



Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

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Dear Dr. Collier,

This technical review was prepared by the National Center for Environmental Health, Division of Environmental Health Science and Practice in response to your July 20, 2018 letter requesting CDC's review of the December 2017 Indiana State Department of Health (ISDH) report titled "Findings of a Cancer Inquiry Investigation Johnson County, Indiana 2015–2017." In addition to a technical review, we compared the approach described in the ISDH report to the 2013 CDC/CSTE Guidelines for Investigating Suspected Cancer Clusters and Responding to Community Concerns (MMWR 2013). This letter summarizes the findings of CDC's review.

During the initial contact and response phase of the investigation, ISDH noted that the concern from citizens and media was of a higher than normal number of childhood cancers in Johnson County since 2010. CDC defines 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." By definition, the cancer cases under investigation should all be of the same type, known to be related to one another, or scientifically proven to have the same cause. The broad categories of "childhood cancers" and "common childhood cancers" do not meet the 2013 CDC/CSTE definition of a suspected cancer cluster because the different cancer types included in these categories are not known to be related to one another and are unlikely to share a common, environmental etiology. According to the CDC/CSTE Guidelines, the investigation could have closed at this point because the factors presented during step 1 did not support further investigation into a suspected cancer cluster.

CDC concurs with the methods and conclusions described in the ISDH report, but offers the following comments for your consideration:

1. ISDH calculated a standardized incidence ratio (SIR) for "all cancer types" and for "common childhood cancers" comparing Johnson County to the rest of Indiana. As stated in the CDC/CSTE Guidelines, calculating an all-cancer SIR is not useful for exploring potential etiologies but can be useful for health communication and educational purposes. ISDH should clearly communicate the limitations of an all-cancer SIR for investigating suspected cancer clusters and explain why SIRs for specific pediatric cancer types were not calculated or presented.
2. Although the conclusions and interpretation of the SIR statistical significance in the ISDH are correct, the description of SIR statistical significance in the Technical Notes section of the report contains errors. Specifically, the statements "If the SIR falls within the

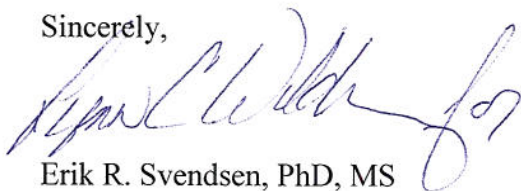
confidence interval, it is not significant” and “A SIR falling within the confidence interval would not be statistically significant” are incorrect and should be revised to indicate that the SIR is not statistically significant if the confidence interval around the SIR includes 1.0. We recommend deleting the first mention and revising the second mention highlighted in grey below.

~~“If the SIR falls within the confidence interval, it is not significant. For instance, a SIR of 1.2 would indicate 20% more reported cases within the study population than expected. In order to figure out significance, 95% confidence intervals are calculated to provide the upper and lower boundaries within which the true observed ratio might fall. A SIR falling within the confidence interval would not be statistically significant and considered to be the same as what would be expected.”~~

CDC is aware that additional investigations of environmental contamination have been initiated in Johnson County since the publication of the ISDH report in 2017. CDC recommends that if those investigations find evidence of community exposure to chemical contaminants that are potential risk factors for pediatric cancer, that ISDH compare incidence data (calculate SIRs) for those specific pediatric cancer types. To address small sample sizes, it is appropriate to combine rare cancers that are related to one another or that share a common cause. In addition, CDC recommends that ISDH consider three additional actions for future analyses. First, consider using other geographic boundaries that more closely align with known or suspected routes of exposure to environmental contaminants (e.g., city of Franklin boundaries could be used if municipal water supply is a suspected route of exposure). Second, if data are available, review longer-term historical trends in pediatric cancer incidence rates (overall and for specific cancer types) to determine whether local and state rates are increasing or decreasing over time. Third, continue to monitor Indiana cancer registry data for new cases of pediatric cancer in Johnson County and calculate updated incidence rates and SIRs when new data become available.

Please let us know if you have any questions or would like to discuss the items included in this technical review. As stated in previous correspondence, CDC and ATSDR staff will continue to provide technical assistance to ISDH as requested.

Sincerely,



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cc: Pam Protzel-Berman, NCEH/ATSDR
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