contamination (vertical delineation) should be completed early in 2018. To date, the precise source of contamination at the Houghland Tomato Factory has not been identified. Evidence suggests that the source of this contamination reached the Webb Wellfield.

Currently, based on the US EPA's most recent assessment[2], there is "inadequate information to assess the carcinogenic potential" of trans-1,2-DCE and cis-1,2-DCE. This designation is based on a lack of both epidemiologic studies in humans and animal studies to evaluate the carcinogenic potential of these chemicals.

Municipal water suppliers are required to follow federal guidelines to test and treat water to meet established standards set by the Safe Drinking Water Act. For those using well water, current recommendations advise routine private well water testing to detect chemical or biological exposures that could potentially cause adverse health effects. Private well water safety cannot be ensured without appropriate testing. Many factors play a role in the composition (make-up) of the

well water, creating variability among users. Even if well water testing indicates a contaminant, its presence does not prove that it caused cancer.

CONCLUSION

IDOH determined that the criteria for a cancer cluster remained unmet after analyzing available data, reviewing information gathered during interviews, and comparing findings to the established definition of a cancer cluster. The difference between the observed number of childhood cancers (either for all cancer types or for the subset of most common childhood cancers) diagnosed in Johnson County and the number expected during the time period of interest was not statistically significant. At this time, unless the IDOH receives new information that warrants additional review, the investigation is closed.

RECOMMENDATIONS

- Concerned citizens could advocate for and support greater scientific research to help identify causes and risk factors for childhood cancers.
- The local health department could conduct local educational campaigns to promote private well testing to identify exposures to chemicals or bacteria that might contribute to other illnesses.
- The IDOH will update this analysis upon request.

ADDITIONAL INFORMATION AND RESOURCES

For additional information about cancer clusters, visit the CDC "About Cancer Clusters" web page at www.cdc.gov/nceh/clusters/about.htm and/or the NCI "Cancer Clusters" web page at www.cancer.gov/cancertopics/factsheet/Risk/clusters.

For additional information on childhood cancer, visit the ACS "Cancer in Children" web page at www.cancer.org/acs/groups/cid/documents/webcontent/002287-pdf.pdf.

Additional online resources:

- IDOH
  - Guidelines for the Management of Inquiries Related to Cancer Concerns or Suspected Cancer Clusters in Indiana
  - Questions and Answers about Suspected Cancer Clusters
  - Childhood Cancer Fact Sheet
- Indiana Cancer Consortium

- o [Indiana Cancer Facts and Figures 2015](#)
  - o [Childhood Cancer Toolkit](#)
- [Indiana Department of Environmental Management](#)
  - o [Webb Wellfield Fact Sheet](#)
- [Agency for Toxic Substances and Disease Registry](#)
  - o [1,2-Dichloroethene Fact Sheet](#)
- [National Water Quality Monitoring Council](#)
- [Safe Drinking Water Act](#)

Questions or comments regarding this investigation may be directed to Keylee Wright, M.A., Director, Cancer Control Section, for IDOH at 317-234-2945 or kwright@isdh.in.gov.

References

1. The Centers for Disease Control and Prevention and the National Public Health Information Coalition. Cancer Clusters: A Toolkit for Communicators. The National Public Health Information Coalition; 2013, https://www.nphic.org/toolkits/cancer-cluster. Accessed March 20, 2017.

2. United States Environmental Protection Agency. *cis-1,2-Dichloroethylene.* Environmental Protection Agency, 2017, https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=418. Accessed on March 20, 2017.

2018 ADDENDUM

With initial concerns raised about the number of childhood cancer cases diagnosed in Johnson County in 2014 and 2015, IDOH revised this analysis in June 2017 to evaluate a new 15-year cohort ending in 2015 (2001-2015). Currently, the Indiana State Cancer Registry is complete through 2015, meaning that all cases reported as of December 31, 2015, have been verified and have undergone quality control processes to meet registry standards. Table 3 presents the updated age-adjusted cancer incidence rates, observed versus expected numbers of cases, SIRs and 95% confidence intervals for cancers diagnosed among children aged 0-19 years between 2001 and 2015. The incidence rate for all cancer types in Johnson County was 6.1 cases per 100,000 children compared to the incidence rate for Indiana: 5.6 cases per 100,000 children. When restricting to the subset of common childhood cancers, the incidence rate for Johnson County was 4.3 cases per 100,000 children and the rate for Indiana was 3.9 cases per 100,000 children.

Table 3. SIRs for all cancer types and common childhood cancers, children aged 0-19 years, Johnson County compared to Indiana, 2001 to 2015.

| | Age-adjusted Incidence Rate[1] | | Observed/Expected Cases[2] (#) | SIR | 95% Confidence Interval | | *p*-value |
	Johnson County	Indiana			Lower Limit	Upper Limit	
All cancer types	6.1	5.6	123/113	1.09	0.90	1.28	0.37
Common childhood cancers[3]	4.3	3.9	88/80	1.10	0.87	1.33	0.38

[1] Age-adjusted incidence rates are number of cases per 100,000 children and age-adjusted to the 2000 U.S. Standard Population. This is done to account for differences in the age structure of the populations of Johnson County and Indiana, which is necessary to make these two rates directly comparable. These rates are not directly comparable to the observed or expected counts.

[2] Expected cases equals the number of cancers that would have been expected to occur if age-specific cancer incidence in Johnson County was equal to age-specific cancer incidence throughout the state of Indiana.

[3] Common childhood cancers include leukemia, brain and other central nervous system tumors, neuroblastoma, Wilms tumor, lymphoma (Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma and bone cancer (including osteosarcoma and Ewing sarcoma).

For all cancer types, the actual number of cases diagnosed between 2001 and 2015 was similar to what was expected (123 cases observed, 113 cases expected, SIR = 1.09, 95% confidence interval = 0.90-1.28). The results were similar for the subset of the most common childhood cancers (88 cases observed, 80 cases expected SIR = 1.10, 95% confidence interval = 0.87-1.33). While the number of cases observed and expected are higher for 2001 to 2015 than 1999 to 2013, neither SIR indicated a

statistically significant difference between the number of cases observed and the number expected. Statistical significance refers to the likelihood that an event has not occurred solely by random chance, and refers only to the process and results of the statistical calculations. It in no way implies any judgment about the importance or significance of cancer (see Technical Notes for more information). The inclusion of the additional data does not change the findings of the initial investigation.

IDOH also assessed the impact of Trevor's Law on its processes for responding to inquiries related to suspected cancer clusters. On June 22, 2016, 42 U.S.C. §280g-17, also known as Trevor's Law, was enacted. This federal law requires the Secretary of the United States Department of Health and Human Services (HHS) to develop criteria for the designation of cancer clusters, as well as develop, publish, and periodically update guidelines for the investigation of potential cancer clusters. In addition, the law requires that HHS provide assistance to state and local health departments. IDOH's current [guidelines](#) for responding to inquiries related to suspected cancer clusters align with the 2013 [guidelines](#) from the CDC and the Council of State and Territorial Epidemiologists. These guidelines have not changed since the passage of Trevor's Law. IDOH will continue to monitor for new guidance or changes in resources provided by federal partners.

2023 ADDENDUM

With initial concerns raised about the number of childhood cancer cases diagnosed in Johnson County in 2014 and 2015, the Indiana Department of Health (IDOH) revised this analysis in 2018 to evaluate a new 15-year cohort ending in 2015 (2001-2015). It is standard practice at IDOH to revisit cancer cluster investigations when a new year of data becomes available in the Indiana State Cancer Registry due to the lag time that occurs with the registry to continue to assess the amount of cancer in the area of concern. Currently, the Indiana State Cancer Registry is complete through 2019, meaning that all cases reported as of December 31, 2019, have been verified and have undergone quality control processes to meet registry standards. Considering recent questions from members of the public into the Indiana State Cancer Registry's processes into collecting cancer data, a review of the processes of the Indiana State Cancer Registry is necessary.

In 1986, a law was passed to start the Indiana State Cancer Registry and mandated that beginning in January 1987 all reportable cancers must be reported to the Indiana State Cancer Registry. This means that since 1987 the Indiana State Cancer Registry has collected every single case of cancer from a variety of hospitals, clinics, labs, and other entities. This database is extremely extensive with data that covers the patient from first diagnosis of cancer through death. Information on patient demographics, diagnosis data, treatment information is collected, in addition to information about any additional or reemergence cancer diagnosis and cause of death information.

The cancer registry staff works to collect this data from each entity, perform extensive quality control and review of the data to ensure accuracy and completeness, work with Vital Records to identify and record if any patients have passed away, and finally prepare the data for analysis by the cancer epidemiologist and appropriate dissemination to researchers and concerned public. The Indiana State Cancer Registry also has agreements with other state registries to ensure the completeness of the cancer registry regardless of where the cancer patient received a diagnosis, treatment, or passed away. This ensures that the Indiana State Cancer Registry represents all Hoosiers' cancer patient data. Unfortunately, due to the time that it takes to receive data for each case from each entity, the time for quality control, and for analysis, cancer registries are known nationally to have a time lag, which is why it's ensured that review investigation analysis continues as a new year of data becomes available.

The CDC reviewed the findings from the initial investigation. While the CDC agreed that the inquiry in question did not support further investigation, it shared recommendations for future analyses, such as not including overall cancer analysis and continuing to monitor Indiana cancer registry data for new cases and calculate updated SIRs as new data becomes available. These changes are also in accordance with the updated guidance document from the CDC titled Guidelines for Examining Unusual Patterns of Cancer and Environmental Concerns that were updated in 2022. IDOH's current guidelines for responding to inquiries related to suspected cancer clusters continue to align with these newest 2022 guidelines from the CDC and the Council of State and Territorial Epidemiologists. The new guidelines allow for a larger focus on the environmental concerns related to cancer inquiries and push for environmental investigation and data review even if the analysis of the available cancer data does not show statistically significant results. Our current process had already been conducting this environmental investigation and data review regardless of statistically significant results.

The one larger aspect that IDOH changed in accordance with the new guidelines is to provide the initial inquirer with a short report of the analysis and investigation done at the conclusion of our investigation. The IDOH cancer section partners with IDOH's Environmental Health Division and the Indiana Department of Environmental Management (IDEM) on a cancer cluster inquiry work team that meets biweekly to review and investigate any pending inquiries or concerns. When a new inquiry comes in from a concerned member of the public, the cancer section goes through an initial investigation questionnaire and review of available cancer data. While this is done the division of Environmental Health reviews environmental contaminants or concerns that could be related to the cancer of concern. IDEM investigates the area of the concern and environmental sites. This team works together throughout the investigation to look at all sides of possible cancer clusters. Regarding this specific concern, IDOH worked closely with the Indiana Department of Environmental Management to provide its services to the Franklin Community. IDEM conducted environmental investigations in the targeted area to complement the IDOH Cancer Assessment. Details of IDEM's environmental activities and findings can be found at this link IDEM: Environmental Cleanups: Franklin IN.

Table 4 presents the updated observed versus expected numbers of cases, SIRs and 95% confidence intervals for cancers diagnosed among children aged 0-19 years since the last addendum of this report. In its review of the initial investigation, the CDC shared that the definition of a cancer cluster should include only "cancers of the same type, known to be related to one another, or scientifically proven to have the same cause," instead of all or common childhood cancers. Thus, the investigation could have been closed prior to further investigation or completion of this initial report as the cancers of concern did not meet that definition. For the purpose of this addendum, the same childhood cancers are included in this analysis for consistency. As can be seen in this table, IDOH has continued to perform the analysis of this concern due to the nature of the registry data being behind to ensure nothing was missed.

Table 4. SIR for Common childhood cancers[3], children aged 0-19 years, Johnson County, and Indiana

	Observed/Expected Cases[2] (#)	SIR	95% Confidence Interval Lower Limit	Upper Limit	*p*-value
2002-2016	74/69	1.1	0.83	1.32	0.54
2003-2017	79/70	1.1	0.89	1.40	0.26
2004-2018	84/70	1.2	0.94	1.45	0.13
2005-2019	85/71	1.2	0.94	1.45	0.12

[1] Age-adjusted incidence rates are number of cases per 100,000 children and age-adjusted to the 2000 U.S. Standard Population. This is done to account for differences in the age structure of the populations, which is necessary to make these two rates directly comparable. These rates are not directly comparable to the observed or expected counts.

[2] Expected cases equals the number of cancers that would have been expected to occur if age-specific cancer incidence in Johnson County was equal to age-specific cancer incidence throughout the state of Indiana.

[3] Common childhood cancers include leukemia, brain and other central nervous system tumors, neuroblastoma, Wilms tumor, lymphoma (Hodgkin and non-Hodgkin), rhabdomyosarcoma, retinoblastoma and bone cancer (including osteosarcoma and Ewing sarcoma).

Regarding common childhood cancer, the actual number of cases diagnosed between 2005 and 2019 (the most recent years available) were similar to the last iteration of this report and were not significantly different to what was expected (85 cases observed, 71 cases expected, SIR = 1.2, 95% confidence interval = 0.94-1.45). While the number of cases observed and expected are higher for 2005-2019 compared to previous years, the ratio is similar with none of the SIRs indicating a statistically significant difference between the number of cases observed and the number expected.

The cancer incidence rates between Johnson County and Indiana were also not statistically significantly different from one another in this iteration. Statistical significance refers to the likelihood that an event has not occurred solely by random chance, and refers only to the process and results of the statistical calculations. It in no way implies any judgment about the importance or significance of cancer (see Technical Notes for more information). The inclusion of the additional data does not change the findings of the initial investigation.

TECHNICAL NOTES

Age-adjusted rates: The rates of almost all causes of disease, injury, and death vary by age. Age adjustment is a technique to reduce the effects of age on crude or raw cancer rates. This allows comparisons across groups of people of different ages. For example, comparing the crude rate of heart disease in Florida with that of California is misleading, because the older population in Florida leads to a higher crude death rate. For such a comparison, age-adjusted rates are better. All mortality and incidence rates in this publication were age-adjusted using the direct method. This method weights the age-specific rates (i.e., rates calculated for each age group) for a given sex, race, or geographic area by the age distribution of the standard population. The 2000 United States standard million population and five-year age group population numbers were used to calculate all the age-adjusted rates in this report.

Confidence interval: A confidence interval is a measure of how precise a number is in a statistical study. Statistics help people estimate actual numbers. In a statistical study, confidence intervals are usually set at 95%. For example, suppose investigators find an age-adjusted breast cancer rate in a town of 10 cases per 1,000 women, with a confidence interval of plus or minus five. This means that the number of cases could range from 5 (i.e., 10 minus 5) to 15 (i.e., 10 plus 5). That indicates a 95% chance that the rate is between 5 and 15 and a 5% chance that the rate is below 5 or above 15. The confidence interval is a reminder that there is always a possibility that findings are due to chance. However, a larger sample size produces more accurate and reliable findings.

SIR : SIR stands for *standardized incidence ratio*. The SIR is the number of observed cases divided by the number of expected cases of a given disease. The expected number is the number of cases that would occur in a community if the disease rate in a larger reference population (like a county, state,

or country) occurred in that community. An SIR over 1 indicates a higher-than-expected number of cases, an SIR of 1 indicates the number of cases is what would be expected, and a SIR below 1 indicates the number of cases is less than expected. For instance, an SIR of 1.2 would indicate 20% more reported cases within the study population than expected. To determine statistical significance, 95% confidence intervals are calculated to provide the upper and lower boundaries within which the true observed ratio might fall. The SIR is not statistically significant if the confidence interval around the SIR includes 1.0.

Statistically significant : Another step in evaluating whether the number of observed cases is higher than what would be expected is to evaluate whether the difference between these two numbers is statistically significantly different. The term "statistical significance" refers only to the process and results of the statistical calculations and in no way implies any judgment about the importance or significance of cancer. For more information, please see the current [guidelines] for investigating suspected cancer clusters and responding to community concerns from the CDC and the Council of State and Territorial Epidemiologists.