Cancer Incidence Assessment in ZIP Codes with Suspected PFAS Exposure, Rock Island County, Ill., 1996-2019

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The Illinois Department of Public Health, Illinois State Cancer Registry (ISCR), makes these data available as a public service.

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Abstract

Background: At the request of the U.S. Environmental Protection Agency (USEPA), the Division of Epidemiological Studies, Illinois Department of Public Health (IDPH), assessed cancer incidence in the Illinois populations downstream of, and surrounding, an emitter of perfluoroalkyl and polyfluoroalkyl substances (PFAS), 3M manufacturing, near Cordova, Illinois. Current scientific evidence suggests that PFAS are possibly carcinogenic to humans.

Methods and Data: Cancer cases were obtained from the Illinois State Cancer Registry (ISCR) for diagnosis years 1996-2019. The study area consisted of 16 ZIP codes selected by the USEPA. They include ZIP codes 61282, 61256, 61264, 61244, 61265, 61282, 61240, 61239, and 61241 (referred to as the small-urban group of ZIP codes); and ZIP codes 61252, 61251, 61250, 61230, 61257, 61242, and 61275 (referred to as the rural group of ZIP codes). Each ZIP code group was compared to a referent group of Illinois counties that are similar in population density and racial ethnic make-up, adjusting for age. The small-urban ZIP code group was compared to a group of 12 Illinois counties. The rural ZIP code group was compared to a group of 83 rural Illinois counties. Cases were geocoded into the study areas using a combination of GIS software and manual review. Twenty-three common cancer sites were examined with a particular interest in kidney, testicular, and female breast cancers. These three specific sites are of high concern due to their documented association with PFAS exposure. Standardized incidence ratios (SIRs) and their 99% confidence intervals (CI) were calculated with comparable county populations as references.

Results: Over the 24-year time period, SIRs for men living in the small-urban group of ZIP codes, displayed significantly lower than expected numbers of colorectal, lung, kidney, and leukemia cases. An elevated number of testicular cancer cases was observed but was not statistically significant ($p = 0.02$). In the rural ZIP code group, we observed a significantly lower than expected number of lung cancer cases in men. Among women living in the small-urban ZIP code group, we saw significantly higher than expected cases of cervical and uterine cancer. Also observed were significantly lower numbers of female lung, kidney, myeloma, and leukemia cases. In the rural ZIP code group females displayed significantly higher numbers of melanoma and significantly lower numbers of colorectal and lung cancer.

Discussion: This assessment included 82 SIRs and found 11 where the observed rates of specific cancers were significantly lower in the populations being examined, and two with significantly elevated cancer rates (cervix and uterus, in the small-urban population of women.) There was no consistent evidence for an association between cancer and PFAS exposure in the populations examined. While testicular cancer, one of the cancers previously seen to be associated with PFAS exposure, appeared at a higher rate than expected among men living in the small-urban study area, this finding was not statistically significant at the $p <= 0.01$ level and this elevation was not seen in the rural study area. Kidney cancer, the other site suspected to be associated with PFAS exposure, was statistically significantly lower in both men and women living in the small-urban area. The pattern of cancer rates observed in this study differ from the findings of other studies that observed elevations in testicular, kidney, and female breast cancers. Additional study of PFAS at the population level is recommended.

Background

In May 2022, the U. S. Environmental Protection Agency (USEPA) requested that the Division of Epidemiological Studies, Illinois Department of Public Health (IDPH), assess cancer incidence in the Illinois populations downstream of, and surrounding, an emitter of per-fluoroalkyl and poly-fluoroalkyl substances (PFAS). The PFAS emission source is a manufacturing facility owned by 3M and is located north of Cordova, Illinois on the banks of the Mississippi River. Several individual chemicals in the PFAS family of chemicals have classified as possibly carcinogenic to humans by the International Agency for Research on Cancer (IARC 2016). The USEPA concluded that there was suggestive evidence of the carcinogenic potential of PFAS (US EPA 2016, US EPA 2016).

PFAS are a family of synthetic chemicals that do not occur naturally in the environment. There are thousands of different PFAS, and they are widely dispersed in the environment throughout the world. These compounds are known to be very persistent in the environment and resistant to normal environmental decomposition avenues. Common applications of PFAS include protectants for paper and cardboard packaging, carpets, leather products, and textiles (acting to protect against water, grease, and soil); and in firefighting foams (ATSDR 2021).

Past studies of PFAS and their associations with human disease and health outcomes have shown evidence for associations with decreased antibody response (in adults and children), dyslipidemia (in adults and children), and decreased infant and fetal growth. Of import to the current investigation, past studies into PFAS have shown evidence for an association with increased risk of kidney and testicular cancer in adults (Steeland 2021, Viera

2013, Barry 2013). In addition, past studies have found limited or suggestive evidence for increased risk of breast cancer in adults (NASEM 2022).

In response to the USEPA's request, IDPH has produced the following analysis to assess cancer incidence in the area surrounding, and downstream of the 3M facility.

Data Sources and Methods

The USEPA provided IDPH with a list of ZIP codes that approximated the area of concern. Selection of specific ZIP codes were driven by two lines of reasoning. First, ZIP codes within a 10-mile radius of the facility were thought to be at risk of PFAS exposure through airborne emissions of PFAS from the facility. Secondly, ZIP codes that are suspected to have drinking water contaminated with PFAS from the facility were also included. ZIP codes were reviewed to ensure a contiguous geographical area and are presented in Table 1 and Map 1.

Cancer cases were identified through the Illinois State Cancer Registry (ISCR). All malignant cancer cases from 1996 through 2019 were included in this assessment. This timeframe was selected for several reasons. It represents the most recent and most complete years of data in the registry that are a part of the operational period of the facility, the 24-year period provides a large number of cases and populations to examine, and it also allows for the typical cancer latency period, which would be 10 to 15 years for solid tumors.

Cancer cases were assigned to ZIP codes using geocoding. Geocoding is a process through which cancer cases are assigned to specific geographic locations based on address data received from reporting facilities at the time of diagnosis. The geocoding process in this study

was carried out in multiple steps using a series of computer programs (i.e., MapMarker®, Accurint™), in combination with manual examination of residential address data to ensure that cancer cases were being placed in the correct ZIP codes. First, all malignant cancer cases from 1996-2019 were selected for the 16 ZIP codes comprising the study area (N=22,387). Initially, two more ZIP codes, 61299 and 61204, were included in the study area. These two ZIP codes were later identified to be post office boxes. Twenty-four cancer cases that were assigned these ZIP codes were reviewed and residential address information sought in Accurint™. Residential ZIP codes were obtained for 11 cases found to have the 61204 post office box. Nine cases originally assigned to 61204 were reallocated to the 61201 ZIP code, one to 61265, and one to 61275. Residential address information could not be found for 13 cases (0.06%) and these were excluded. With this process finished, a total of 22,374 cases were identified for the study area.

In order to capture out-of-state cases, ISCR has standing agreements with other central cancer registries to identify Illinois resident cases that are identified outside the state and to share that data with ISCR. These registries include Arkansas, California, Florida, Indiana, Iowa, Kentucky, Michigan, Mississippi (through August 2004), Missouri, North Carolina, Washington, Wisconsin, Wyoming (through February 2008), and the Mayo clinic in Minnesota (through October 2005). Out-of-state diagnoses among residents of the study area accounted for 19.3% of the total number of cases reported between 1996 and 2019 and were included in the study. While identification of cancer cases in Illinois is dependent upon reporting by diagnostic and therapeutic facilities as mandated by state law, completeness of out-of-state reporting depends upon the years of operation of these other central registries, the extent of

their identification of out-of-state residents, and their standards of quality. To benchmark the performance of population-based cancer registries for data completeness, timeliness, and quality, the North American Association of Central Cancer Registries (NAACCR) has developed a certification process to review registry data for completeness, accuracy, and timeliness of reporting. As of May 2022, ISCR data met the highest performance criteria for Gold Certification for cancer diagnosis years 1996 through 2019. The statewide completeness of case reporting from all reporting sources, assessed using the NAACCR standard, is estimated to be 100% complete for all years between 1996 and 2019. The criteria for Silver and Gold certification can be found on the NAACCR website at https://www.naaccr.org/certification-criteria/.

All cancer cases from the study area were grouped by tumor site, sex, and age. These are referred to as the *observed* cases. Age- and sex-specific rates from comparable populations in Illinois were applied to each age group of the study population (indirect age adjustment) and to each tumor site to obtain an *expected* number of cases for the study area (Mattson 1986). For both observed and expected cases, two groups of cancer sites were considered in this study. The first group includes kidney, testicular, and female breast cancers. This cancer group of concern was selected because of its documented associations with PFAS exposure in scientific studies (NASEM 2022, Steeland 2021, Viera 2013, Barry 2013). The second group includes other tumor sites that ISCR routinely examines when conducting a cancer assessment study. This group included oral cavity, esophagus, stomach, colon and rectum, liver, pancreas, lung and bronchus, bone, melanoma, cervix, uterus, ovary, prostate, bladder, brain, nervous system, Hodgkin's lymphoma, non-Hodgkin's lymphoma, myeloma, leukemia, and all other

cancers. This second group of tumor sites was examined to capture any other possible cancer increases and to help generate new hypotheses for future studies. The site recode scheme used in this analysis was the International Classification of Diseases for Oncology version 3 (ICD-O-3) with adjustment for hematopoietic histologies as defined by the Surveillance Epidemiology and End Results Program (SEER) of the National Cancer Institute (NCI) (https://seer.cancer.gov/siterecode/index.html).

According to longstanding ISCR practice, cancer incidence in a study area is compared to a population with a similar population density, race distribution, and a large enough size to provide stable estimates (Howe and Keller et al 1993). In addition to state and county geographies, ISCR has defined and maintained four routinely used reference groups (Cook County, five suburban collar counties, small urban with 13 counties, and rural with 83 counties) for Illinois based on population density, rate of growth, Beale codes, and with a total population of at least 2 million. The study area in this examination was determined to be comprised of both small urban and rural areas. The southern study area ZIP codes 61201, 61264, 61265, 61240, 61241, 61256, 61244, 61282, and 61239 contained the majority of the small urban areas covered by the study area (i.e., the cities of Rock Island, Moline, East Moline, Milan, Silvis, Hampton, Carbon Cliff, Coal Valley, Green Rock, Colona, and Oak Grove) and was seen to be predominantly urban. In contrast, the northern ZIP codes 61252, 61251, 61250, 61230, 61257, 61242, and 61275 were observed to be predominantly rural. Given the urban-rural differences within the study area it was split into two study areas, a small urban and a rural study area, to aid in achieving demographically similar comparisons with referent groups. Additionally, PFAS exposure in the small urban study area is thought to be through

contaminated water, whereas exposure in the rural study is thought to be through both water and air contamination within 10 miles of the emission source. Total incident cancer cases for the small urban and rural study areas were 19,962 and 2,412 respectively. The small urban study area was compared to a group of 12 Illinois counties that comprised the small urban comparison group. Likewise, the rural study area was compared to 83 Illinois counties that male up the rural comparison group.

Age- and sex-specific population counts for ZIP codes in Illinois for each year between 1996 and 2019 were required in order to compute the observed and expected cases in this cancer assessment. While this level of population information is available for census years 2000 and 2010, it was not available for non-census years. Because of this, non-census year population figures were estimated from the 2000 and 2010 U.S. Census, the most reliable sources for small area population. Age- and sex-specific population counts for ZIP codes were created through application of a linear function to interpolate and extrapolate counts from the 2000 and 2010 census to other years. These estimates were then aggregated to form age- and sex-specific population figures for both study areas.

The observed number of cases was compared with the expected number of cases for all age-, sex-, and site-specific categories. Standardized incidence ratios (SIR) and their 99% confidence intervals (CI) were calculated. An SIR is the ratio of observed cases to the expected number of cases, and an SIR greater than 1.0 or less than 1.0 indicates that observed cases are higher or lower than the expected cases, respectively. The SIR is considered statistically significant when the SIRs confidence interval (CI) does not include 1.0. A statistically

significant SIR means that the SIR, as judged by statistical significance, is unlikely to have occurred by chance. More technically, a statistically significant SIR indicates that there is a low probability (less than 1% chance) of getting a result as extreme or more extreme than what is observed, if there is truly no difference between the expected and observed numbers, and all assumptions related to the statistical test are true. The SIR, CIs, and resulting statistical significance are affected by the strength of the exposure, incidence of the disease, the size of the population studied, and many other factors, such as quality of the data, choice of the study areas, and changes in cancer reporting (Aschengrau and Seage 2003, Last 2001). See appendix A for formulas used in the calculation of SIRs.

Results

Kidney, Testicular, and Female Breast Cancers

Over the 24-year time period, the SIRs for kidney cancer were significantly lower than expected in males and females of the small urban study area. Among women residing in the small urban study area, breast cancer was also observed to be significantly lower than expected. Testicular cancer was observed to be slightly elevated, but not statistically significant ($p = 0.02$). In the rural study area, no significant differences in SIRs were observed in kidney, testicular, or female breast (Table 2 and 3).

Other Cancer Sites

In the small urban study area, cervical and uterine cancers were observed to be significantly elevated in women, 20% and 10% respectively. Also, lung, myeloma, and

leukemia cancers were seen to be significantly depressed. In men, no significant elevations were observed, but colorectal, lung, and leukemia cancers were observed to be significantly lower than expected. The rural study area displayed a significant excess of melanoma cases in females (50% higher than expected), and a significant depression of colorectal cancer in females and lung cancer in males and females.

Discussion

This cancer assessment used two study areas, two reference groups, and examined not only kidney, testicular and female breast cancers, the cancers of concern due to their documented associations with PFAS, but also other cancer sites that have not been shown to be related to PFAS exposure. The assessment included 82 SIRs and found 11 where the observed rates of specific cancers were significantly lower in the populations being examined, and three with significantly elevated cancer rates (cervix and uterus in the small urban study area and female melanoma in the rural study area).

With respect to the PFAS-related cancer sites, we observed testicular cancer to be elevated above expected, albeit not significantly (p=0.02), in one of the study areas. This observation, however, was accompanied by lower female breast cancer and kidney cancer incidence in the small urban study area. The lack of elevations within cancer sites of concern and differences between study areas means this study does not provide consistent evidence for an association between PFAS and cancer in the populations examined.

In addition to kidney, testicular, and female breast cancers, this study examined a number of other common cancer sites and found increases in one, melanoma in females of the

rural study area, and significant decreases in several others. These results should be viewed with an abundance of caution, as none of these sites have yet been reported by previous studies as having an association with PFAS exposure. Likewise, decreases observed in cancer sites should not be interpreted as a possible protective effect of PFAS.

The present assessment has several important limitations that need to be considered. First, with just over 80 age, sex, cancer site, and reference group combinations being compared, it is likely that this process may produce some "false significant values" by chance. In statistical terms, this is called the multiple comparison problem. The more comparisons made, the more pronounced the problem is. Clearly, simultaneously examining many cancer sites would exacerbate the problem. The potential consequence is that chance occurrences cannot be ruled out in explaining differences between the observed and expected numbers. The confidence interval was set at 99%, which means that there was a 1 out of 100 chance that a significant finding was a false positive.

Second, due to the lack of annual population data from the census for the study area, the 2000 and 2010 census population numbers were used in interpolating and extrapolating population counts for non-census years. These imprecise denominator numbers, when used to derive sex-specific expected numbers, might have introduced errors and biases into the comparison, of which neither the direction nor the magnitude is known.

Third, many potential risk factors for cancer, including occupational exposure, smoking, diet, lifestyle, family history, and other medical conditions, are not collected by the current registry system and, as a result, their inclusion for analysis was not possible. Living in a study

area at the time of diagnosis was a crude proxy for exposure to PFAS. This is because a cancer patient could have either left or moved into the study area right before or after their cancer diagnosis, resulting in either a case under-count or a case over-count. This lack of individual-level information on the history of residence and other risk factors for cases in the study areas and the reference population made more refined analysis and comparison impossible. Therefore, any observed increase, in and of itself, is insufficient to draw conclusions regarding the potential impact of PFAS exposure.

Fourth, the lack of specific information on PFAS exposure in study area residents as well as comparison populations could be a source of potential confounding. Without this information, it is possible that ZIP codes selected for each study area could have included areas with very little PFAS exposure, thus diluting the exposed population. Also, since PFAS are widespread in the environment, it is possible that the comparison groups also contain some level of exposure. Without any measure of PFAS exposure the magnitude and direction of any confounding influence is unknown.

Finally, small numbers could lead to unstable SIRs and decreased statistical power to detect true differences. The total cancer cases (small urban N=19,962, rural N=2,412) seemed to be adequate for overall analyses in this assessment. However, in stratifying by gender and cancer site some comparisons were made using case counts less than 10. These SIRs are not very stable and should not be given too much weight as a result. The direct consequence of small numbers is the lack of statistical power for the study to identify a difference when indeed a true difference could exist. The problem could be further amplified by the presence of the

study's other limitations (e.g., imprecise measures of PFAS exposure and lack of measures on other risk factors), resulting in false negative findings.

In conclusion, this cancer assessment examined several cancer sites that included cancers that have a recognized association with PFAS, and other common cancer sites that have no such association with PFAS, in adults of the study areas, over the years 1998 through 2017. For kidney, testicular, and female breast, a cancer group of concern due to their documented PFAS associations, the study found a non-significant elevation in testicular cancer but no elevations in other sites. However, the simultaneous presence of other cancer sites displaying significant decreases raised valid questions about the overall findings regarding kidney, testicular, and female breast cancers, as a group. For other common cancer sites, the study found increased cervical and uterine cancer in females of the small urban study area, but again, other cancers, such as kidney, lung, myeloma, and leukemia, showed decreases, and these differences were also reflected between genders. Several important limitations in methodology and data could be identified. Continuous tracking of the area's cancer incidence, with a particular focus on PFAS related sites, and conducting more studies elsewhere with larger populations are recommended.

References

Agency for Toxic Substances and Disease Registry (ATSDR). 2021. Toxicological Profile for Perfluoroalkyls. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Available from https://wwwn.cdc.gov/TSP/ToxProfiles/ToxProfiles.aspx?id=1117&tid=237

Aschengrau A, Seage G. Essentials of Epidemiology in Public Health. Sudbury MA: Jones and Bartlett; 2003:222-223.

Barry V, Winquist A, Steeland K. Perfluorooctanoic Acid (PFOA) Exposures and Incident Cancer among Adults Living Near a Chemical Plant. Environmental Health Perspectives. 2013;121:1313-1318.

Howe HL, Keller JE, Lehnherr M. Relation between Population Density and Cancer Incidence, Illinois 1986-1990. Am J Epidemiol 1993;138:29-36.

International Agency for Research on Cancer (IARC). Some Chemicals used as Solvents and in Polymer Manufacture / IARC Monographs on the Evaluations of Carcinogenic Risks to Humans. 2016: Lyon, France.

Last J. A Dictionary of Epidemiology. New York NY: Oxford University Press; 2001: 172.

Mattson DE. Statistics: Difficult Concepts, Understandable Explanations. Oak Park, Ill.: Bolchazy-Carducci Publishers Inc.;1986:386-389.

National Academies of Sciences, Engineering, and Medicine (NASEM) 2022. Guidance on PFAS Exposure, Testing, and Clinical Follow-Up. Washington, DC: The National Academies Press. https://doi.org/10.17226/26156.

Steeland K, Winquist A. PFAS and cancer, a scoping review of the epidemiologic evidence. Environ Res 2021;194:110690.

United States Environmental Protection Agency. Drinking Water Health Advisory for Perfluorooctanoic Acid (PFOA). 2016: Washington, DC. Available from: https://www.epa.gov/sites/default/files/2016-05/documents/pfoa_health_advisory_final-plain.pdf

United States Environmental Protection Agency. Drinking Water Health Advisory for Perfluorooctane Sulfonate (PFOS). 2016: Washington, DC. Available from: https://www.epa.gov/sites/default/files/2016-05/documents/pfos_health_advisory_final-plain.pdf

Viera VM, Hoffman K, Shin HM, Weinberg JM, Webster TF, Fletcher T. Perfluorooctanoic Acid Exposure and Cancer Outcome sin a Contaminated Community: A Geographical Analysis. Environmental Health Perspectives 2013; 121: 318-323

Figures and Tables

Table 1: ZIP Codes Comprising the Study Areas

Small Urban	Rural
61201	61230
61239	61242
61240	61250
61241	61251
61244	61252
61256	61257
61264	61275
61265	
61282	

Map 1:Small Urban and Rural Study Area ZIP Codes

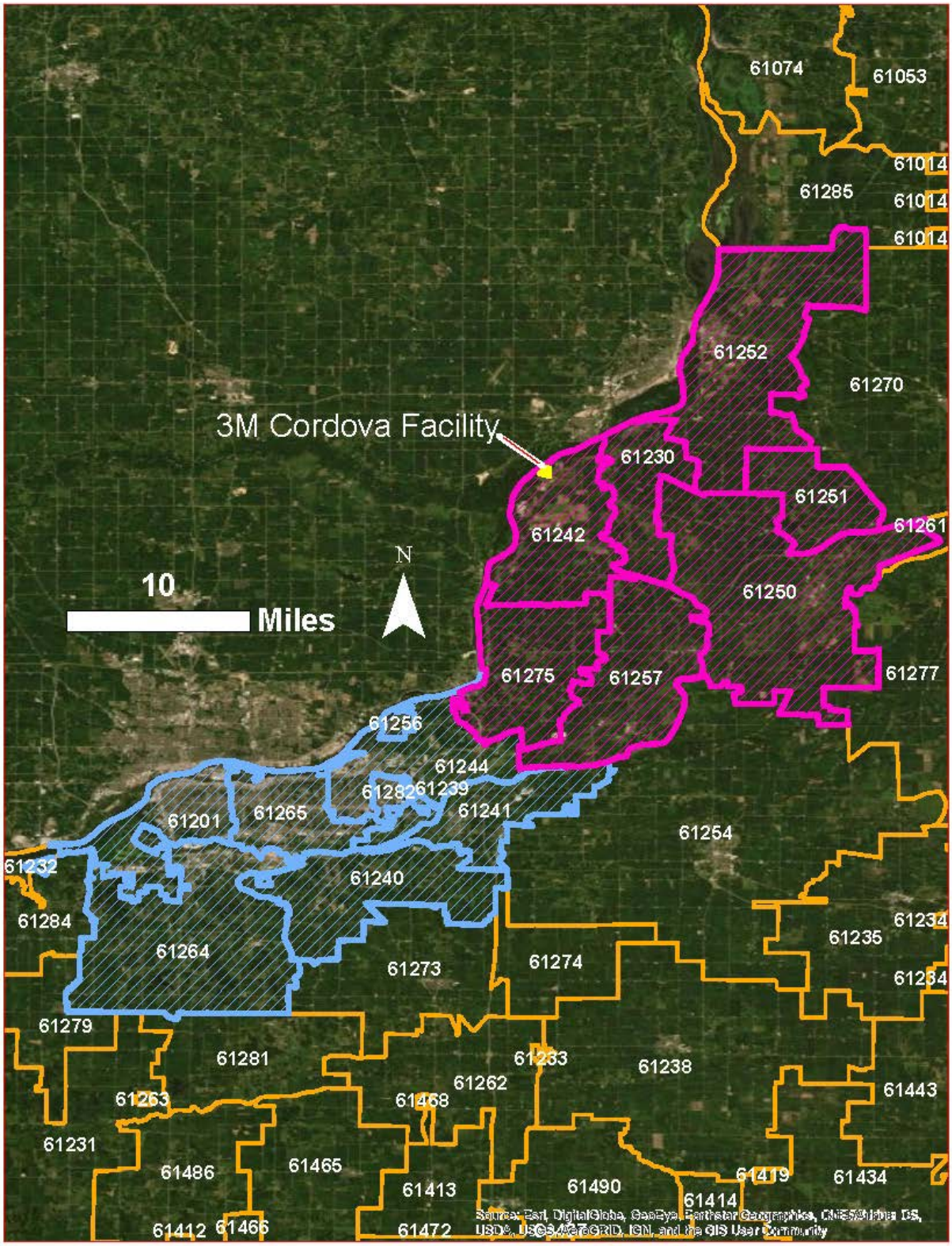

Table 2: Standardized Incidence Ratios for Common Cancer Sites for Males by ZIP Code Group, 1996-2019

	Small-Urban ZIP Codes					Rural ZIP Codes				
SITES	**Obs.**	**Exp.**	**SIR**	**99% LCI**	**99% UCI**	**Obs.**	**Exp.**	**SIR**	**99% LCI**	**99% UCI**
Males										
Oral Cavity	354	355.3	1.0	0.9	1.1	54	49.6	1.1	0.7	1.5
Esophagus	196	188.7	1.0	0.9	1.2	24	26.7	0.9	0.5	1.5
Stomach	128	157.2	0.8	0.6	1.0	17	19.3	0.9	0.4	1.6
Colorectal*	*973*	*1,085.0*	*0.9*	*0.8*	*0.9*	145	159.3	0.9	0.7	1.1
Liver	165	164.5	1.0	0.8	1.2	16	19.1	0.8	0.4	1.5
Pancreas	270	272.0	1.0	0.8	1.2	28	36.1	0.8	0.4	1.2
Lung*	*1,680*	*1,792.8*	*0.9*	*0.8*	*0.9*	*175*	*256.4*	*0.7*	*0.6*	*0.8*
Bone	17	17.3	1.0	0.5	1.8	2	2.1	1.0	0.0	4.5
Melanoma	480	471.8	1.0	0.9	1.1	71	63.3	1.1	0.8	1.5
Breast Invasive	20	24.0	0.8	0.4	1.4	1	0.1	8.8	0.0	65.5
Testis	109	89	1.2	0.9	1.6	8	10.6	0.8	0.2	1.8
Prostate	2,765	2,733.1	1.0	1.0	1.1	342	357.8	1.0	0.8	1.1
Bladder	745	742.9	1.0	0.9	1.1	109	101.7	1.1	0.8	1.4
Kidney*	*386*	*477.8*	*0.8*	*0.7*	*0.9*	67	60.0	1.1	0.8	1.5
Nervous System	130	145.5	0.9	0.7	1.1	14	18.3	0.8	0.3	1.5
Hodgkin's Lymphoma	71	56.2	1.3	0.9	1.7	6	6.3	0.9	0.2	2.5
Non-Hodgkin's Lymphoma	394	443.9	0.9	0.8	1.0	63	58.3	1.1	0.8	1.5
Myeloma	143	145.9	1.0	0.8	1.2	19	18.7	1.0	0.5	1.8
Leukemia*	*250*	*335.3*	*0.8*	*0.6*	*0.9*	28	44.3	0.6	0.4	1.0
All Other Sites	1,003	1,019.4	1.0	0.9	1.1	123	135.8	0.9	0.7	1.1

* SIRs in **bold** indicate significantly higher incidence at the p<=0.01 level, SIRs in *italics* indicate significantly lower incidence at the p<=0.01 level

Source: Illinois State Cancer Registry, data as of November 2021

Table 3: Standardized Incidence Ratios for Common Cancer Sites for Females by ZIP Code Group, 1996-2019

	Small Urban ZIP Codes					Rural ZIP Codes				
SITES	**Obs.**	**Exp.**	**SIR**	**99% LCI**	**99% UCI**	**Obs.**	**Exp.**	**SIR**	**99% LCI**	**99% UCI**
Females										
Oral Cavity	156	154.9	1.0	0.8	1.2	17	17.5	1.0	0.5	1.8
Esophagus	43	49.7	0.9	0.6	1.3	5	5.2	1.0	0.2	2.7
Stomach	95	95.6	1.0	0.8	1.3	8	8.8	0.9	0.3	2.1
Colorectal*	985	1,060.7	0.9	0.9	1.0	*86*	*128.7*	*0.7*	*0.5*	*0.9*
Liver	46	60.6	0.8	0.5	1.1	10	6.4	1.6	0.6	3.3
Pancreas	253	270.2	0.9	0.8	1.1	33	28.6	1.2	0.7	1.8
Lung*	*1,437*	*1,539.3*	*0.9*	*0.9*	*1.0*	*117*	*168.9*	*0.7*	*0.5*	*0.9*
Bone	7	14.0	0.5	0.1	1.2	1	1.8	0.6	0.0	4.2
Melanoma*	387	359.8	1.1	0.9	1.2	**65**	**43.3**	**1.5**	**1.1**	**2.1**
Breast Invasive*	*2,726*	*2,900.2*	*0.9*	*0.8*	*0.9*	334	323.9	1.0	0.9	1.2
Cervix*	**189**	**154.9**	**1.2**	**1.0**	**1.5**	16	21.0	0.8	0.4	1.4
Uterus*	**666**	**607.4**	**1.1**	**1.0**	**1.2**	73	74.5	1.0	0.7	1.3
Ovary	265	279.8	0.9	0.8	1.1	35	32.0	1.1	0.7	1.7
Bladder	234	253.8	0.9	0.8	1.1	17	26.5	0.6	0.3	1.2
Kidney*	*253*	*303.8*	*0.8*	*0.7*	*1.0*	36	34.4	1.0	0.7	1.6
Nervous System	113	116.7	1.0	0.7	1.2	19	14.0	1.4	0.7	2.4
Hodgkin's Lymphoma	43	42.5	1.0	0.7	1.5	7	4.8	1.5	0.4	3.6
Non-Hodgkin's Lymphoma	366	390.5	0.9	0.8	1.1	44	43.9	1.0	0.7	1.5
Myeloma*	*92*	*125.7*	*0.7*	*0.5*	*0.9*	11	12.6	0.9	0.3	1.8
Leukemia*	*179*	*248.5*	*0.7*	*0.6*	*0.9*	27	28.0	1.0	0.6	1.6
All Other Sites	1,118	1,192.0	0.9	0.9	1.0	139	131.0	1.1	0.8	1.3

* SIRs in **bold** indicate significantly higher incidence at the p<=0.01 level, SIRs in *italics* indicate significantly lower incidence at the p<=0.01 level

Source: Illinois State Cancer Registry, data as of November 2021

APPENDIX A: Standardized Incidence Ratio and Confidence Limits

Various authors discuss the standardized mortality ratio (SMR) and provide exact and approximate confidence limits for the true SMR. These results are also applicable to the standardized incidence ratio (SIR). The following sections provide a brief outline of the results and give references to more detailed discussions.

Definition of the SIR

Suppose the person-time from the study group (i.e., cohort) is allocated among *M* cells defined by the cross-classification of various adjustment variables, such as gender, race, attained age group, and attained calendar year group. Let t_k represent the person-time and D_k represent the observed events that the cohort subjects contribute to the *k*th cell, and let λ_k^* represent the standard rate for the *k*th cell, where *k* = 1, 2, ..., *M*. Given this notation, the SIR is defined as

$$\mathrm{SIR} = \frac{\sum_{k=1}^{M} D_k}{\sum_{k=1}^{M} t_k \lambda_k^*} = \frac{D}{E^*}$$

where the total number of events observed in the cohort is $D = \sum_{k=1}^{M} D_k$, and the total number of expected events is $E^* = \sum_{k=1}^{M} E_k^* = \sum_{k=1}^{M} t_k \lambda_k^*$ (Breslow and Day,1987; Sahai and Khurshid,1996).

Approximate Confidence Limits for the True SIR

The approximate limits for the true SIR, Φ, are $\mathrm{SIR}_{\tilde{L}} = \frac{D}{E^*}\left(1 - \frac{1}{9D} + \frac{Z_{\alpha/2}}{3\sqrt{D}}\right)^3$ and

$$\mathrm{SIR}_{\tilde{U}} = \frac{D+1}{E^*}\left(1 - \frac{1}{9(D+1)} + \frac{Z_{1-\alpha/2}}{3\sqrt{D+1}}\right)^3$$

where Z_α is the 100α percentile of the standard normal distribution (Rothman and Boice, 1979,

1982; Breslow and Day, 1987; Sahai and Khurshid, 1993, 1996). Rothman and Boice (1979, 1982) mention that these limits were first proposed by Byar (unpublished).

References

Breslow NE, Day NE (1987). Statistical Methods in Cancer Research. Vol. II, The Design and Analysis of Cohort Studies (IARC Scientific Publication No. 82). Lyon, France: International Agency for Research on Cancer.

Rothman KJ, Boice JD, Jr. (1979). Epidemiologic Analysis with a Programmable Calculator (NIH Publication 79-1649). Washington DC: US Government Printing Office.

Rothman KJ, Boice JD, Jr. (1982). Epidemiologic Analysis with a Programmable Calculator, New Edition. Boston, MA: Epidemiology Resources, Inc.

Sahai H, Khurshid A (1993). Confidence Intervals for the Mean of a Poisson Distribution: A Review. *Biometrical J*, 35: 857-67.

Sahai H, Khurshid A (1996). Statistics in Epidemiology: Methods, Techniques, and Applications. Boca Raton, FL: CRC Press, Inc.

Wilson EB, Hilferty MM (1931). The Distribution of Chi-Square. *Proc Natl Acad Sci USA*, 17: 684-8