Ewing's Family of Tumors, Childhood Cancer and Total Cancer Standard Incidence Ratio Results for Washington, Fayette, Greene and Westmoreland Counties in Pennsylvania

Bureau of Epidemiology, Division of Community Epidemiology

March 2020

pennsylvania
DEPARTMENT OF HEALTH

Executive Summary

Background

Since 2018, the Pennsylvania Department of Health (department) has been responding to resident concerns regarding cancer concerns in Westmoreland and Washington counties, specifically focusing on childhood cancers, Ewing's family of tumors (hereinafter referred to as 'Ewing's tumors' in this document) and overall cancer rates, as well as the potential role of select environmental exposures in causing cancer.[1]

Ewing's tumors are a group of malignant tumors that occur in bones or soft tissues, such as cartilage or nerves. Studies of children with Ewing's tumors have not found links to radiation, chemicals or other environmental exposures. It occurs most often in individuals who are between 10 and 20 years old, in males more than in females, and is more common among whites than in other ethnic groups.[2]

Nationally, childhood cancer rates have been rising slightly for the past few decades,[2] and cancer is the leading cause of death by disease past infancy.[3] In 2018, it was estimated that nationally 15,590 children and adolescents ages 0 to 19 would be diagnosed with cancer and 1,780 would die of the disease.[3] Familial and genetic factors are identified in 5 to 15% of childhood cancer cases. In less than 10% of cases, there are known environmental exposures and exogenous factors, such as prenatal exposure to tobacco, X-rays, or certain medications. However, for the remaining 75 to 90% of cases, the causes remain unknown.[4, 5]

This report is a supplementary analysis to the department's original report "Ewing's Family of Tumors, Childhood Cancer and Radiation-Related Cancer Incidence Review for Washington County and Canon-McMillan School District in Pennsylvania," published in April 2019.

Feedback from an October 10, 2019, community meeting at Canon-McMillan School District further emphasized the importance of conducting this analysis. This review allowed for a deeper look at the number of cancer cases in the southwestern part of the state compared to statewide cases to determine if there are any persistent or abnormally high (or statistically significant) increases in this area.

Key Questions

As follow-up to the 2019 report, the department sought to provide more information to the community for the following questions related to cancer and fracking:

- What are the number of cancer cases (overall, childhood, and Ewing's tumors) in each of the four counties and the area overall? Is this area experiencing an increase in cancer rates?

- Compared to the rest of the state, is the four-county area experiencing a higher proportion of childhood cancers as a proportion of all cancers?

- Considering the entire state, is the rate of childhood cancer in counties with fracking higher than in counties without fracking?

- Considering the entire state, is the rate of Ewing's tumors in counties with fracking higher than in counties without fracking?

- If you analyze the cancer data annually, do fracking counties have a higher rate of childhood cancer or Ewing's tumors than non-fracking counties?

Key Findings

The department's source for cancer data is the Pennsylvania Cancer Registry. By law all health care providers diagnosing or treating cancer patients are required to report those cases to the registry. The Pennsylvania Cancer Registry started receiving data in 1984, and 1985 was the first year the registry received completed data from all facilities. This analysis used cancer incidence data reported to the registry, as well as estimated population data by school district and county from the U.S. Census Bureau. Cancer data were analyzed for three time periods: 1985−1994; 1995−2004; and 2005−2017. These three time periods were used to assess trends over time.

Key findings from a review of this data include:

- Childhood cancer rates, as well as overall cancer rates, were similar to or lower than the rest of state rates for all three time periods. However, there were some exceptions. There was a slightly higher rate of female childhood cancers from 1985-1994 in Washington County when compared to the rest of the commonwealth. Ewing's tumors in females also were higher in the four-county area from 2005-2017, and higher in females in Westmoreland County for the 1995-2004 and 2005-2017 time periods as well as overall in 1995 to 2004 when compared to the rest of the commonwealth.

- Childhood cancer in the four-county area was found to be a lower proportion of all cancers than is seen for the rest of the state.

- Although the all childhood cancer rate was slightly higher in fracking counties than in other counties, the elevation was not statistically significant.

- Although the rate of Ewing's tumors was slightly higher in fracking counties than non-fracking counties, the difference also was not statistically significant.

- Annual trends of age-adjusted all childhood cancer and Ewing's tumor incidence rates are very similar between fracking and non-fracking counties, with no notable differences.

Next Steps

We know that in terms of dealing with cancer, one case is too many for those who are affected by it. Cancer can be a very serious illness that can take a toll on the individual, their family and the entire community's lives. The treatment for cancer can be difficult and the prognosis, unfortunately, may not always be good. We know that there are many concerned parents, friends,

family members and loved ones who are concerned about what may be causing the Ewing's tumors and other childhood cancers in southwestern Pennsylvania.

The department is committed to working with the community on this issue and will continue to monitor the data for Ewing's tumors and childhood cancers in the area over the next several years as more data become available.

In the next few years, we will advance two research studies in partnership with an academic center. These studies will run concurrently and add, in different ways, to existing scientific literature.

One project will be a case control study of childhood cancers, including Ewing's tumors, in response to concerns raised about the prevalence of rare cancers in the southwestern area of the state, and will use data from the cancer registry and cancer referral centers to determine characteristics of cancer cases and to also gather data from cases controls through interviews. This study is designed to explore if those being diagnosed with Ewing's tumors or childhood cancers are more often exposed to fracking than controls.

The other study will look at acute conditions, such as asthma and birth outcomes, that have previously showed some relationship to certain industries in existing published research. Doing this specifically in Southwestern Pennsylvania will serve to potentially replicate study findings from other regions using similar methodology and will greatly add to the understanding of the potential health effects related to natural gas development. Replication of prior findings in a different population is one of the steps that strengthen the confidence in existing findings.

The anticipated cost of both studies is approximately $1 million per year for three years. More precise funding details will be known once an agreement with the academic center is executed.

Methods

The Pennsylvania Cancer Control, Prevention and Research Act of 1980 and the Pennsylvania Department of Health's regulations concerning reporting of communicable and noncommunicable diseases require all health care providers diagnosing or treating cancer patients to report those cases to the Pennsylvania Cancer Registry (PCR). Cancer data are reported by hospitals, clinics, laboratories, radiation facilities, cancer centers, surgical centers, doctor's offices, death certificates, and through data exchange when Pennsylvania residents are diagnosed or treated in other states. The Pennsylvania Cancer Registry started receiving data in 1984, and 1985 was the first year the registry received completed data from all facilities. This analysis used cancer incidence data reported to the PCR, as well as estimated population data by school district and county from the U.S. Census Bureau.

Ewing's family of tumors, which is being referred as "Ewing's tumors" in this report are defined as any cancer diagnosis with histologic/behavior codes of:

1. 9260/3 (Ewing sarcoma) -- not limited by primary site;
2. 9364/3 (Peripheral neuroectodermal tumor/pPNET) -- all primary sites except C70.0-C72.9 (including sites in the brain, meninges, spinal cord, cranial nerves and other parts of the central nervous system);
3. 9473/3 (Primitive neuroectodermal tumor, NOS) -- all primary sites except C70.0-C72.9 (including sites in the brain, meninges, spinal cord, cranial nerves and other parts of the central nervous system); and
4. 9365/3 (Askin tumor).

This definition is based on the Stanford University School of Medicine surgical pathology criteria and is referenced on the National Cancer Institute's website in the SEER Inquiry System, question: 20160028.[6, 7]

Childhood cancer is defined as cancers in children diagnosed between 0 and 19 years of age using the International Classification of Childhood Cancer (ICCC) variables, which includes ICD-O-3 site, ICD-O-3 histology and ICD-O-3 behavior codes for grouping. All cancers occurring in this age group were included as childhood cancer. Childhood cancer sub-group analyses were not performed due to the small incidence counts.

The category of "all cancers" is defined as all cancers reported to the Pennsylvania Cancer Registry regardless of topography, histology and behavior codes. We included the "all cancer" age-adjusted standardized incidence ratios (SIRs) in this analysis, so that the readers can see the overall cancer rate change compared to the rest of the state. We also included the "all cancer" ratios in the calculation of the proportion of a specific cancer over all cancers. The proportion of a specific cancer over all cancers were not calculated in this analysis.

Cancer data were analyzed for three time periods: 1985−1994; 1995−2004; and 2005−2017. These three time periods were used to assess cancer incidence trends over time. This analysis used the mid-time period census population (1990, 2000 and 2010 census data) for age-adjustment. Age-adjusted standardized incidence ratios for cancers and their 95% confidence intervals (CIs) for Washington County, Westmoreland County, Fayette County, Greene County,

and the four counties combined were calculated, respectively, by gender to determine whether the residents experienced a statistically significant excess of cancer incidence compared to the rest of the Pennsylvania population. SIRs were calculated as the ratios of the number of cancer cases observed in residents in Washington County, Westmoreland County, Fayette County, Greene County, and the four counties combined during the three time periods, compared to the number of cases expected in that population if the county were experiencing the same age- and sex-specific cancer incidence rates as a reference area (the rest of Pennsylvania). An SIR greater than 1.0 indicates more cancer cases occurred than expected. An SIR is considered statistically significant if the 95% CI does not include 1.0.

The proportion of childhood cancer over all cancers is calculated using the total number of cancer cases diagnosed among those residents less than 20 years of age divided by the total number of cancer cases among all age groups diagnosed in the year. The proportion trend is graphed, and the trend evaluated.

In this analysis, we also compared age-adjusted all childhood cancers and childhood Ewing's tumors incidence rate trends between counties with and without unconventional gas production. Allegheny, Armstrong, Beaver, Blair, Bradford, Butler, Cameron, Centre, Clarion, Clearfield, Clinton, Crawford, Fayette, Forest, Greene, Huntingdon, Indiana, Jefferson, Lycoming, McKean, Mercer, Potter, Somerset, Sullivan, Tioga, Venango, Warren, Washington, Westmoreland and Wyoming counties are defined as fracking counties, and the rest of the counties in the state are defined as non-fracking counties.[8] Age-adjusted all childhood cancer and Ewing's tumors incidence rates for the time periods 2005-2017 between fracking counties and non-fracking counties were compared using direct age-adjustment with the 2000 U.S. standard population. We also used the segmented regression analysis of interrupted time-series method to estimate the changes in the level and trend in all childhood cancers and childhood Ewing's tumors age-adjusted incidence rates pre- and post-2005 (which is the boom year for unconventional gas production in Pennsylvania).[9] We also explored ratios of childhood cancer over all cancers and Ewing's tumors over all childhood cancers between fracking and non-fracking counties. SAS software version 9.4 (SAS Institute Inc., Cary, North Carolina) was used for all the statistical analyses. The Hosmer-Lemeshow test was used for autoregressive model fit diagnosis. A two-sided P-value of less than 0.05 was considered significant.

One Ewing's tumors case was reported with both address at diagnosis and current address in Westmoreland County. Upon further investigation with the diagnosing hospital and the patient's family, PCR corrected the patient's address to Washington County instead of Westmoreland County. This represents a change from the original report "Ewing's Family of Tumors, Childhood Cancer, and Radiation-Related Cancer Incidence Review for Washington County and Canon-McMillan School District in Pennsylvania, April 2019."

Results

All results below are organized according to the five questions in the Executive Summary with tables and figures following the text in pages 11-14.

Question 1. What are the number of cancer cases (overall, childhood, and Ewing's tumors) in each of the four counties and the area overall? Is this area experiencing an increase in cancer rates?

Summary Answer 1. Childhood cancer rates, as well as overall cancer rates, were similar to or lower than state rates for all three time periods (1985-1994, 1995-2004, 2005-2017). Exceptions to this occurred in Washington County where there was a higher rate of female childhood cancers in the earliest time period, and a slightly higher rate of overall cancer rates among females during 1995-2004. Ewing's tumors were higher in the four-county area, specifically among females, for the most recent time period. For Westmoreland County, Ewing's tumors were also higher females for the 1995-2004 and 2005-2017 time periods and overall in the 1995-2004 period. Fayette, Greene and Washington rates for Ewing's tumors were no different than state rates. Details are below.

Results for the Four County area (Table 1)

- Ewing's Family of Tumors (Ewing's tumors) incidence:
  - There were more Ewing's tumors incident cases in the recent time period than the earlier time periods. The Ewing's tumors incidence rate for females was 84% (SIR = 1.84, 95% CI: 1.05, 2.98), higher than the rest of the state in the most recent time period. However, Ewing's tumors incidence rates for both males and females were lower than the rest of the state in the 1985-1994 time period and were not statistically significant.
- Childhood cancer incidence:
  - Both male and female childhood cancer incidence rates were not statistically significantly different from the rest of the state during any of the three time periods.
- All cancers (children plus adults) incidence:
  - Both male and female incidence rate for all cancers were statistically significantly lower than the rest of the state during all three time periods.

Results for Fayette County (Table 2)

- Ewing's Family of Tumors (Ewing's tumors) incidence:

    - There were more Ewing's tumors incident cases in the recent time period than the earlier time periods, but Ewing's tumors incidence rates for both males and females were not statistically significantly different from the rest of the state during any of the three time periods.
- Childhood cancer incidence:
    - Both male and female childhood cancer incidence rates were not statistically significantly different from the rest of the state during any of the three time periods.
- All cancers (children plus adults) incidence:
    - 1985-1994: The male incidence rate for all cancers was 3% (SIR = 0.97, 95% CI: 0.94, 0.99) lower than the rest of the state, but the female incidence rate for all cancers was not statistically significantly different from the rest of the state.
    - 1995-2004: The female incidence rate for all cancers was 7% (SIR = 0.93, 95% CI: 0.91, 0.96) lower than the rest of the state, but the male incidence rate for all cancers was not statistically significantly different from the rest of the state.
    - 2005-2017: The female incidence rate for all cancers was 4% (SIR = 0.96, 95% CI: 0.93, 0.98) lower than the rest of the state, but the male incidence rate for all cancers was not statistically significantly different from the rest of the state.

Results for Greene County (Table 3)

- Ewing's Family of Tumors (Ewing's tumors) incidence:
    - The Ewing's tumors incidence rates for both males and females were not statistically significantly different from the rest of the state during any of the three time periods.
- Childhood cancer incidence:
    - There were more childhood cancer incident cases for both males and females in the most recent time period (2005-2017) than earlier time periods.
    - The female childhood cancer incidence rate was 63% (SIR = 0.37, 95% CI: 0.10, 0.95) lower than the rest of the state in the 1985-1994 time period.
- All cancers (children plus adults) incidence:
    - 1985-1994: The incidence rate for all cancers (children plus adults) was statistically significantly lower for males, females and combined.
    - 1995-2004: The incidence rate for all cancers (children plus adults) was statistically significantly lower for males and combined but not statistically different from the rest of the state for females.
    - 2005-2017: The incidence rate for all cancers (children plus adults) combined was statistically significantly lower for males and combined but not statistically different from the rest of the state for females.

Results for Washington County (Table 4)

- Ewing's Family of Tumors (Ewing's tumors) incidence:

    - There were more Ewing's tumors incident cases in the recent time period than the earlier time periods, but Ewing's tumors incidence rates for both males and females were not statistically significantly different from the rest of the state for all three time periods.
- Childhood cancer incidence:
    - The female childhood cancer incidence rate was 34% (SIR = 1.34, 95% CI: 1.03, 1.71) higher than the rest of the state in the 1985-1994 time period; however, this rate decreased during the 1995-2004 and 2005-2017 time periods and was not statistically significantly different from the rest of the state in those same periods.
    - The male and combined childhood cancer incidence rates were not statistically significantly different from the rest of the state during any of the three time periods.
- All cancers (children plus adults) incidence:
    - 1985-1994: The incidence rate for all cancers (children plus adults) was statistically significantly lower for males, females and combined.
    - 1995-2004: The incidence rate for all cancers (children plus adults) combined in Washington County was slightly higher (SIR = 1.03, 95% CI: 1.01, 1.05) than the rest of the state for females but slightly lower for males (SIR=0.98, 95% CI: 0.96, 1.01).
    - 2005-2017: The incidence rate for all cancers (children plus adults) combined was slightly lower for males (SIR=0.98, 95% CI: 0.96, 0.99) but not statistically different from the rest of the state for females or combined.

Results for Westmoreland County (Table 5*)*

- Ewing's Family of Tumors (Ewing's tumors) incidence:
    - The Ewing's tumors incidence rates for females were statistically significantly higher than the rest of the state during the 1995-2004 time period. The Ewing's tumors incidence rate for females was also statistically significantly higher than the rest of the state during the 2005-2017 time period, but not for males. There were more Ewing's tumors incident cases for females in the recent two time periods than during the 1985-1994 time period.
    - The Ewing's tumors incidence rates for both males and females were lower than the rest of the state in the 1985-1994 time period and were not statistically significant.
- Childhood cancer incidence:
    - Both male and female childhood cancer incidence rates were not statistically significantly different from the rest of the state during any of the three time periods.
- All cancers (children plus adults) incidence:
    - Both male and female all cancers incidence rates were statistically significantly lower than the rest of the state during all three time periods except for the incidence rate among males in the 1985-1994 time period.

Question 2. Compared to the rest of the state, is the four-county area experiencing a higher level of childhood cancers as a proportion of all cancers?

Summary Answer 2: No, childhood cancer in the four-county area was found to be a lower proportion of all cancers than is seen statewide. Details are below.

Results for the proportion of childhood cancer over all cancer yearly trend (Figure 1)

- The percentage of childhood cancer over all cancer is generally lower in the four-county combined area than the rest of the state in most of the years. The yearly linear trend is also similar which indicates that the four-county area is not experiencing more childhood cancer as a proportion of all cancers than the rest of state in recent years.

Question 3. Considering the entire state, is the rate of childhood cancer in counties with fracking higher than in counties without fracking?

Summary Answer 3. Although the all childhood cancer rate was slightly higher in fracking counties than in other counties, the elevation was not statistically significant. Details are below.

Detailed results for age-adjusted childhood cancers and childhood Ewing's tumors incidence rate trends between counties with and without fracking. Additionally, results for the ratio of childhood cancer over all cancers and Ewing's tumors over all childhood cancer between fracking and non-fracking counties analysis is summarized below:

- The age-adjusted all childhood cancers incidence rate was slightly higher in fracking counties than in non-fracking counties (21.1 vs. 20.6 per 100,000 population) for the time period 2005-2017 but was not statistically different. The estimated rate ratio is 1.02 with a confidence interval of 0.98, 1.07. (Figure 2)
- The age-adjusted childhood Ewing's tumors incidence rate was slightly higher in fracking counties than in non-fracking counties (0.52 vs. 0.42 per 100,000 population) for the time period 2005-2017 but was not statistically different. The estimated rate ratio is 1.02 with a confidence interval of 0.98, 1.07. (Figure 3)

Question 4. C**onsidering the entire state, is the rate of Ewing's tumors higher in counties with fracking than in counties without fracking?**

Summary Answer 4. Although the rate of Ewing's tumors was slightly higher in fracking counties than counties without fracking, the difference was also not statistically significant. Details are below.

Detailed results for yearly linear trends for childhood cancers are below:

- The yearly linear trend of the age-adjusted all childhood cancers incidence rates between fracking and non-fracking counties was similar. There were no age-adjusted all childhood cancer cancers incident rate changes between the two areas before and after 2005. (Figure 4)

Question 5. If you analyze the data annually, do counties with fracking have higher a higher rate of childhood cancer or Ewing's tumors than counties without fracking?

Summary Answer 5. Cancer incident trends were compared between fracking and non-fracking counties and there were no notable differences. Details are below.

Detailed results for yearly linear trends for Ewing's tumors and other yearly comparisons are below:

- The yearly linear trend of the age-adjusted childhood Ewing's tumors incidence rates between fracking and non-fracking counties was similar. There was no age-adjusted childhood Ewing's tumors incident rate changes between the two areas before and after 2005. (Figure 5)
- The linear trend of the ratios of childhood cancer over all cancers diagnosed in counties with fracking activities was similar to the linear trend of the ratios of childhood cancer over all cancers in counties without fracking activities from 1985 to 2017. (Figure 6)
- The linear trend of the ratios of childhood Ewing's tumors over all childhood cancers diagnosed in counties with fracking activities was slightly steeper than the linear trend of the ratios of childhood Ewing's tumors over all childhood cancers in counties without fracking activities from 1985 to 2017, but this difference was not statistically significant. (Figure 7)

Limitations

This analysis has several limitations. First, cancer is not just one disease, but a collection of a complex group of diseases with many possible causes. Different cancers will have different causes and risk factors. Childhood cancer includes many different types of subgroups. We could not analyze those subgroups individually due to an extremely small number of cases. However, analysis of all childhood cancers provides the ability to assess elevations in childhood cancers overall but may mask subgroup differences.

In addition, people may migrate from one location to another, from one state to another, or even from one country to another, and, therefore, it becomes difficult to find the source of exposure that may have caused a particular cancer. This is true for childhood cancer evaluation, since we do not usually know the parents' migration and environmental exposure histories. Cancers diagnosed in Pa. residents are only reported to the PCR. Diagnoses made after the individual moved out of state may not be included in the PCR. Likewise, diagnoses made to people who have recently moved into the commonwealth (with exposures happening elsewhere) will be included in the PCR.

An additional limitation is that a simple SIR calculation does not test for associations between risk factors and disease outcomes. It is an assessment of whether what you observe is more or less than what you would expect in a population. It does not provide cause-effect association.

Furthermore, using SIRs in cluster analysis has its own inherent issues, especially in small geographic areas and/or sparsely populated areas. Most of the SIRs in this report were calculated based on a small number of cases. Thus, stability of the SIRs should be considered when interpreting those results, especially for those SIRs calculated based on a small number such as five or less observed or expected cases.

Finally, even with a statistically significant SIR in one area or time period, statistical significance could still be caused by chance alone. For example, if the probability of observing a higher SIR in one county in Pennsylvania is 1% (which is extremely low), the probability of observing a statistically significantly higher SIR in at least one county among all 67 counties in Pennsylvania could be as high as 49 percent. If the probability of observing a higher SIR in one time period is 5%, there could still be as high as a 14.3% chance of seeing one higher SIR among the three time periods. Thus, extreme caution should be exercised when interpreting SIRs in this report.

The proportion of childhood cancer over all cancers trend is assumed to be linear for this analysis.

As mentioned in the methods section, there was one Ewing's tumors case reported with both an address at diagnosis and a current address in Westmoreland County; this was later determined to be a Washington County resident as a result of hospital and family member input. The PCR relies solely on hospitals and reporting physicians to use their best judgement inputting accurate addresses at diagnosis. There could be other cases with the address at diagnosis listed incorrectly in the PCR.

Conclusions

The all cancer incidence rates and childhood incidence rates in the all four counties combined area is similar or slightly lower than the rest of the state during the time periods 1995-2004 and 2005-2017. The Ewing's tumors incidence rate in the four-county combined area is higher than the rest of the state during the last two time periods but not statistically different from the rest of the state. The female Ewing's tumors incidence rate reached statistical significance during 2005-2017. This is mostly driven by a higher than expected number of cases in Fayette County and especially Westmoreland County. The Ewing's tumors incidence rates in Washington County and Greene County were lower than the rest of the state during the last time period of 2005-2017. The Ewing's tumors incidence rate in Westmoreland County was 64% higher overall than the rest of the state in the 2005-2017 time period and was statistically significant based on a total number of 17 cases during the 13-year time frame. However, the Ewing's tumors incidence rate in Westmoreland County in 2005-2017 was lower than the prior time period of 1995-2004 (SIR of 2.07 in 1995-2004 vs. 1.64 in 2005-2017). In summary, Westmoreland County experienced an elevated rate of Ewing's tumors for the last two consecutive time periods..

The proportion of childhood cancer over all cancers yearly trend in the four-county area is similar to the rest of the state.

All childhood cancer incidence was evaluated in this analysis, but no individual childhood cancer types were analyzed. Even though the causes of childhood cancer have been systematically studied for several decades, apart from high-dose radiation and prior chemotherapy, there are few strong external risk factors.[10] On the other hand, inherent risk factors including birth weight, parental age and congenital anomalies are consistently associated with many types of pediatric cancer.[10, 11] The types of cancers children more commonly develop are often different from the types of cancers which develop in adults. Childhood cancers are not thought to be strongly linked to lifestyle or environmental risk factors.

In conclusion, age-adjusted childhood cancer rates and age-adjusted childhood Ewing's tumors incidence rates were slightly higher for the time period of 2005-2017 in fracking counties vs. non-fracking counties, but the difference was small and did not reach statistical significance. Yearly trends for the age-adjusted childhood cancer incidence rates and childhood Ewing's tumors incidence rates were similar between fracking and non-fracking counties.

The childhood cancer incidence rates in the four-county area were similar to the rest of the state and were not elevated in any of the three time periods evaluated. The linear trend of the ratios of childhood cancer over all cancers and the ratios of childhood Ewing's tumors over all childhood cancer in counties with fracking activities were similar to those in counties without fracking activities from 1985 to 2017.

The Ewing's tumors incidence rate in the four-county area was elevated for the time period 2005-2017 but not statistically significantly elevated (except among females), and the Ewing's tumors incidence rates fluctuated among the four counties and over the time period. Only Westmoreland county showed an elevation for Ewing's tumors in the two latter time periods (total and for females, but not for males). No environmental causes are known to be associated with Ewing's

tumors. This analysis was not designed to evaluate an environmental association but, given the fluctuation in rates and with no consistent patterns in each of the four counties, it does not strongly suggest a common environmental exposure. In addition, analysis of statewide cancer data for fracking versus non-fracking counties did not show notable differences in trends, and there were no statistically significant differences for Ewing's tumors and childhood cancers between fracking and non-fracking counties for the latest time period, The department will continue to monitor the data for Ewing's tumors and childhood cancers in the area over the next several years as more data become available.

References

1. Ewing's Family of Tumors, Childhood Cancer, and Radiation-Related Cancer Incidence Review for Washington County and Canon-McMillan School District in Pennsylvania. Pennsylvania Department of Health, Bureau of Epidemiology. https://mediaweb.wpxi.com/document_dev/2019/04/23/Ewings_washington_fmt_15094776_ver1.0.pdf.Published April 22,2019. Assessed 01/07/2020.
2. Risk factors for Ewing tumors. American Cancer Society. https://www.cancer.org/cancer/ewing-tumor/causes-risks-prevention/risk-factors.html#references. Updated May 31, 2018. Accessed on 10/10/2019.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA: A Cancer Journal for Clinicians 2018; 68(1):7-30.
4. Lichtenstein P, Holm NV, Verkasalo PK. et al. Environmental and heritable factors in the causation of cancer: analyses of cohorts of twins from Sweden, Denmark, and Finland. N Engl J Med. 2000; 343:78-85
5. Anderson LM, Diwan BA, Fear NT, Roman E. Critical windows of exposure for children's health: cancer in human epidemiological studies and neoplasms in experimental animal models. Environ Health Perspect. 2000;108 Suppl 3(Suppl 3):573–594. doi:10.1289/ehp.00108s3573
6. Peripheral primitive neuroectodermal tumor definition. Standford University, School of Medicine. http://surgpathcriteria.stanford.edu/softmisc/ppnet/printable.html. Published February 2, 2007. Accessed 04/22/2019.
7. SEER Inquiry System – View, question question:20160028. SEER. https://seer.cancer.gov/seerinquiry/index.php?page=view&id=20160028&type=q. Published 07/25/2016. Updated 10/31/2016. Access 04/22/2019.
8. PA oil and gas mapping. Pennsylvania department of environmental protection. http://www.depgis.state.pa.us/PaOilAndGasMapping/. Accessed 01/07/2020.
9. Wagner AK, Soumerai SB, Zhang F, et al. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther2002;27:299-309.
10. Spector LG, Pankratz N, Marcotte EL. Genetic and nongenetic risk factors for childhood cancer. Pediatr Clin North Am. 2015;62(1):11–25. doi:10.1016/j.pcl.2014.09.013
11. Stacy SL, Buchanich JM, Ma ZQ, Mair C, Robertson L, Sharma RK, Talbott EO, Yuan JM. Maternal obesity, birth size, and risk of childhood cancer development. American Journal of Epidemiology. 2019 May 20; 188(8): 1503-1511

Table 1: Ewing's tumors, Childhood Cancer and All Cancers Incidence Rates in Four Counties (Fayette, Greene, Washington, and Westmoreland) Compared to the Rest of State for Three Time Periods, 1985–1994, 1995–2004 and 2005–2017, PCR 1985–2017

Cancer Type	Gender	1985 to 1994				1995 to 2004				2005 to 2017			
		Obs[a]	Exp[b]	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Ewing's tumors	Female	2	4.9	0.41	0.05 - 1.49	11	8.1	1.37	0.68 - 2.44	16	8.7	1.84**	1.05 - 2.98
	Male	4	6.5	0.62	0.17 - 1.58	11	9.4	1.18	0.59 - 2.11	15	12.8	1.17	0.66 - 1.93
	Total	6	11.3	0.53	0.19 - 1.15	22	17.4	1.26	0.79 - 1.92	31	21.4	1.45	0.98 - 2.05
Childhood cancer	Female	192	178.4	1.08	0.93 - 1.24	144	159.8	0.90	0.76 - 1.06	209	212.5	0.98	0.86 - 1.13
	Male	170	181.6	0.94	0.80 - 1.09	164	173.9	0.94	0.80 - 1.10	238	238.8	1.00	0.87 - 1.13
	Total	362	360.3	1.00	0.90 - 1.11	308	333.8	0.92	0.82 - 1.03	447	451.3	0.99	0.90 - 1.09
All cancers	Female	22267	23253.6	0.96*	0.95 - 0.97	25322	26286.8	0.96*	0.95 - 0.98	36857	37399.7	0.99*	0.98 - 0.99
	Male	21632	23150.4	0.93*	0.92 - 0.95	25829	26579.4	0.97*	0.96 - 0.98	34817	36408.3	0.96*	0.95 - 0.97
	Total	43899	46218.1	0.95*	0.94 - 0.96	51151	52859.6	0.97*	0.96 - 0.98	71674	73818.9	0.97*	0.96 - 0.98

[a]Obs = Observed number of cancer cases
[b]Exp = Expected number of cancer cases
*SIR is statistically significantly lower than 1.0.
**SIR is statistically significantly higher than 1.0.

Table 2: Ewing's tumors, Childhood Cancer and All Cancers Incidence Rates in Fayette County Compared to the Rest of State for Three Time Periods, 1985–1994, 1995–2004 and 2005–2017, PCR 1985–2017

Cancer Type	Gender	1985 to 1994				1995 to 2004				2005 to 2017			
		Obs[a]	Exp[b]	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Ewing's tumors	Female	1	0.9	1.09	0.03 - 6.09	0	1.6	0.00	0 - 2.51	5	1.6	3.06	0.99 - 7.13
	Male	1	1.2	0.80	0.02 - 4.46	2	1.9	1.07	0.13 - 3.88	3	2.3	1.28	0.26 - 3.73
	Total	2	2.2	0.92	0.11 - 3.34	2	3.5	0.57	0.07 - 2.06	8	4.0	2.02	0.87 - 3.98
Childhood cancer	Female	37	35.2	1.05	0.74 - 1.45	27	31.7	0.85	0.56 - 1.24	28	38.5	0.73	0.48 - 1.05
	Male	25	36.5	0.69	0.44 - 1.01	27	34.9	0.77	0.51 - 1.13	45	42.8	1.05	0.77 - 1.41
	Total	62	71.8	0.86	0.66 - 1.11	54	66.6	0.81	0.61 - 1.06	73	81.4	0.90	0.70 - 1.13
All cancers	Female	4636	4523.2	1.02	0.99 - 1.06	4802	5144.2	0.93*	0.91 - 0.96	6462	6758.0	0.96*	0.93 - 0.98
	Male	4267	4419.4	0.97*	0.94 - 0.99	5076	5056.7	1.00	0.98 - 1.03	6406	6548.2	0.98	0.95 - 1.00
	Total	8903	8928.4	1.00	0.98 - 1.02	9878	10233.1	0.97*	0.95 - 0.99	12868	13323.3	0.97*	0.95 - 0.98

[a]Obs = Observed number of cancer cases
[b]Exp = Expected number of cancer cases
*SIR is statistically significantly lower than 1.0.
**SIR is statistically significantly higher than 1.0.

Table 3: Ewing's tumors, Childhood Cancer and All Cancers Incidence Rates in Greene County Compared to the Rest of State for Three Time Periods, 1985–1994, 1995–2004 and 2005–2017, PCR 1985–2017

Cancer Type	Gender	1985 to 1994				1995 to 2004				2005 to 2017			
		Obs[a]	Exp[b]	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Ewing's tumors	Female	0	0.3	0.00	0 - 13.75	1	0.4	2.30	0.06 - 12.81	0	0.5	0.00	0 - 7.92
	Male	1	0.3	2.86	0.07 - 15.9	0	0.6	0.00	0 - 6.50	1	0.7	1.39	0.04 - 7.75
	Total	1	0.6	1.61	0.04 - 8.99	1	1.0	1.00	0.03 - 5.59	1	1.2	0.84	0.02 - 4.70
Childhood cancer	Female	4	10.8	0.37*	0.10 - 0.95	6	8.6	0.70	0.26 - 1.52	15	11.4	1.32	0.74 - 2.18
	Male	5	10.6	0.47	0.15 - 1.10	7	9.4	0.74	0.30 - 1.53	16	12.7	1.26	0.72 - 2.05
	Total	9	21.4	0.42*	0.19 - 0.80	13	18.0	0.72	0.38 - 1.24	31	24.0	1.29	0.88 - 1.83
All cancers	Female	789	1128.2	0.70*	0.65 - 0.75	1086	1211.5	0.90*	0.84 - 0.95	1700	1673.5	1.02	0.97- 1.07
	Male	815	1126.6	0.72*	0.68 - 0.78	1219	1271.4	0.96	0.91 - 1.01	1568	1744.1	0.90*	0.86 - 0.95
	Total	1604	2239.3	0.72*	0.68 - 0.75	2305	2486.8	0.93*	0.89 - 0.97	3268	3421.0	0.96*	0.92 - 0.99

[a]Obs = Observed number of cancer cases
[b]Exp = Expected number of cancer cases
*SIR is statistically significantly lower than 1.0.
**SIR is statistically significantly higher than 1.0.

Table 4: EFOT, Childhood Cancer and All Cancers Incidence Rates in Washington County Compared to the Rest of State for Three Time Periods, 1985–1994, 1995–2004 and 2005–2017, PCR 1985–2017

Cancer Type	Gender	1985 to 1994				1995 to 2004				2005 to 2017			
		Obs[a]	Exp[b]	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Ewing's tumors	Female	0	1.3	0.00	0 - 2.90	1	2.2	0.45	0.01 - 2.51	1	2.60	0.38	0.01 - 2.14
	Male	0	1.7	0.00	0 - 2.13	1	2.5	0.39	0.01 - 2.21	4	3.63	1.10	0.30 - 2.82
	Total	0	3.0	0.00	0 - 1.23	2	4.8	0.42	0.05 - 1.53	5	6.23	0.80	0.26 - 1.87
Childhood cancer	Female	64	47.8	1.34**	1.03 - 1.71	31	42.9	0.72	0.49 - 1.03	57	60.86	0.94	0.71 - 1.21
	Male	44	48.9	0.90	0.65 - 1.21	44	46.5	0.95	0.69 - 1.27	70	68.10	1.03	0.80 - 1.30
	Total	108	96.8	1.12	0.92 - 1.35	75	89.4	0.84	0.66 - 1.05	127	128.92	0.99	0.82 - 1.17
All cancers	Female	6001	6277.5	0.96*	0.93 - 0.98	7157	6968.9	1.03**	1.01 - 1.05	10358	10159.03	1.02	1.00- 1.04
	Male	5853	6238.4	0.94*	0.91 - 0.96	6925	7035.6	0.98	0.96 - 1.01	9559	9801.35	0.98*	0.96 - 0.99
	Total	11854	12478.7	0.95*	0.93 - 0.97	14082	13996.9	1.01	0.99 - 1.02	19917	19956.33	1.00	0.98 - 1.01

[a]Obs = Observed number of cancer cases
[b]Exp = Expected number of cancer cases
*SIR is statistically significantly lower than 1.0.
**SIR is statistically significantly higher than 1.0.

Table 5: Ewing's tumors, Childhood Cancer and All Cancers Incidence Rates in Westmorland County Compared to the Rest of State for Three Time Periods, 1985–1994, 1995–2004 and 2005–2017, PCR 1985–2017

Cancer Type	Gender	1985 to 1994				1995 to 2004				2005 to 2017			
		Obs[a]	Exp[b]	SIR	95% CI	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Ewing's tumors	Female	1	2.28	0.44	0.01 - 2.44	9	3.80	2.37**	1.08 - 4.49	10	4.25	2.35**	1.13 - 4.33
	Male	2	3.06	0.65	0.08 - 2.36	8	4.42	1.81	0.78 - 3.57	7	6.16	1.14	0.46 - 2.34
	Total	3	5.34	0.56	0.12 - 1.64	17	8.22	2.07**	1.21 - 3.31	17	10.37	1.64	0.95 – 2.62
Childhood cancer	Female	87	85.13	1.02	0.82 - 1.26	80	75.80	1.06	0.84 - 1.31	109	101.47	1.07	0.88 - 1.30
	Male	96	84.91	1.13	0.92 - 1.38	86	82.60	1.04	0.83 - 1.29	107	115.27	0.93	0.76 - 1.12
	Total	183	170.01	1.08	0.93 - 1.24	166	158.41	1.05	0.90 - 1.22	216	216.78	1.00	0.87 - 1.14
All cancers	Female	10841	11272.3	0.96*	0.94 - 0.98	12277	12919.7	0.95*	0.93 - 0.97	18337	18786.5	0.98*	0.96 - 0.99
	Male	10697	11287.9	0.95	0.92 - 1.38	12609	13187.0	0.96*	0.94 - 0.97	17284	18245.1	0.95*	0.93 - 0.96
	Total	21538	22450.1	0.96	0.93 - 1.24	24886	26070.7	0.95*	0.94 - 0.97	35621	37025.9	0.96*	0.95 - 0.97

[a]Obs = Observed number of cancer cases

[b]Exp = Expected number of cancer cases

*SIR is statistically significantly lower than 1.0.

**SIR is statistically significantly higher than 1.0.

Figure 1: Percent of Childhood Cancer Over All Cancer Yearly Trend Comparison Between the Four-county Area and the Rest of the State, PCR, 1985-2017

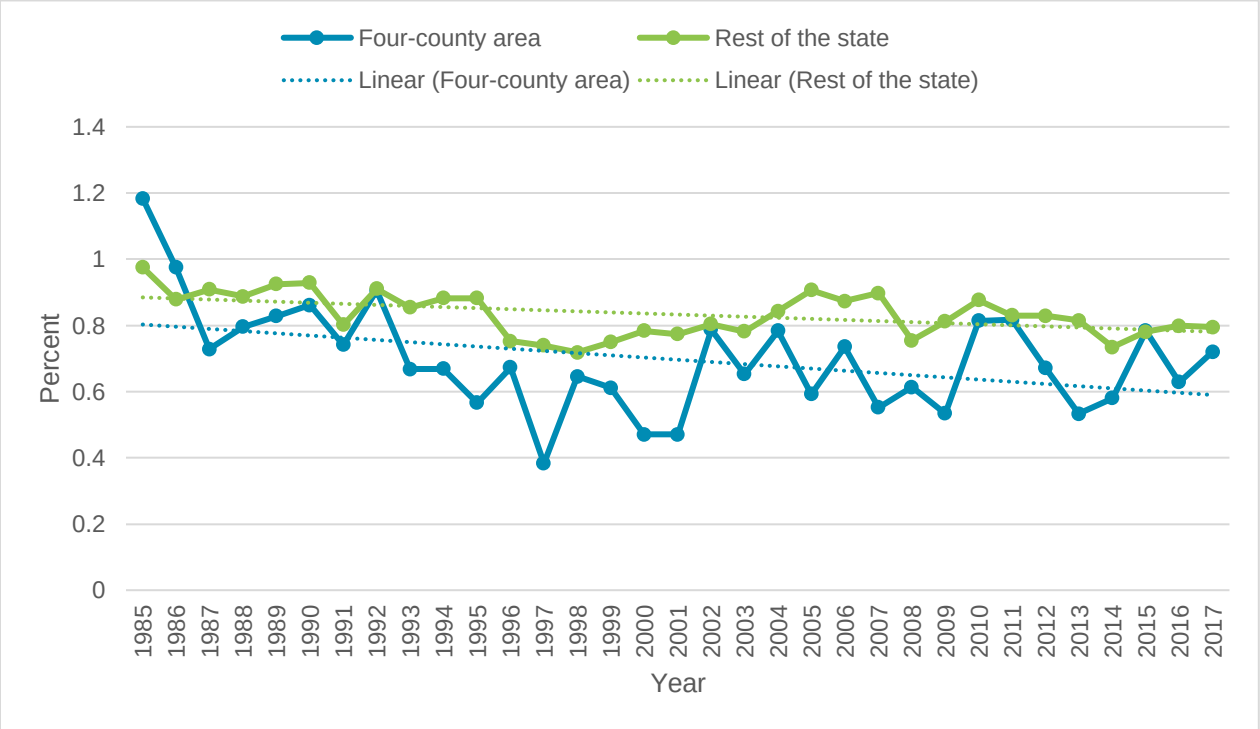

Figure 2: Age-adjusted All Childhood Cancers Incidence Rate for the Time Period 2005-2017 Between Counties With and Without Non-conventional Gas Production, PCR

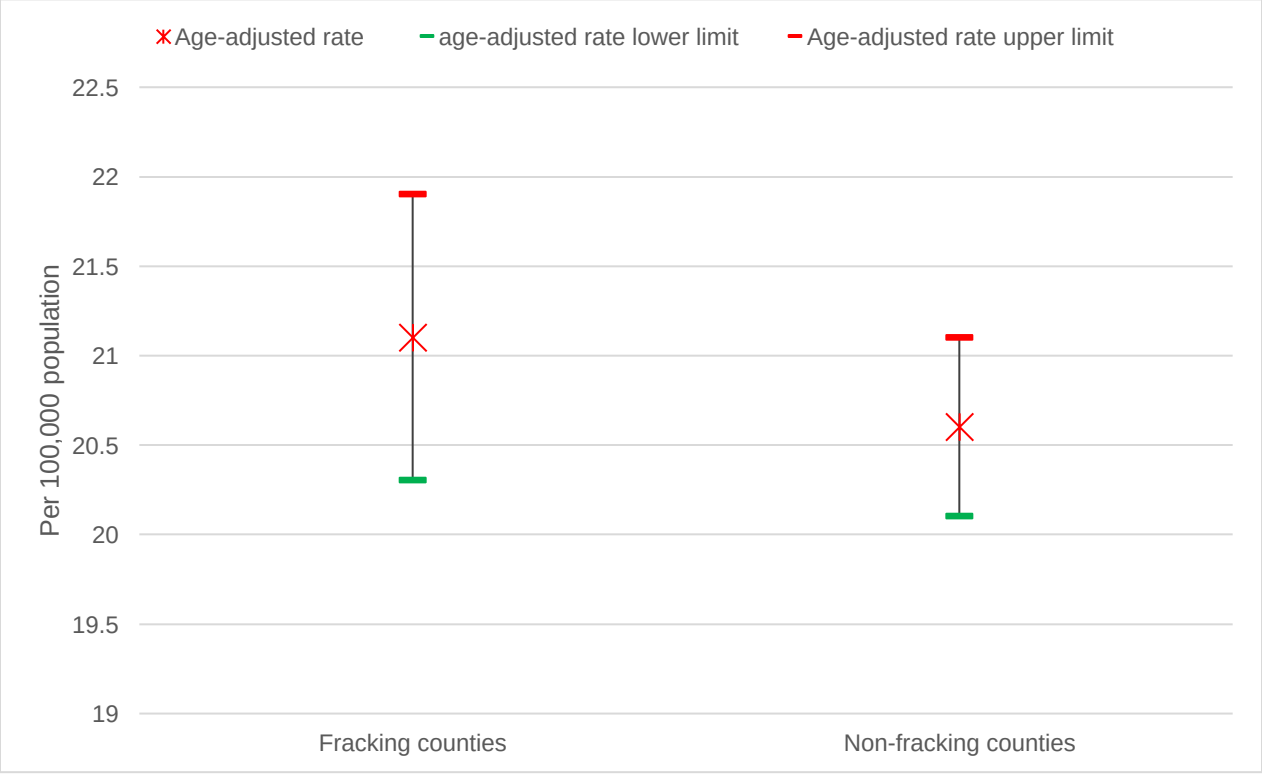

Figure 3: Age-adjusted Childhood Ewing's tumors Incidence Rate for the Time Period 2005-2017 Between Counties With and Without Non-conventional Gas Production, PCR

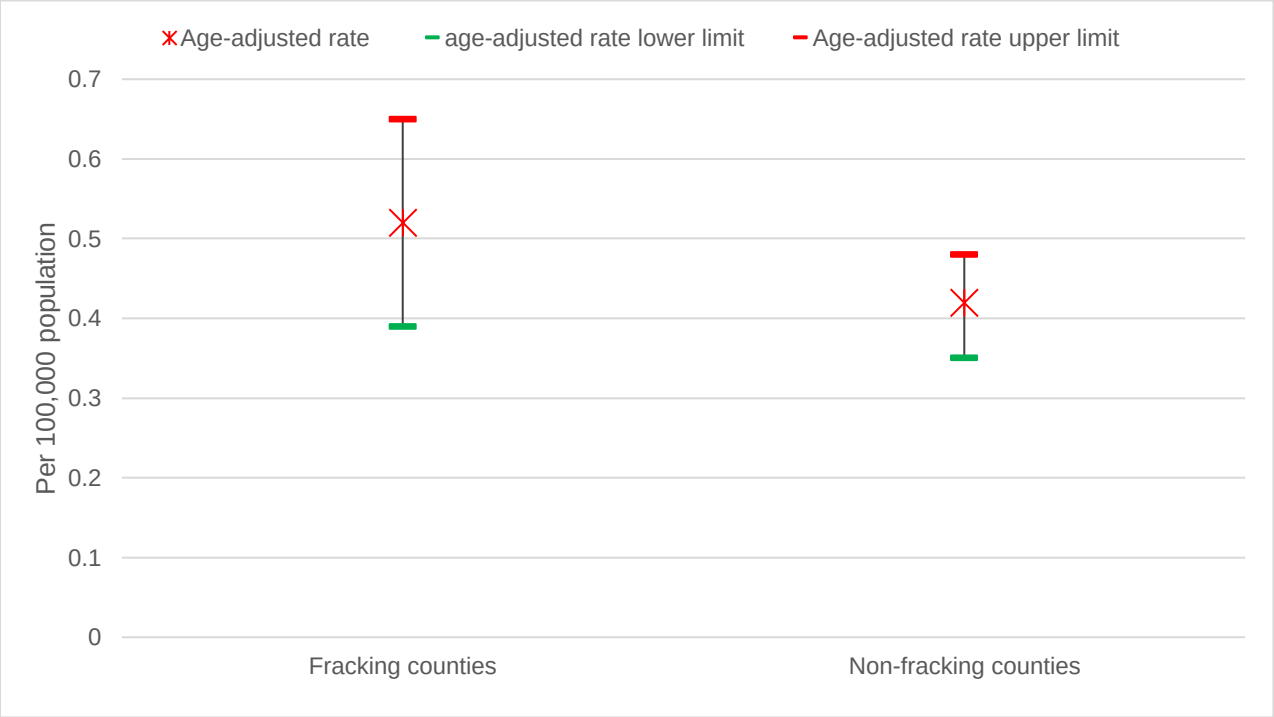

Figure 4: Age-adjusted All Childhood Cancers Incidence Rate Trends Between Counties With and Without Non-conventional Gas Production, PCR, 1985-2017

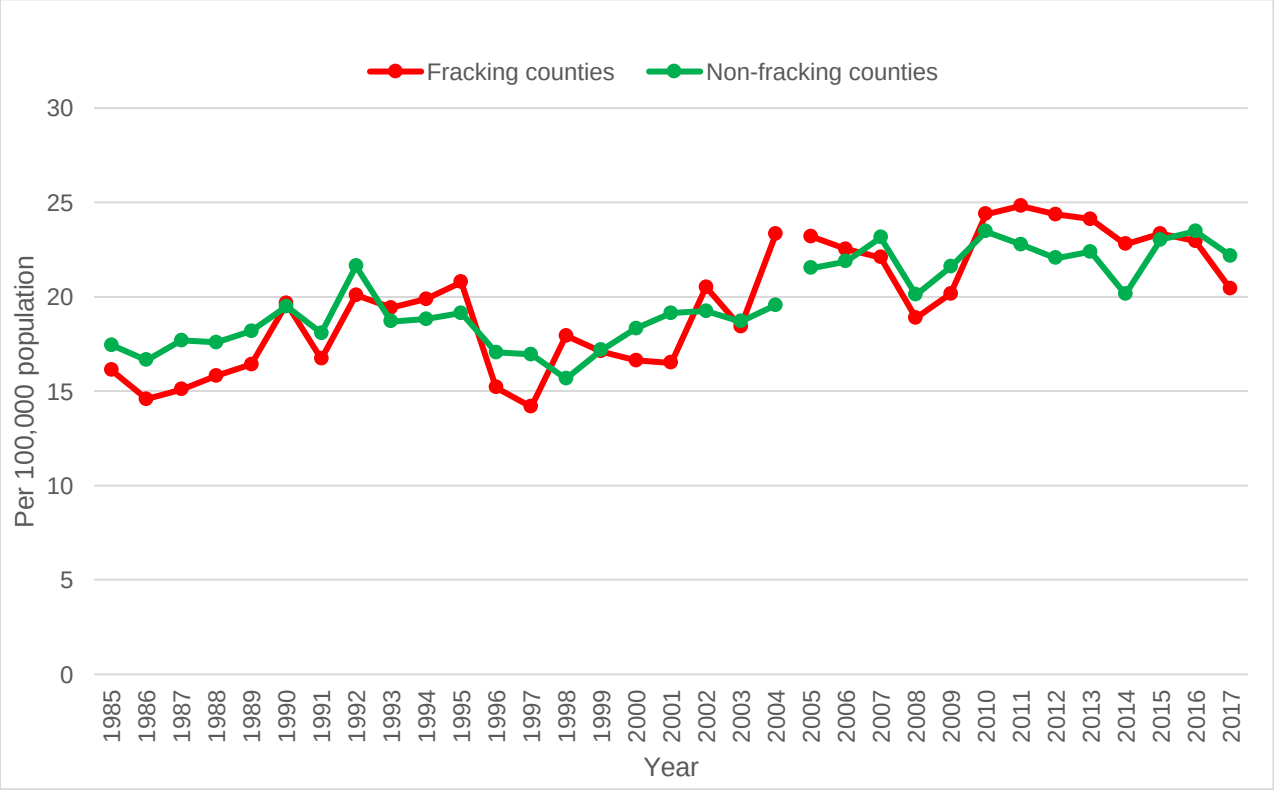

Figure 5: Log Transformed Ewing's tumors Incidence Trends Between Counties With and Without Non-conventional Gas Production, PCR, 1985-2017

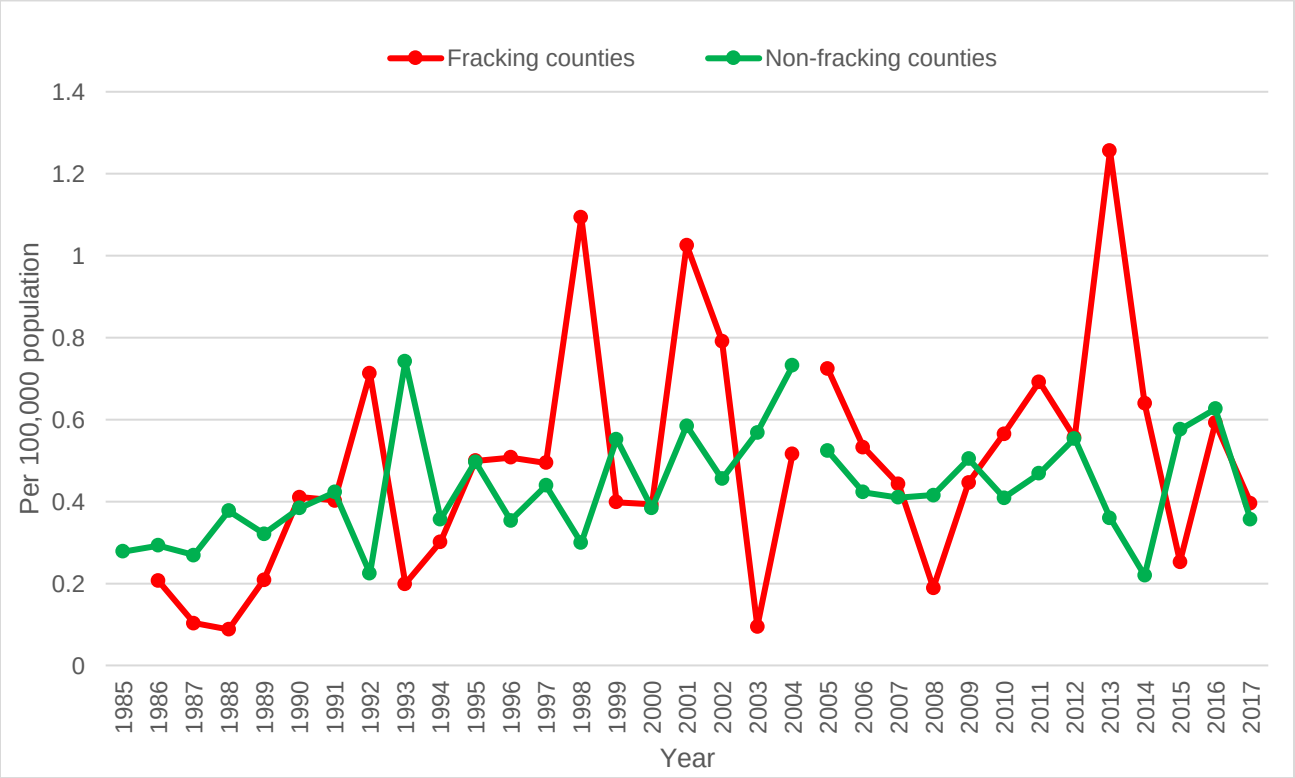

Figure 6: Ratio of Childhood Cancer Over All Cancers Between Fracking and Non-fracking Counties, PCR, 1985-2017

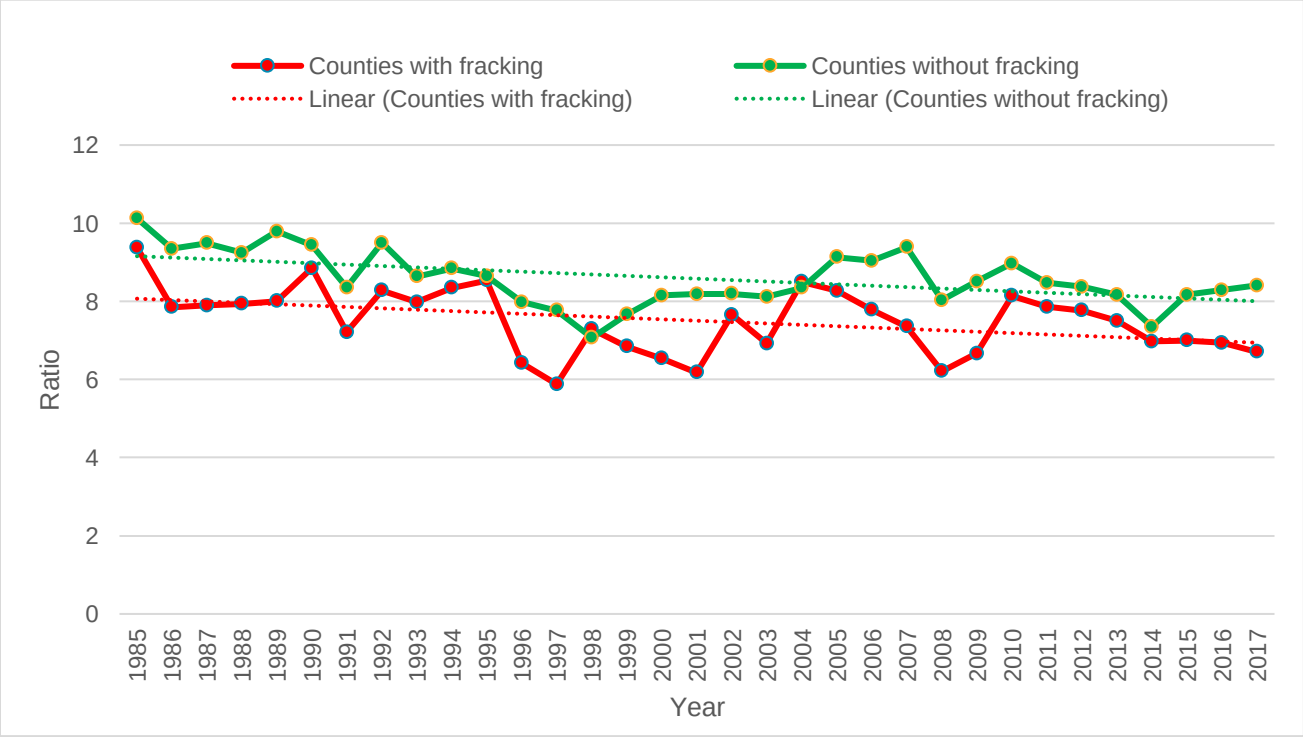

Figure 7: Ratio of Childhood Ewing's tumors Over All Childhood Cancer Between Fracking and Non-fracking Counties, PCR, 1985-2017