October 2017 Addendum 1 to the August 2016 Cancer Data Review (1985-2013) – Selected Zip Codes of Warminster (18974), Warrington (18976) and Horsham (19044), Pennsylvania

Division of Environmental Health Epidemiology

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pennsylvania
DEPARTMENT OF HEALTH

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Executive Summary

This update is addendum 1 to the cancer review and update for the Warminster, Warrington and Horsham community released in August 2016. The Pennsylvania Department of Health (DOH) completed this update in response to community questions about pancreatic and pediatric cancer rates in the area.

- For pancreatic cancer, there appears to be an increase in the number of new pancreatic cancer cases in the zip codes reviewed relative to the state when comparing the time periods evaluated in this update.
    - Further analysis of the pancreatic cancer rates for this community is recommended. Additional mapping and other analyses will help us better understand the pancreatic cancer rates in this area.
    - It is important to keep in mind the limited information supporting links between chemical exposures and pancreatic cancer.

- Cancers and birth defects in children have been of special concern in this community for many years. The number of pediatric cancer cases reported to the state cancer registry was too small to support analysis at the individual zip code level. Therefore, pediatric cancers were evaluated across all three zip codes of interest combined in this analysis. Pediatric cancer rates did not show any statistically significant change in comparison to the state rates in the zip codes (combined) over the three time periods of interest or over the entire duration of 1985-2013.

- Given these findings and the legacy of environmental contamination in this area, DOH remains committed to evaluating new data or additional information as it becomes available for this community. Further, an addendum 2 to this work is also planned. This second update will produce new calculated rates for all of the cancer types in the original 2016 document (as well as these two additional cancer types) using the public water system boundaries instead of zip codes as the basis of for the population in the evaluation. This will more accurately represent the population of

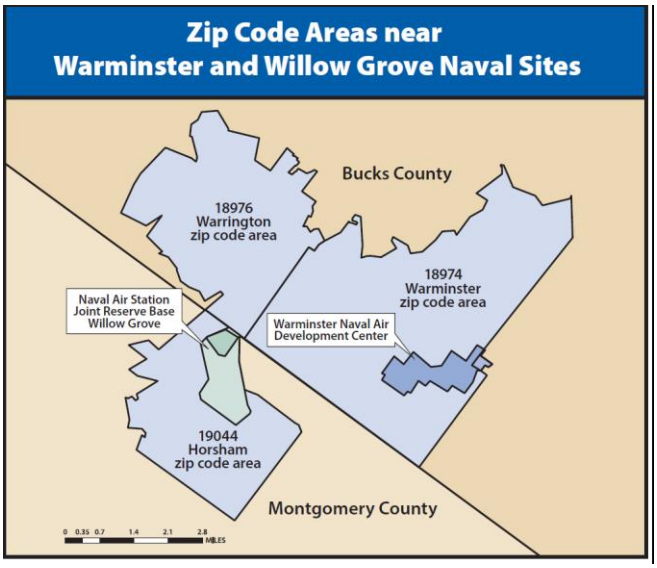
people exposed to the contaminate on in the public drinking water supply. DOH will also consider further analyses of the pancreatic cancer information for this area, including mapping the locations of the pancreatic cases over time.

Purpose

DOH developed this addendum to provide information about pancreatic and pediatric cancer incidence rates for communities living in zip codes surrounding the former Naval Air Warfare Center in Warminster, Bucks County, Pa. and the Willow Grove Naval Air and Air Reserve Station, Horsham, Montgomery County, Pa. for the period 1985–2013.

Previously, the Agency for Toxic Substances and Disease Registry (ATSDR) and DOH assessed incidence rates of seven selected cancers (bladder, kidney, liver, non-Hodgkin's lymphoma, multiple myeloma, prostate and testicular) in communities living in zip codes 18974, 18976 and 19044 (Figure 1). The cancer review was published in a document released in August 2016 and is available at https://www.atsdr.cdc.gov/HAC/pha/CancerDataReviewPA/CancerDataReview_PA_508.pdf. These original seven cancers were selected based on associations in the literature of these cancer types and the historical environmental contaminants of concern in drinking water in this area. Please see the background section below for a description of the specific chemicals found in drinking water in this community.

Figure 1: Zip Code Areas Near Warminster and Willow Grove



Source: August 2016 Cancer Data Review Report

This addendum was prepared to respond to requests from the public to also examine the incidence rates of pancreatic and pediatric cancers (pediatric cancers in this review are defined as cancers diagnosed in newborns through adolescence, or children 0-19 years of age) in the same region and over the same time period previously assessed. Note: previous studies have not reported firm associations between pancreatic and pediatric cancers and the contaminants of concern identified in drinking water in the area.

Background

Residents have raised concerns about environmental contamination and health problems over many years in the Warminster and Willow Grove area. Specific contaminants detected in public and/or private drinking water in the area include:

- in the 1970s, volatile chemicals such as tetrachlorethene (PCE), trichloroethylene (TCE), 1,2-dichloroethene (1,2, DCE) and carbon tetrachloride); and
- more recently in 2014, perfluoroalkyl substances (PFAS) such as perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA). These chemicals were likely used in firefighting foams for decades in this area.

Methodology

A cancer incidence analysis is the primary tool used by DOH to investigate the possibility of excess cancer in a community. For a cancer incidence analysis, DOH calculates incidence rates using information reported by hospitals and health care providers to the Pennsylvania state cancer registry and compares this information at the zip code level to state- or county-wide rates by calculating standardized incidence ratios. A cancer incidence analysis is specifically intended to address the question “Is there an excess of cancer in the area or population of concern?” It cannot determine if past exposures to contaminants caused, or contributed to, the observed cancer cases. DOH follows guidelines recommended by CDC and the Council of State and Territorial Epidemiologists (CSTE) for investigating concerns about cancer clusters available at https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6208a1.htm. If DOH determines that further investigation into a cancer cluster concern is warranted, DOH will consider further epidemiologic evidence and analyses, as feasible, and site-specific circumstances. DOH must also factor into consideration that excesses of cancer may occur by chance alone. For this community, DOH and ATSDR evaluated time trends by evaluating three time periods: 1985 to 1994, 1995 to 2004 and 2005 to 2013. DOH also reviewed cancer incidence rates for the combined three zip codes over these time periods.

To determine whether a statistically significant excess of cancer existed in the geographic areas of concern, the number of observed cases was compared to what would be "expected" based on the state cancer rates. Calculating the expected number(s) of cancer cases takes into consideration the sex and ages of people who are diagnosed with cancer. This is important because sex and age impact cancer rates. If we are trying to determine if there is more or less cancer in a community compared to the rest of the state or county, we must make sure that the difference in cancer rates is not simply due to one of these factors.

For this cancer incidence analysis as well as in the August 2016 review, DOH calculated incidence rates of pancreatic and pediatric cancers using information reported to the Pennsylvania state cancer registry and compared this information at the zip code level to statewide rates by calculating standardized incidence ratios (SIRs). DOH also reviewed cancer incidence rates for the combined three zip codes over these time periods. To determine whether a statistically significant excess of cancer existed in the geographic areas of concern, the number of observed cases was compared to what would be “expected” based on the state cancer rates.

Statistical significance implies that less than a certain percent chance (usually selected as 5 percent) exists that the observed difference is merely the result of random fluctuation in the number of observed cancer cases. Statistical significance is impacted by variability (or random fluctuations in the number of cancer cases reported) and sample size. Differences between populations may not achieve statistical significance if sample sizes are small, even if an actual difference exists. Statistical significance can be determined by examining the confidence interval, which is the computed interval with a given confidence (usually 95 percent) that the true value of an estimate is contained within the interval. For example, if the confidence interval does not include 1.0 and the interval is below 1.0, then the number of cases is significantly lower than expected. Similarly, if the confidence interval does not include 1.0 and the interval is above 1.0, then a statistically significant excess exists in the number of cases. If the confidence interval includes 1.0, then the true ratio may be 1.0, and the conclusion cannot be made with sufficient confidence that the observed number of cases reflects a real excess or deficit. As long as the 95% confidence interval contains 1.0, the indication is that the SIR is still

within the range expected on the basis of the disease experience of the comparison population. Note, it may be worthwhile to further consider cancer rates in a community that do not reach statistical significance if there is strong scientific information supporting an association between the cancer(s) of interest and an identified chemical exposure in a community, as well as plausibility with the exposure scenario. As stated in the CDC and CSTE cancer cluster guidelines referenced earlier, “In addition to whether the SIR is statistically significant, the investigators should consider the suspected cluster in the context of the plausibility that the cancers could share a common etiology based on the latency, on community patterns of migration in and out, known risk factors for the cancer of concern, and the potential for exposure to a contaminant of concern, as well as other factors.”

The width of the confidence interval also reflects the stability of the ratio estimate. For example, a narrow confidence interval (e.g., 1.03–1.15) allows a fair level of certainty that the calculated ratio is close to the true ratio for the population. A wide interval (e.g., 0.85–4.50) leaves considerable doubt about the true ratio, which could be much lower or much higher than the calculated ratio[1].

DOH summed together cases of different cancer types in children aged 0-19 to evaluate rates of pediatric cancers in this community. The cancer types considered were leukemia, myeloproliferative diseases and myelodysplastic diseases; lymphomas and reticuloendothelial neoplasms; CNS and miscellaneous intracranial and intra-spinal neoplasms; neuroblastoma and other peripheral nervous cell tumors; soft tissue and other extra osseous sarcomas; retinoblastoma; renal tumors; hepatic tumors; malignant bone tumors; germ cell tumors, trophoblastic tumors and neoplasms of gonads; other malignant epithelial neoplasms and malignant melanomas; and other unspecified malignant neoplasms. Due to small numbers for pediatric cancers (1) the zip codes were combined for calculating pediatric SIRs for the three separate time periods; and (2) the time periods were combined for calculating pediatric SIRS for the three separate zip codes.

Results

Pancreatic Cancer Results (all ages)

Table 1 summarizes the pancreatic cancer results for this community. In the earliest time period reviewed (1985-1994), the rates for pancreatic cancer were lower than the state rates for both sexes in all the three zip codes, including few statistically significant reductions.

- For males, 1985-1994, pancreatic incidence rate was approximately 0.4 times lower than the statewide rate in zip code 18974.
- For females, 1985-1994, pancreatic incidence rate was approximately 0.3 times lower than the statewide rate in zip code 18976.
- For males, 1985-1994, pancreatic incidence rate was approximately 0.5 times lower than the statewide rate in the three zip codes combined (18974, 18976, 19044).
- For females, 1985-1994, pancreatic incidence rate was approximately 0.6 times lower than the statewide rate in the three zip codes combined (18974, 18976, 19044).

Table 1. Pancreatic Cancer Incidence in Warminster, Warrington and Horsham, Pa. (1985-2013)

Zip code	Sex	1985-1994				1995-2004				2005-2013			
		Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI
18974	Male	9	25	0.36**	0.16 - 0.68	29	24	1.21	0.81 - 1.74	38	22	1.71*	1.21 - 2.35
	Female	19	29	0.65	0.39 - 1.02	25	22	1.12	0.73 - 1.66	47	20	2.36*	1.73 - 3.14
18976	Male	9	9	0.95	0.44 - 1.81	8	7	1.07	0.46 - 2.11	9	7	1.3	0.59 - 2.47
	Female	3	10	0.29**	0.06 - 0.85	11	6	1.72	0.86 - 3.07	14	6	2.09*	1.2 - 3.67
19044	Male	2	6	0.34	0.04 - 1.24	12	7	1.76	0.91 - 3.07	9	6	1.52	0.69 - 2.88
	Female	4	6	0.68	0.19 - 1.74	4	6	0.67	0.18 - 1.72	13	6	2.23*	1.19 - 3.81
Combined (3 Zips)	Male	20	40	0.50**	0.3 - 0.77	49	38	1.28	0.95 - 1.69	56	35	1.60*	1.21 - 2.08
	Female	26	45	0.57**	0.37 - 0.84	40	35	1.15	0.82 - 1.57	74	32	2.30*	1.81 - 2.89

**Statistically significant, lower relative to state; $p < 0.05$; *Statistically significant, higher relative to state; $p < 0.05$; Data source – Pennsylvania Cancer Registry, U.S. Census Bureau

From 1995-2004, none of the rates for pancreatic cancer were statistically different from those of the state in any of the zip codes.

In the most recent time period reviewed (2005-2013), the pancreatic rates for both sexes in all of the three zip codes combined and in the three individual zip codes were significantly higher than the statewide rates, with the exception of the rate for males in zip codes 18976 and 19044.

- For males, 2005-2013, pancreatic incidence rate was approximately 1.7 times higher than the statewide rate in zip code 18974.
- For females, 2005-2013, pancreatic incidence rate was approximately 2.4 times higher than the statewide rate in zip code 18974.
- For females, 2005-2013, pancreatic incidence rate was approximately 2.1 times higher than the statewide rate in zip code 18976.
- For females, 2005-2013, pancreatic incidence rate was approximately 2.2 times higher than the statewide rate in zip code 19044.
- For males, 2005-2013, pancreatic incidence rate was approximately 1.6 times higher than the statewide rate in the three zip codes combined (18974, 18976, 19044).
- For females, 2005-2013, pancreatic incidence rate was approximately 2.3 times the statewide rate in the three zip codes combined (18974, 18976, 19044).

Pediatric (0-19 years) Cancers Results

There were fewer than 50 pediatric cancer cases for each time period for the combined three zip codes area (see Table 2). This number of pediatric cancer cases was too small to support analysis at the individual zip code level. Therefore, pediatric cancers were only evaluated across all three zip codes of interest combined in this analysis.

Table 2: Pediatric Cancer Incidence in Warminster, Warrington and Horsham, Pa. (1985-2013)

Sex	1985-1994				1994-2004				2005-2013			
	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI
Male	21	17.2	1.22	0.76 - 1.87	21	18.62	1.13	0.7-1.72	26	19.61	1.33	0.87-1.94
Female	19	16.5	1.15	0.69 - 1.8	24	16.85	1.42	0.91-2.12	18	17.98	1	0.59-1.58

Data source – Pennsylvania Cancer Registry, U.S. Census Bureau

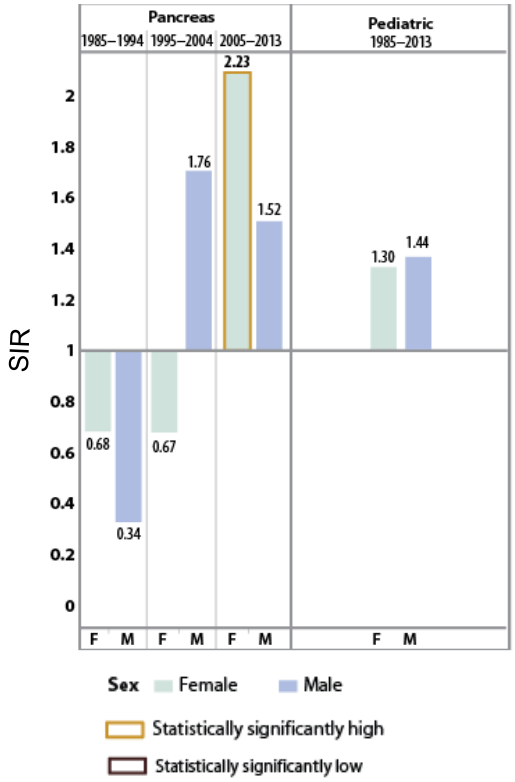
The observed numbers of childhood cancers in three zip codes combined were not statistically different from the expected numbers in all three time periods (1985-1994, 1995-2004 and 2005-

2013). Further, no statistically significant childhood cancer elevations were found in any of the three zip codes comparing to statewide rates for the overall time period of 1985-2013.

Discussion

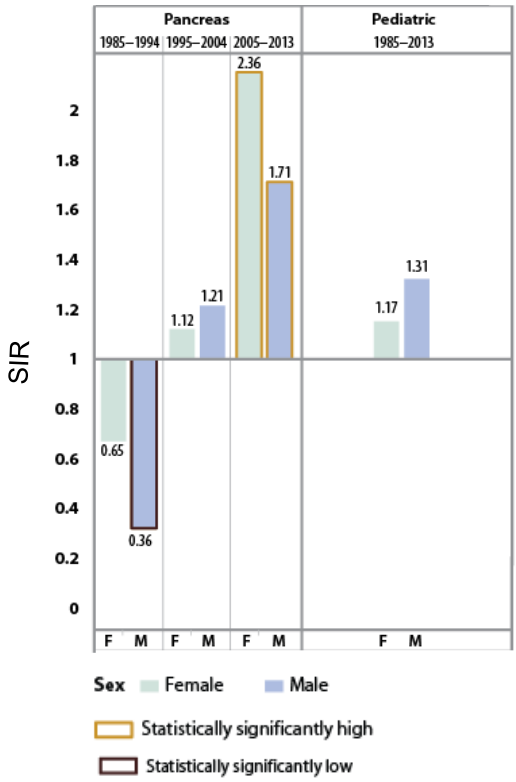
Figures 2-5 depict the pancreatic and pediatric cancer rates relative to statewide rates in the three zip codes individually and combined over the time periods of interest.

Figure 2. SIR for Horsham (19044)
By Cancer Type, Year and Sex



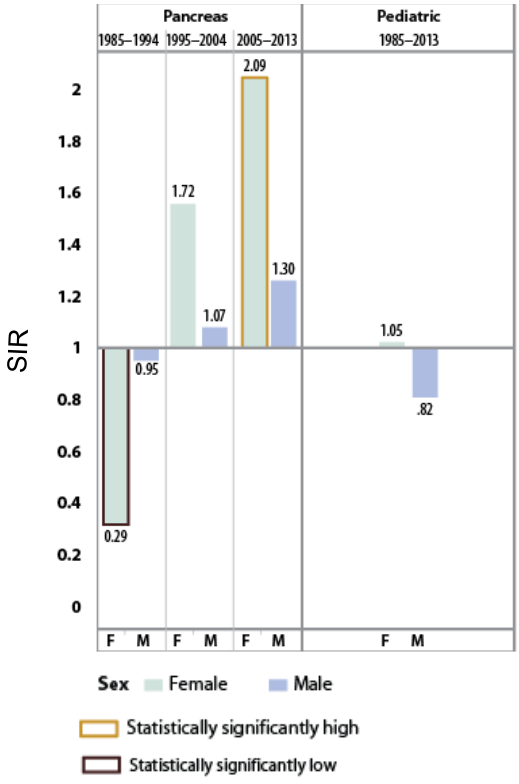
Data source – Pennsylvania Cancer Registry, U.S. Census Bureau

Figure 3. SIR for Warminster (18974)
By Cancer Type, Year and Sex



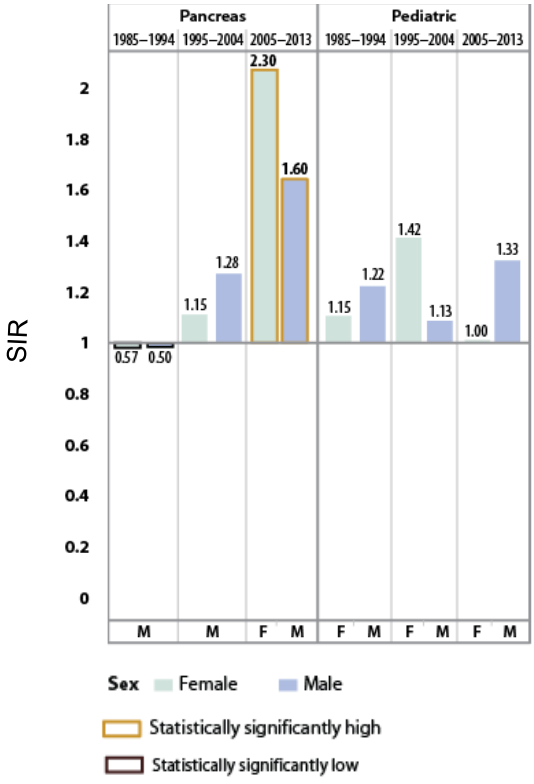
Data source – Pennsylvania Cancer Registry, U.S. Census Bureau

Figure 4. SIR for Warrington (18976) By Cancer Type, Year and Sex



Data source – Pennsylvania Cancer Registry, U.S. Census Bureau

Figure 5. SIRs for Combined Zip Codes (19044, 18974 and 18976) By Cancer Types, Year and Sex



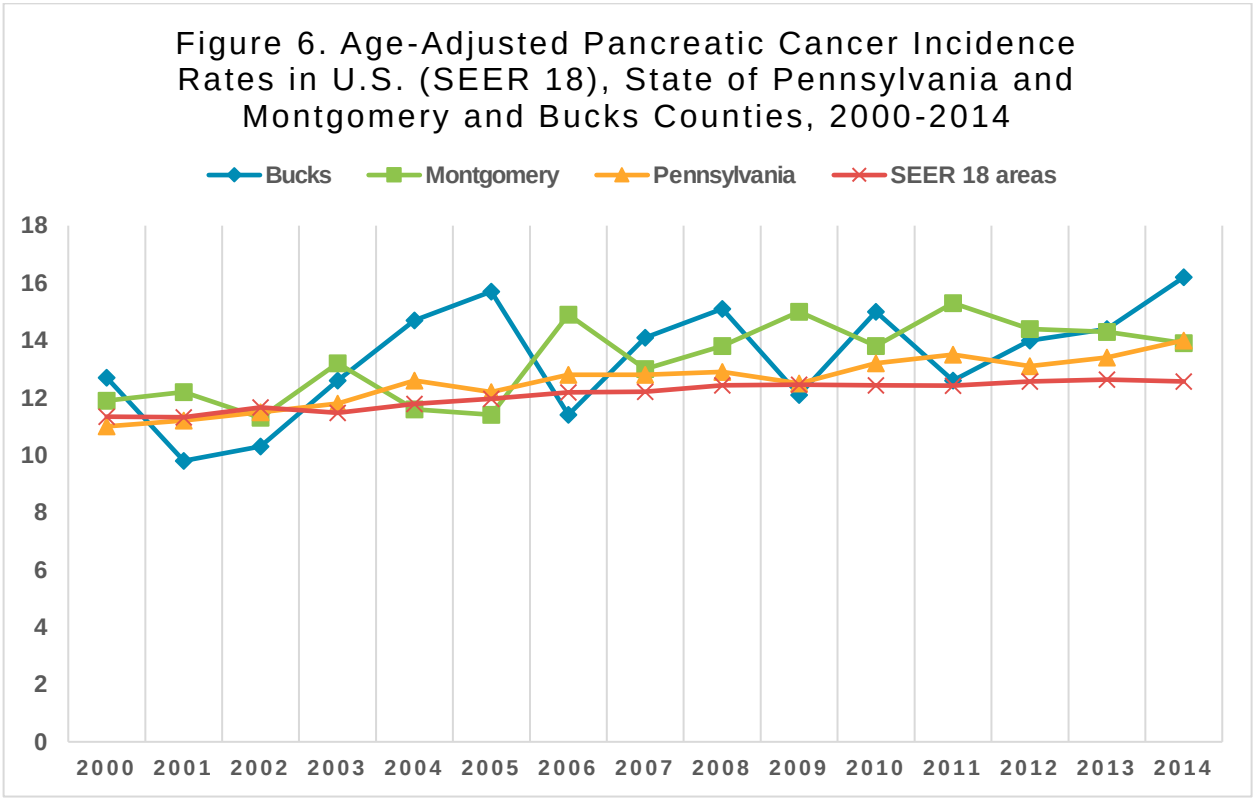
Data source – Pennsylvania Cancer Registry, U.S. Census Bureau

Pancreatic Cancer Discussion

There appears to be an increase in the number of new pancreatic cancer cases relative to the state when comparing the time periods evaluated in this update. A formal trend analysis was not performed for these specific zip codes in Bucks and Montgomery counties. However, as shown in Table 1, contrasting the different time periods shows the earliest time period with fewer pancreatic cancers than expected compared to the state, the middle time period showing what is expected compared to the state, and the most recent time period with more than expected pancreatic cancer cases compared to the state. Note, pancreatic cancer is a relatively

rare cancer and, therefore, these calculations for some of the zip codes of interest are based on small numbers of cases resulting in wide confidence intervals.

Figure 6 displays pancreatic cancer rates at the county, state and national level. The national cancer incidence information is based on the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute (NCI). SEER currently collects and publishes cancer incidence and survival data from population-based cancer registries covering approximately 28 percent of the U.S. population.



Data source: Pennsylvania Cancer Registry, U.S. Census Bureau, SEER cancer incidence data.
Note: "SEER 18" refers to national cancer incidence information from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). SEER currently collects and publishes cancer incidence and survival data from population-based cancer registries covering approximately 28 percent of the US population in 18 different cancer registries with data going back to 2000.

It is important to keep in mind the limited information supporting links between chemical exposures and pancreatic cancer. The data available at this time are very limited and the

studies are often inconclusive. As reviewed in ATSDR's Toxicological Profiles available at https://www.atsdr.cdc.gov/toxprofiles/index.asp and summarized by the American Cancer Society at https://www.cancer.org/cancer/pancreatic-cancer/causes-risks-prevention/risk-factors.html, some studies have suggested that exposure to pesticides, asbestos, benzene and chlorinated hydrocarbons may increase pancreatic cancer risk, but a causal relationship has not been confirmed. Although benzene and chlorinated hydrocarbons have been contaminants of concern in some of the historical drinking water contamination in this area, exposures to these chemicals in drinking water were addressed via public water hookups and treatment systems in the 1990s. Exposure to PFAS was the most recent widespread chemical exposure in this community's drinking water supply, and a link between pancreatic cancer and this class of chemicals has not been established. Two community-based studies[2,3] looking at community drinking water exposures to PFAS did not find an association with pancreatic cancer, but one PFAS (PFOA) has been found to cause pancreatic tumors in rodents[4]. As stated in ATSDR's Draft Toxicological Profile for Perfluoroalkyls, a number of factors related to differences between rodents and humans suggest that PFOA probably does not represent a significant pancreatic cancer hazard for humans. Studies of PFOA exposure and pancreatic cancer in worker populations are limited by very small numbers of exposed cases. It is more firmly established that people with certain risk factors such as smoking, diabetes, pancreatitis, obesity and certain genetic factors may be more likely than others to develop pancreatic cancer. However, the information contained in cancer registry records available for this review does not include these risk factors. Therefore, the analysis in this addendum was not able to consider the important prevalence of these risk factors in the populations studied, limiting the interpretation of these pancreatic cancer results.

Pediatric Cancer Discussion

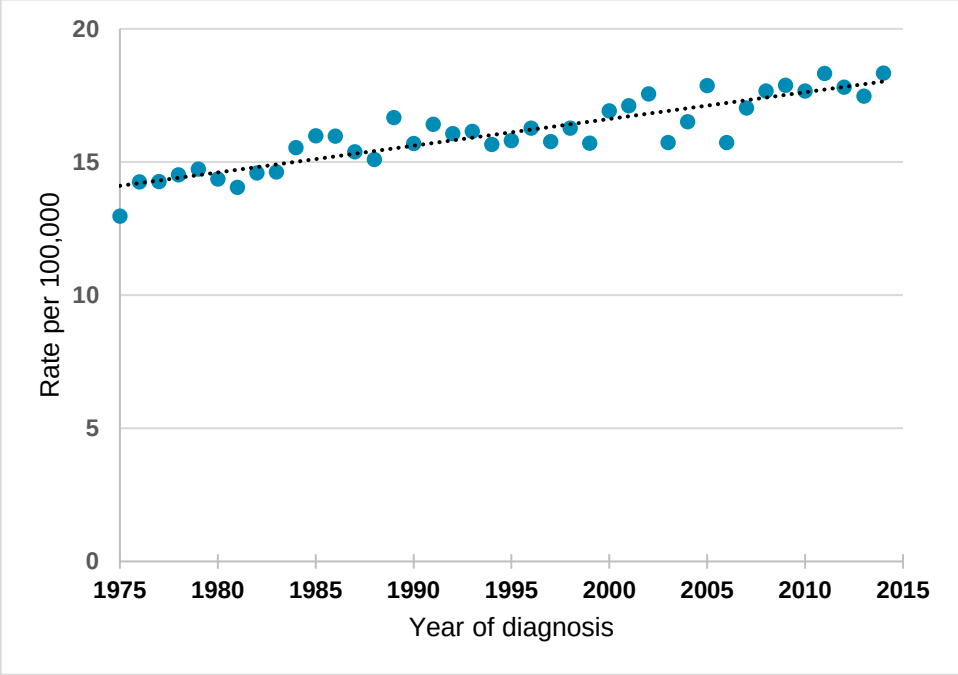
Cancers and birth defects in children have been of special concern in this community for many years. Reviews by public health agencies to date have not found statistical elevations in the available health outcome statistics for children diagnosed while living in the area. An early 1980s study by the Bucks County Health Department, DOH and CDC examined the rates of birth defects within Warminster Township, Northampton Township, Upper Southampton

Township and Ivyland Borough. Results showed the birth defect rate in the area was within expected levels. In 2006, DOH published a report reviewing cases of brain cancer in children and young adults under the age of 25 living in the Warminster area from 1993–2004. The information available at that time did not indicate a higher occurrence in the number of brain cancers among that age group in the Warminster area.

For this addendum, DOH evaluated rates for pediatric cancers in the Warminster, Warrington and Horsham zip codes from 1985-2013. Results showed that all cancer types diagnosed in children from 0-19 years of age from this area were similar to statewide rates.

Diagnoses of cancer in younger populations have been increasing nationally. Based on CDC's analysis of SEER data, Figure 7 depicts cancer diagnoses of all types in people ages 19 and younger and mortality in the United States from 1975-2014.

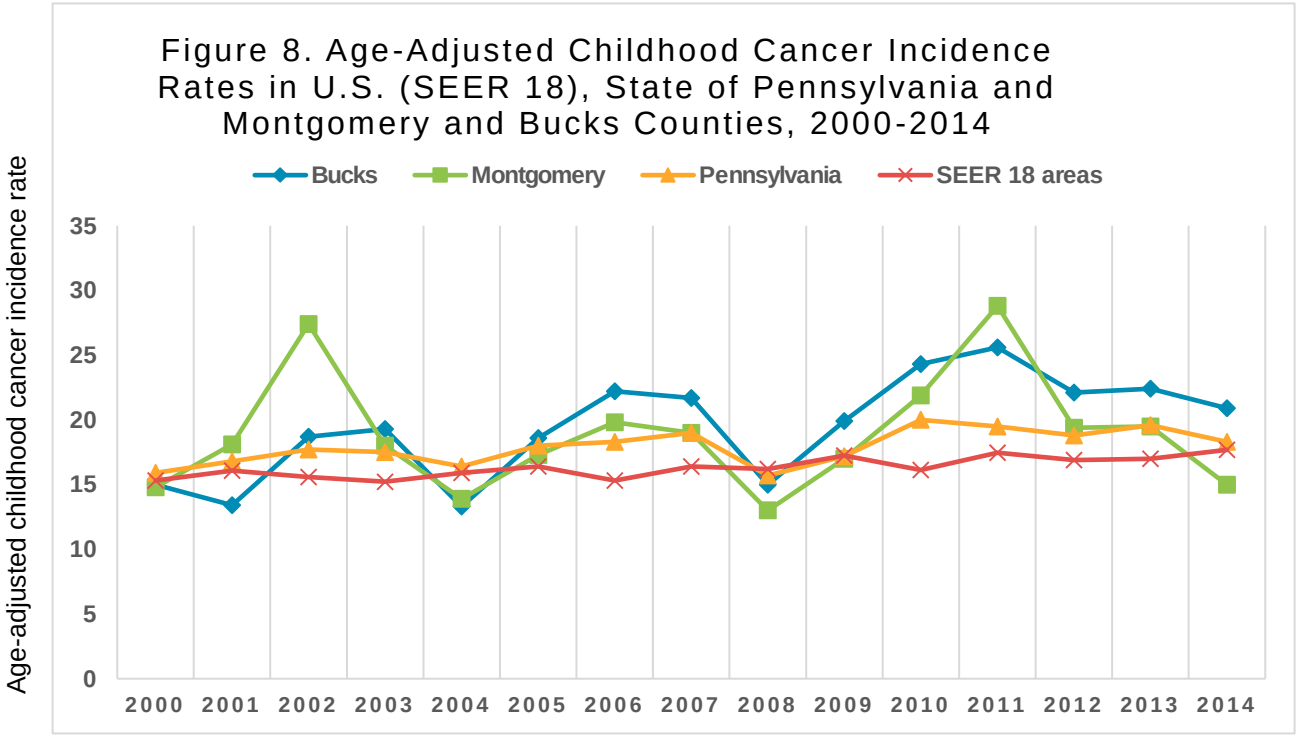
Figure 7. Age-Adjusted Childhood Cancer Incidence Rate in U.S. (SEER 9), 1975-2014



Reference: https://seer.cancer.gov/faststats/

Note: "SEER 9" refers to national cancer incidence information from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). SEER 9 includes cancer incidence and survival data from nine population-based cancer registries that includes data going back to 1975. Cancer sites include invasive cases only unless otherwise noted.

Figure 8 depicts age-adjusted childhood cancer incidence rates in Pennsylvania, Montgomery and Bucks counties, as well as nationally across 18 SEER areas.



Data source: Pennsylvania Cancer Registry, U.S. Census Bureau, SEER cancer incidence data.
Note: "SEER 18" refers to national cancer incidence information from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). SEER currently collects and publishes cancer incidence and survival data from population-based cancer registries covering approximately 28 percent of the U.S. population in 18 different cancer registries with data going back to 2000.

Researchers still do not know much about what causes cancer in children. Most children's cancers are caused by random genetic mutations. For some of these mutations, there are some environmental and genetic factors that can contribute to the cancer, but we still do not know what causes most childhood cancers.

Limitations

Caution should be exercised when interpreting an SIR. The interpretation of an SIR depends on both the size and the stability of the SIR. Two SIRs can have the same size but not the same stability. For example, an SIR of 150 based on four expected cases and six observed cases indicates a 50 percent excess in cancer, but the excess is actually only two cases. Conversely, an SIR of 150 based on 400 expected cases and 600 observed cases represents the same 50 percent excess in cancer, but, because the SIR is based on a greater number of cases, the estimate is more stable. It is very unlikely that 200 excess cases of cancer would occur by chance alone.

There may be underreporting of cancers diagnosed in veterans and their families from the area. Veterans who worked at the Willow Grove and Warminster bases and their families may have moved out of the state by the time their cancers were diagnosed. Further, DOH notes that there appears to be incomplete cancer incidence reporting from the Veterans Administration hospitals to the Pennsylvania Cancer Registry.

As summarized in the August 2016 cancer data review for this community, overall limitations in this kind of zip code level cancer data review include the following:

- A review of cancer incidence data does not determine the cause of any observed increases or decreases in cancer types.
- Zip code level analyses can provide a helpful preliminary screen of cancer registry data, but zip code boundaries may only approximate potential geographic areas of interest.
- Cancer registry incidence data are based on residence location at the time of diagnosis. Cancers can take years, or even decades, to develop following exposure to a cancer-causing agent. Cancers diagnosed in people right now may have been influenced by something that happened somewhere else a long time ago.
- Although cancer overall is a common diagnosis, there may only be a small number of a particular cancer type in a particular zip code. Researchers need larger numbers of

persons in order to have a more accurate and representative picture of the reality of a community.

- Cancer registry data only includes very limited or no information on lifestyle, demographic or occupational risk factors. Science does not know the causes of most types of cancer. For each person, cancer is thought to be a caused by a combination of many factors, genetic and environmental.

Conclusions

The 2016 cancer data review showed an inconclusive picture of cancer incidence rates in the area. Statistically significant increases were found for bladder, myeloma, non-Hodgkin's lymphoma and testis for different time periods, gender and zip codes, and statistically significant decreases were found for bladder and prostate cancer for males in different time periods and zip codes. This 2017 addendum adds two other cancer categories (pancreatic cancer and all cancer types in pediatric populations) to the prior review. For pancreatic cancer, there appears to be an increase in the number of new pancreatic cancer cases in the zip codes reviewed relative to the state when comparing the time periods evaluated in this update. Pediatric cancer rates did not show any statistically significant change in comparison to the state rates in the zip codes (combined) over the three time periods of interest or over the entire duration of 1985-2013.

Further analysis of the pancreatic cancer rates for this area is recommended. More refined geospatial analyses will help us better understand the pancreatic cancer rates in this area. It is important to keep in mind the limited information supporting links between chemical exposures and pancreatic cancer and the history of chemical contamination in drinking water in this area. Data are very limited and the studies are often inconclusive for links between chemical exposures and pancreatic cancer. It is more firmly established that people with certain risk factors such as smoking, diabetes, pancreatitis, obesity and certain genetic factors may be more likely than others to develop pancreatic cancer. However, the information contained in cancer registry records available for this review does not include these risk factors. Therefore,

the analysis in this addendum was not able to consider the important prevalence of these risk factors in the populations studied, limiting the interpretation of these pancreatic cancer results.

There are important limitations with these kinds of zip code level cancer incidence reviews, including likely underreporting of cancers diagnosed in veterans and their families from the area. Even when a statistically significant increase in cancer incidence is detected, determining the validity of an association between an environmental agent and the development of cancer is difficult as behavioral, genetic and environmental factors interact and affect cancer growth. These factors may act together or in sequence to initiate or promote cancer. Furthermore, difficulties in identifying the mode of transmission or a biological pathway, the level of exposure, and amount of exposure time all contribute to the complexities of cancer inquiry investigations.

Given these findings and the legacy of environmental contamination in this area, DOH remains committed to evaluating new data or additional information as it becomes available for this community. Further, an addendum 2 to this work is also planned. This second update will produce new calculated rates for all of the cancer types in the original 2016 document (as well as these two additional cancer types), using the public water system boundaries instead of zip codes as the denominator population. DOH will also consider further analyses of the pancreatic cancer information for this area, including additional geographic analyses.

Citations

1. Pennsylvania Department of Health, Tools of the Trade, Data Analysis. http://www.statistics.health.pa.gov/StatisticalResources/UnderstandingHealthStats/ToolsoftheTrade/Documents/Comparing_Age_Adjusted_Rates.pdf accessed April 2017.

2. Eriksen KT, Sørensen M, McLaughlin JK, Lipworth L, Tjønneland A, Overvad K, Raaschou-Nielsen O. Perfluorooctanoate and perfluorooctanesulfonate plasma levels and risk of cancer in the general Danish population. *J Natl Cancer Inst* 101 (2009):605-609.

3. Steenland K, Fletcher T, Savitz DA. Epidemiologic Evidence on the Health Effects of Perfluorooctanoic Acid (PFOA). *Environmental Health Perspectives* 118(2010):1100-1108.

4. Biegel LB, Hurtt ME, Frame SR, et al. Mechanisms of extrahepatic tumor induction by peroxisome proliferators in male CD rats. *Toxicol Sci* 60(2001):44-55; as cited in ATSDR Draft Toxicological Profile for Perfluoroalkyls. August 2015. Available at: https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf.