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Two Suspected Worksite or Occupational Cancer Clusters Investigated Using the Cancer Data Registry and Multiple Primary Standardized Incidence Ratios in SEER*Stat—Idaho, 2013–2014

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Abstract

Background: Investigations of suspected cancer clusters are resource intensive and rarely identify true clusters: among 428 publicly reported US investigations during 1990–2011, only 1 etiologic cluster was identified. In 2013, the Cancer Data Registry of Idaho (CDRI) was contacted regarding a suspected cancer cluster at a worksite (Cluster A) and among an occupational cohort (Cluster B). We investigated to determine whether these were true clusters.

Methods: We derived investigation cohorts for Cluster A from facility-provided employee records and for Cluster B from professional licensing records. We used Registry Plus™ Link Plus to conduct probabilistic linkage of cohort members to the CDRI registry and completed matching through manual review by using LexisNexis®, Accurint®, and the Social Security Death Index. We calculated standardized incidence ratios (SIR) using the MP-SIR session type in SEER*Stat and Idaho and US referent populations.

Results: For Cluster A, we identified 34 cancer cases during 9,689 person-years; compared with Idaho and US rates, 95% CIs for SIRs included 1.0 for 24 of 24 primary site categories. For Cluster B, we identified 78 cancer cases during 15,154 person-years; compared with Idaho rates, 95% CI for SIRs included 1.0 for 23 of 24 primary site categories and was less than 1.0 for lung and bronchus cancers, and compared with US rates, 95% CI for SIRs included 1.0 for 22 of 24 primary site categories and was less than 1.0 for lung and bronchus and colorectal cancers.

Conclusion: We identified no statistically significant excess in cancer incidence in either cohort. SEER*Stat's MP-SIR is an efficient tool for performing SIR assessments, a Centers for Disease

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Control and Prevention/Council of State and Territorial Epidemiologists–recommended step when investigating suspected cancer clusters.

Keywords

cancer; cancer registry; cluster; occupational group; workplace

Introduction

Sometimes a greater-than-expected number of cancer cases is perceived in the worksite or among an occupational cohort and attributed to exposure to a shared occupational hazard. Central cancer registries and local public health officials might be asked to respond to reports of these events, referred to as cancer clusters. However, investigations of suspected cancer clusters are resource intensive and rarely result in the identification of a cluster with a common etiology. Among 428 publicly reported US investigations during 1990–2011, only 1 etiologic cluster was identified.[1] Challenges surrounding cancer cluster investigations include studying a disease with multiple causal factors and a sometimes decades-long latency period between exposure to a disease-causing agent and the onset of disease symptoms. Nonetheless, these investigations remain an important function of public health agencies. Investigations of cancer in occupational settings have contributed significantly to our understanding of cancer risks and etiologies.[2] An estimated 4% to 10% of cancers in the United States are caused by occupational exposures.[3] Moreover, approximately a third of human carcinogens were first documented via well-designed cohort or nested case-control worksite studies with a priori etiologic hypotheses.[2]

Participants from several disciplines and sectors who all study or perform cancer cluster investigations held a workshop, “Advancing Cancer Cluster Assessments: Starting the Dialogue,” in April 2013 aiming to advance the search for new investigative approaches. Results of this workshop were published with the intention of encouraging consideration of new ways of thinking about cancer cluster investigations.[4] To add to a set of emerging methods in the field, we describe here a novel procedure used in the investigation of a suspected cancer cluster at a worksite and among an occupational cohort: the use of the Multiple-Primary–Standardized Incidence Ratios (MP-SIR) session type in SEER*Stat.[5] MP-SIR sessions are generally used to compare cancer incidence in a defined cohort of persons previously diagnosed with cancer to the cancer incidence in the general population. We used them to compare cancer incidence in a worksite cohort and among an occupational cohort to the cancer incidence in the general population.

Methods

In 2013, the Cancer Data Registry of Idaho (CDRI) was contacted regarding a suspected cancer cluster at a worksite (Cluster A) and another (Cluster B) among an occupational cohort. CDRI and the Division of Public Health (DPH) at the Idaho Department of Health and Welfare investigated to determine if these were true clusters, meaning the cancer incidence rates were elevated compared to those expected in the general population. While

both investigations happened separately and at different times, the methodology implemented was similar and will therefore be described conjointly.

CDRI reviewed a list of cancer cases submitted by the inquirers against the CDRI database. In addition, CDRI requested a roster of all current and former worksite employees (Cluster A) and of all members of the occupational cohort (Cluster B), so that CDRI and DPH could review it against the CDRI database to look for any additional unreported cancer cases among roster members. To conduct a linkage between the rosters and the CDRI database, to ascertain cancer cases, we requested the following information from the worksite inquirer (Cluster A): first name, middle name, last name, date of birth (at the least, month and year), sex, home and employment address, Social Security number, and start and end dates of employment or time spent at workplace or occupation. From the occupational group inquirer (Cluster B), we requested first name, last name, date of birth (at the least, month and year), sex, home and/or employment address, professional certification or license status (ie, active, inactive, or historical), and start and end dates of occupational licensure. Cancer cases that occurred among persons who were diagnosed with cancer prior to working in the suspected facility or occupation were not included in the investigations. We matched the entire worksite and occupational group rosters, instead of simply the initial lists submitted by the inquirers, to the CDRI database to confirm cancer primary site and allow for a statistical assessment of the existence of a cancer cluster.

We cleaned the roster data before linking with the CDRI population-based cancer registry. We scanned for and removed duplicate records using Registry Plus™ Link Plus, a program developed at the Center for Disease Control and Prevention (CDC)'s Division of Cancer Prevention and Control in support of the National Program of Cancer Registries (NPCR). We populated missing data such as dates of birth and changes of residence among former workers, by using Accurint®, an online subscription-based public records service from LexisNexis®. Additionally, we imputed missing values for sex by using a file of name frequencies by sex from the National Center for Health Statistics.

We linked the cleaned roster data to the CDRI database using Link Plus, in which probabilistic record linkage scores were computed based on the theoretical framework developed by Fellegi and Sunter.[6] If more than 1 primary cancer case was diagnosed in a patient, every cancer case was selected for inclusion in the resulting analytic data set. During linkage, we identified candidate matching pairs using the following data fields: birth date, Social Security number, and Soundex functions of last name, first name, and middle name. Among the candidate matching pairs, we computed match scores using last name, first name, middle name, Social Security number, and birth date. For indeterminate match results, manual review was conducted using additional resources such as Accurint.

CDRI routinely collects vital status information on all cases. By using the Social Security Death Index, we determined the vital status of each person in the cohorts that did not link to the CDRI database. Because CDRI was not population-based until 1971, cancer cases and person-time at risk were not counted or accrued prior to 1971 in the analytic data set. Person-time contributions were calculated from the initial date of hire or licensure (censored to 1971). The end of the study period was the latest date for which CDRI received cancer

reports for all cases in the roster (ie, July 2013). For Cluster B, 2 initial analytic data sets were created for a sensitivity analysis: One data set was created whereby persons whose licenses had expired were censored on the date of license expiration, and another data set was created using July 2013 as the end of study for all records with vital status “alive.” The former data set has a conservative exit date, because it contained the same number of cancer cases as the latter database, while including a shorter person-time accrual, thereby resulting in higher calculated cancer rates. The use of both initial analytic data sets served as a sensitivity analysis in the investigation.

We assumed a latency of 6 months, meaning cancer cases and person-time at risk were counted and accrued starting 6 months after the start of the study period (ie, the date of hire at the worksite for Cluster A and the date of occupational licensure in Cluster B). Thus, no case diagnosed within 6 months of employment or licensure would be considered related to a worksite or occupational hazard. Six months was selected because 1 cancer case was diagnosed within 7 months of employment on the worksite, and it has been our experience that trust among concerned parties is higher if all cancer cases can be included in cluster analyses. If a person ended employment prior to the end of the study period, cancer cases and person-time at risk were still counted and accrued until the end of the study. This is because he or she may have been diagnosed with cancer post-employment, potentially as a result of employment. And, even if no cancer diagnosis was made, the person-time at risk was still meaningful and needed to be accounted for. A mock-up of case and person-time contributions is shown in Figure 1.

Using SEER*Stat, we compared observed malignant cancer and benign brain and other nervous system tumor incidence rates among the worksite or occupational cohort with referent rates—also based on allowance of multiple primary cancers—from the National Cancer Institute’s Surveillance, Epidemiology, and End Results Program (SEER) for whites, and from the CDRI database for Idaho for all races. Cancer cases were coded according to the International Classification of Diseases for Oncology, 3rd edition.[7] SEER 9 registries (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco–Oakland, Seattle–Puget Sound, and Utah) were used for referent rates because incidence data were available for the longest time span, beginning with 1973. For the SEER data, incidence rates for the 1973–1974 period were used for years prior to 1973. Referent rates were stratified by primary site category, age group, sex, and year of diagnosis.

The expected number of incident cancer cases was calculated based upon age-, sex-, and time period-specific referent cancer incidence rates. Age was categorized into 5-year intervals. These rates were multiplied by the person-time for the worksite (Cluster A) and occupational cohort (Cluster B), stratified the same way, to calculate the number of expected incident cancer cases. Standardized incidence ratios (SIR) and 95% CIs were calculated for observed vs expected numbers of cases using the SEER*Stat Multiple Primary-Standardized Incidence Ratio (MP-SIR) session. Results were tabulated using CDRI annual report primary site categories, which include malignant cases (in situ urinary bladder cases are included in bladder category and overall in tables) and benign brain and other central nervous system cases.

Results

For Cluster A, we linked 1,296 employee records from the worksite roster to 177,494 CDRI records, from 1980–2013. Of those, 1,180 (91.0%) did not match to a CDRI cancer case. The linkage identified 56 employee matches to the CDRI database. Some of the linked persons had more than 1 primary cancer case. Among the 59 cancer cases identified in the analytic data set, 21 (35.6%) occurred before the worker's hire date and 3 additional cases (5.1%) were excluded from analysis because they were benign behavior in a site besides brain, or in situ behavior. There were 34 cases of invasive cancer and 1 case of benign brain and other nervous system tumors during 9,689 person-years. Compared with Idaho and US rates, 95% CIs for SIRs included 1.0 for all sites combined and for every primary site category (Table 1).

For Cluster B, we linked 874 occupational cohort records to 201,048 CDRI records, from 1970–2013. We ascertained the vital status for 166 persons for whom vital status was missing. Both analytic data sets contained 881 records. Using the more conservative data set, we identified 78 cancer cases during 15,154 person-years. Compared with Idaho rates, the 95% CI for SIRs included 1.0 for 23 of 24 primary site categories and was less than 1.0 for lung and bronchus cancers; compared with US rates, the 95% CI for SIRs included 1.0 for 22 of 24 primary site categories and was less than 1.0 for lung and bronchus and colorectal cancers (Table 2). Using the less conservative data set for person-years at risk also resulted in 78 cancer cases in the cohort, but more person-time was accrued; therefore, the incidence rates were lower (data not shown) and consequently the SIRs decreased. Compared with Idaho referent rates, there were fewer cases than expected of colorectal cancer, lung and bronchus cancer, and all cancer sites combined in the occupational cohort. These findings were statistically significant.

Discussion

We did not identify a statistically significant excess in cancer incidence among the worksite cohort (Cluster A) or the occupational cohort (Cluster B) in these investigations when compared with referent rates for Idaho or SEER regions. No statistically significant excess in cancer incidence was found among the worksite cohort or among the occupational cohort for every primary cancer site category assessed.

The negative findings in both cancer cluster investigations were not surprising. Many employed populations are healthier than the general population at the time they begin employment and are at lower risk of cancer than the general United States or Idaho populations, which include persons who are chronically ill and hospitalized.[8] Moreover, most occupational cancers manifest 1 or more decades after exposure. Use of longer follow-up periods could result in higher cancer incidence ratios. Cancers diagnosed among members of the worksite cohort and the occupational cohort who moved to other states before diagnosis were not ascertained because they were not reported to CDRI. Using additional state cancer registries might help to account for cohort mobility. Any potential underreporting of cases to CDRI is a potential source of undercounting of cancer cases in the worksite and occupational cohorts and the Idaho referent rates. Because CDRI was not

population-based until 1971, cancer cases and person-time at risk were not counted prior to 1971 in the resulting analytic data sets. This might have resulted in the exclusion of a number of cancer cases in the original employee or occupational cohort data sets. CDRI collects incidence data on all cancer patients who reside in the state of Idaho or who are diagnosed and treated for cancer in the state of Idaho; their records are routinely checked to assure data validity and reliability. Misclassification in the Social Security Death Index might have biased our results, as incorrect records of death have been known to occur.[9] We likely assumed too short a latency period (6 months), resulting in a longer person-time at risk accrual and counting of cases with too short of any purported exposure time to be related to employment. Cancer latency periods are typically assumed to be long.[10,11] Additionally, it is difficult to detect subtle effects, such as a statistically significant excess in cancer cases, when the number of cases is small.

We describe a new methodology used to investigate a suspected cancer cluster at a worksite and among an occupational cohort: the use of the MP-SIR session type in SEER*Stat. SEER*Stat's MP-SIR is an efficient tool for performing SIR assessments, a CDC/Council of State and Territorial Epidemiologists-recommended step when investigating suspected cancer clusters. Results for cancer in all sites are provided quickly and simultaneously. The choice of population-based referent rates to use in the analysis is easily obtained using the MP-SIR session; discrepancies between variables among the 2 data sets (analytic and referent) are highlighted and adjusted. Parameter settings within the session allow the user to easily define study period length; calculated statistics are quickly and easily stratified by variables of your choice. Overall, SEER*Stat's MP-SIR session provides a user-friendly interface and consistent approach to conducting worksite and occupational cancer cluster investigations. While other methods are also available to routinely perform cancer incidence SIR analyses in occupational cohorts,[12,13] we hope this new approach to the analysis of cancer incidence among worksite and occupational cohorts could also be considered by other central cancer registries.

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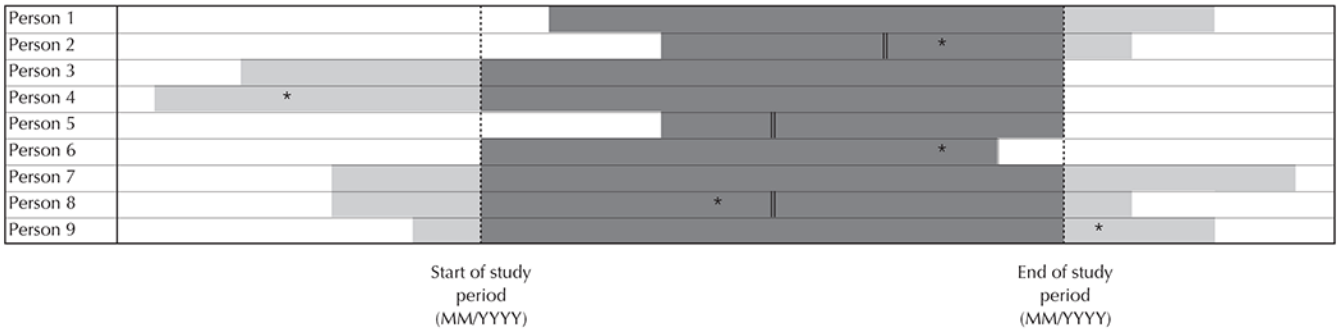

Figure 1. Examples of Case and Person-Time Contributions to a Worksite or Occupational Cohort Cancer Cluster Investigation

Mock-up data are for illustration purposes only and not sourced from any analytic data set. Asterisk (*) indicates cancer diagnosis. Light gray bars indicate no contribution to person-time. Dark gray bars indicate contribution to person-time, from start of study period (eg, the date of hire at the worksite for Cluster A and the date of occupational licensure in Cluster B) to end of study period (chosen to be the latest date for which the Cancer Data Registry of Idaho received cancer reports for all cases in the roster or occupational cohort). Persons 2, 6, and 8 would each contribute cases to the investigation, as denoted by asterisks. Persons 1, 3, 4, 5, 7, and 9 would contribute person-time, but not case counts (no cancer diagnosis within study period). Aside from person 6, who died shortly before the end of the study period, each person would contribute person-time up until the end of the study period, even if they left employment sometime between the start and end of the study period (ie, persons 2, 5, and 8; denoted by double vertical lines). Person 9 would not contribute to the case count because the cancer diagnosis occurred after the end of the study.

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Table 1.

Standardized Incidence Ratios of Cancer Among Cluster A Worksite Employees Compared with Idaho and SEER 9[a] Referent Populations

	Worksite Employees			*Idaho Referent Rates*		*SEER 9 Referent Rates*	
	No. Cancer Cases	**No. Employees**	**Person-Years at Risk**	**SIR**	**95% CI**	**SIR**	**95% CI**
All sites[b]	34	1,171	9,689	0.91	(0.63–1.27)	0.80	(0.56–1.12)
Bladder	1	1,171	9,689	0.86	(0.02–4.77)	0.75	(0.02–4.20)
Brain	0	1,171	9,689	0.00	(0.00–5.46)	0.00	(0.00–5.31)
Brain and other nervous system—benign	1	1,171	9,689	1.22	(0.03–6.77)	1.25	(0.03–6.99)
Breast (females)	12	573	5,174	1.72	(0.89–3.00)	1.43	(0.74–2.50)
Cervix (females)	0	573	5,174	0.00	(0.00–6.58)	0.00	(0.00–6.35)
Colorectal	2	1,171	9,689	0.72	(0.09–2.58)	0.63	(0.08–2.29)
Corpus uteri (females)	1	573	5,174	0.72	(0.02–4.02)	0.63	(0.02–3.50)
Esophagus	0	1,171	9,689	0.00	(0.00–10.20)	0.00	(0.00–10.06)
Hodgkin lymphoma	0	1,171	9,689	0.00	(0.00–13.31)	0.00	(0.00–11.47)
Kidney and renal pelvis	1	1,171	9,689	0.77	(0.02–4.30)	0.73	(0.02–4.04)
Larynx	0	1,171	9,689	0.00	(0.00–15.31)	0.00	(0.00–11.71)
Leukemia	0	1,171	9,689	0.00	(0.00–3.74)	0.00	(0.00–3.97)
Liver and intrahepatic bile duct	0	1,171	9,689	0.00	(0.00–7.88)	0.00	(0.00–6.33)
Lung and bronchus	0	1,171	9,689	0.00	(0.00–1.34)	0.00	(0.00–1.03)
Melanoma of the skin	5	1,171	9,689	1.88	(0.61–4.38)	1.61	(0.52–3.75)
Myeloma	0	1,171	9,689	0.00	(0.00–10.45)	0.00	(0.00–9.68)
Non-Hodgkin lymphoma	1	1,171	9,689	0.69	(0.02–3.86)	0.56	(0.01–3.10)
Oral cavity and pharynx	2	1,171	9,689	1.61	(0.19–5.81)	1.64	(0.20–5.91)
Ovary (females)	0	573	5,174	0.00	(0.00–5.73)	0.00	(0.00–4.74)
Pancreas	0	1,171	9,689	0.00	(0.00–5.48)	0.00	(0.00–5.01)
Prostate (males)	5	598	4,514	0.93	(0.30–2.17)	0.85	(0.27–1.97)
Stomach	0	1,171	9,689	0.00	(0.00–9.80)	0.00	(0.00–8.27)
Testis (males)	0	598	4,514	0.00	(0.00–8.92)	0.00	(0.00–8.71)
Thyroid	3	1,171	9,689	1.50	(0.31–4.40)	1.68	(0.35–4.91)

SEER, Surveillance, Epidemiology, and End Results Program; SIR, standardized incidence ratios.

[a] SEER 9 refers to the Surveillance, Epidemiology, and End Results Program registries in Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco–Oakland, Seattle–Puget Sound, and Utah.

[b] *All Sites* category includes malignant behavior cases for primary site categories shown and miscellaneous sites, and excludes benign and borderline behavior cases.

Table 2.

Standardized Incidence Ratios of Cancer (using Conservative Calculation of Person-Years at Risk) Among Cluster B Occupational Cohort Compared with Idaho and SEER 9[a] Referent Populations

	Occupational Cohort			*Idaho Referent Rates*		*SEER 9 Referent Rates*	
	No. Cancer Cases	**No. Persons**	**Person-Years at Risk**	**SIR**	**95% CI**	**SIR**	**95% CI**
All Sites[b]	78	841	15,154	0.89	(0.70–1.11)	0.79	(0.63–0.99)
Bladder	3	841	15,154	0.56	(0.11–1.62)	0.50	(0.10–1.46)
Brain	2	841	15,154	1.36	(0.16–4.90)	1.33	(0.16–4.81)
Brain and other nervous system—benign	2	841	15,154	2.15	(0.26–7.76)	2.93	(0.36–10.59)
Breast (females)	2	299	3,514	0.52	(0.06–1.89)	0.44	(0.05–1.57)
Cervix (females)	0	299	3,514	0.00	(0.00–9.39)	0.00	(0.00–8.93)
Colorectal	3	841	15,154	0.37	(0.08–1.08)	0.31	(0.06–0.91)
Corpus uteri (females)	2	299	3,514	2.83	(0.34–10.23)	2.47	(0.30–8.92)
Esophagus	0	841	15,154	0.00	(0.00–3.24)	0.00	(0.00–2.90)
Hodgkin lymphoma	0	841	15,154	0.00	(0.00–7.18)	0.00	(0.00–6.23)
Kidney and renal pelvis	3	841	15,154	1.06	(0.22–3.10)	0.95	(0.20–2.79)
Larynx	0	841	15,154	0.00	(0.00–3.61)	0.00	(0.00–2.79)
Leukemia	1	841	15,154	0.39	(0.01–2.15)	0.37	(0.01–2.08)
Liver and intrahepatic bile duct	2	841	15,154	2.24	(0.27–8.09)	1.60	(0.19–5.79)
Lung and bronchus	4	841	15,154	0.35	(0.10–0.90)	0.29	(0.08–0.75)
Melanoma of the skin	4	841	15,154	0.84	(0.23–2.15)	0.73	(0.20–1.87)
Myeloma	2	841	15,154	1.82	(0.22–6.57)	1.81	(0.22–6.53)
Non–Hodgkin lymphoma	2	841	15,154	0.57	(0.07–2.06)	0.48	(0.06–1.72)
Oral cavity and pharynx	3	841	15,154	0.90	(0.18–2.62)	0.92	(0.19–2.69)
Ovary (females)	0	299	3,514	0.00	(0.00–9.91)	0.00	(0.00–8.52)
Pancreas	4	841	15,154	2.06	(0.56–5.28)	1.86	(0.51–4.77)
Prostate (males)	33	542	11,640	1.40	(0.96–1.96)	1.35	(0.93–1.90)
Stomach	0	841	15,154	0.00	(0.00–2.88)	0.00	(0.00–2.26)
Testis (males)	3	542	11,640	3.68	(0.76–10.74)	3.52	(0.73–10.29)

	Occupational Cohort			*Idaho Referent Rates*		*SEER 9 Referent Rates*	
	No. Cancer Cases	**No. Persons**	**Person-Years at Risk**	**SIR**	**95% CI**	**SIR**	**95% CI**
Thyroid	2	841	15,154	1.13	(0.14–4.07)	1.17	(0.14–4.23)

SEER, Surveillance, Epidemiology, and End Results Program; SIR, standardized incidence ratios.

[a] SEER 9 refers to the Surveillance, Epidemiology, and End Results Program registries in Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco–Oakland, Seattle–Puget Sound, and Utah.

[b] *All Sites* category includes malignant behavior cases for primary site categories shown and miscellaneous sites, and excludes benign and borderline behavior cases.