

# Chapter 14

## New Malignancies Following Cancer of the Brain and Central Nervous System

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### Synopsis

The incidence of multiple primary cancers was evaluated in a cohort of 31,336 persons diagnosed with a first primary cancer of the brain and central nervous system (CNS) during 1973-2000 and followed for an average of 3.4 years. The overall incidence of new malignancies was 11% higher than expected (O/E=1.11, O=496, EAR=4 per 10,000 person-years). The O/E ratio increased over the first 10 years of follow-up and then decreased. Although the risk of subsequent cancer was increased only slightly overall, considerably larger, statistically significant relative excesses were observed for several uncommon types, including cancers of the bone, soft tissue, brain and CNS, salivary gland, and thyroid gland, as well as acute non-lymphocytic leukemia and melanoma of the skin. Relative and absolute risks were markedly higher for those with first cancers diagnosed in childhood (age <17 years) than for those first diagnosed at older ages. The risk of new cancers was significantly increased following medulloblastoma, ependymoma, and astrocytoma, but not following glioblastoma or meningioma. Radiotherapy appeared to contribute to the excess of new malignancies of the bone, brain, and thyroid gland, whereas chemotherapy probably played a major role in the excess of subsequent leukemia. The etiology of the new soft tissue cancers and melanoma is unclear, but it may involve shared genetic susceptibility factors.

### Brain and Other Central Nervous System Cancers

Approximately 18,500 cancers of the brain and other central nervous system (CNS) are diagnosed each year in the U.S. (Jemal et al, 2005). Brain and other CNS cancers are relatively uncommon, accounting for 1.3% of all new cancer cases and 2.2% of cancer deaths. Most CNS tumors (94%) arise in the brain. Incidence is higher among males than females and higher among whites than blacks (Ries et al, 2004). The 5-year relative survival rate is 33.1%, but survival is inversely associated with age at diagnosis. Just 6% of persons diagnosed over the age of 65 live more than 5 years (Ries et al, 2004).

*Abbreviations: O=observed number of subsequent (2nd, 3rd, etc.) primary cancers; O/E=ratio of observed to expected cancers; CI=confidence interval; PYR=person-years at risk; EAR=excess absolute risk (excess cancers per 10,000 person-years, calculated as [(O-E)/PYR]×10,000).*

Treatments during 1973-2000 typically included surgery and radiation. Radiation was used more often in the treatment of brain cancer (74%) than for cancers in other parts of the CNS (47%). Because most cancers of the nervous system are intracranial and rarely metastasize outside of the CNS, the volume of tissue that receives high doses of radiation generally is limited and confined to the head or neck regions (Black, 1991a,b; Pollack, 1994). However, for medulloblastoma and anaplastic ependymoma, which may spread throughout the spinal axis, craniospinal irradiation sometimes is given (Pollack, 1994; Levin et al, 2001). Today, cranial radiotherapy often is deferred in very young children to avoid the harmful effects of radiation on the developing nervous system (Pollack, 1994; Packer, 1995). Few chemotherapy agents have been proven effective in the treatment of cancers of the brain and CNS (Levin et al, 2001). The following agents have been used: bleomycin, chloroethylnitrosoureas, cisplatin, cyclophosphamide, doxorubicin, etoposide, procarbazine, temozolomide, and vincristine (Greene et al, 1985; Duffner et al, 1998; Levin et al, 2001).

Very little is known about the etiology of cancers of the brain and CNS. Established risk factors include moderate to high doses of ionizing radiation and certain rare familial cancer syndromes, but these account for a very small percentage of cases (Inskip et al, 1995; Louis and von Deimling, 1995). There is inconsistent evidence linking brain cancer to certain occupational and dietary exposures, reproductive factors, and some medical conditions (Inskip et al, 1995; Preston-Martin and Mack, 1996; Wrensch et al, 2002).

### Results and Discussion

Among 31,336 persons who survived at least 2 months following a first cancer of the brain or CNS, 29,361 patients (93.7%) had brain cancers, and 1,975 (6.3%) had cancers in other parts of the CNS. A total of 496 new primary cancers were identified in 464 persons (O/E=1.11, 95% CI=1.01-1.21, EAR=4 per 10,000 person-years). Exclusive of new cancers of the brain and CNS, the observed and expected numbers of new malignancies were nearly equal (O/E=1.02, 95% CI=0.93-1.12). Risk was higher after a first cancer of the brain (O/E=1.15, O=408) than when the first cancer occurred elsewhere in the CNS (O/E=0.94, O=88). The relative risk (O/E)

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**Table 14.A:** Observed (O) numbers of new malignancies, and measures of relative risk (O/E) and excess absolute risk (EAR), by histopathological subtype of the first brain or other CNS cancer. Numbers of patients, mean age at diagnosis, duration of follow-up (mean PYR), and use of radiotherapy (RT) in treatment of the first cancer also are shown.

First primary tumor subtype	No. patients	Mean age (yr)	Mean PYR	Baseline RT (%)	O	O/E	95% CI	EAR (per 10 <sup>4</sup> PYR)
All types	31,336	48.0	3.38	72.0	496	1.11	1.01-1.21	4.47
Glioblastoma	12,169	59.8	0.91	81.0	75	0.81	0.63-1.01	-16.09
Pilocytic astrocytoma	960	16.6	6.72	25.3	9	1.55	0.71-2.93	4.92
Other astrocytoma	9,083	44.6	4.58	75.2	166	1.22	1.04-1.42	7.19
Oligodendroglioma	1,813	42.1	4.99	62.8	46	1.16	0.85-1.54	6.92
Mixed glioma	676	39.0	5.36	75.9	15	1.14	0.64-1.88	5.12
Ependymoma	1,055	31.1	6.84	57.8	46	1.41	1.03-1.88	18.53
Medulloblastoma/PNET	1,207	14.2	6.28	83.8	23	3.71	2.35-5.57	22.16
Malignant meningioma	591	60.3	5.97	39.8	39	0.85	0.61-1.16	-19.24
Other and unspecified	3,782	44.3	4.17	55.7	77	1.01	0.80-1.26	0.44

Notes: ICD-O Revision 2 morphology (M) codes: glioblastoma and gliosarcoma (M9440-9442); pilocytic astrocytoma (M9421); other astrocytoma (M9400-9420, 9424); oligodendroglioma (M9450-9451); mixed glioma (M9382); ependymoma (M9391-9394); medulloblastoma/PNET (M9470-9473); malignant meningioma (M9530-9539); includes patients surviving 2 months or more after diagnosis; EAR calculated as [(O-E)/PYR] × 10,000.

Abbreviations: RT=initial radiotherapy; PNET=primitive neuroectodermal tumor; O=observed number of subsequent (2nd, 3rd, etc.) primary cancers; O/E=ratio of observed to expected cancers; PYR=person-years at risk; EAR=excess absolute risk (excess cancers per 10,000 person-years, calculated as [(O-E)/PYR] × 10,000).

increased over the first 10 years of follow-up but then decreased. The risk of developing a second cancer within 25 years, adjusted for the competing risk of death from other causes, was 2.5% (95% CI=2.2%-2.8%). Risk for all new malignancies combined was higher for males than for females (O/E=1.18 versus 1.00) and higher for blacks than for whites (O/E=1.34 versus 1.10). Striking differences in the risk of subsequent tumors were apparent between persons diagnosed with cancer of the brain or CNS before age 17 years (mean age, 7.7 years; O/E=6.64, O=54, 95% CI=4.99-8.67, EAR=14) and those diagnosed at older ages (O/E=1.00, O=442, 95% CI=0.91-1.10).

With respect to the histopathology of the first cancer, the excess absolute risks were highest among persons first diagnosed with medulloblastoma or ependymoma; these tumors tend to be diagnosed at younger ages and have better-than-average survival, and they are often treated with radiation (Table 14.A). Intermediate excess absolute risks were observed for new cancers following an initial astrocytoma, oligodendroglioma, or mixed glioma. New malignancies occurred less often than expected following glioblastoma and malignant meningioma. These tumors tend to be diagnosed at older ages, and glioblastoma is associated with poor survival, so there is limited time for treatment-induced cancers to appear.

Significantly elevated subsequent cancer risks were observed only for relatively uncommon cancers, including those of the brain and CNS, bone, soft tissue, salivary gland, and thyroid gland, as well as for acute non-lymphocytic leukemia (ANLL) and melanoma of the skin. The highest relative risk was observed for bone cancer and the highest EAR for subsequent brain and CNS cancer. A statistically significant deficit was seen for breast cancer, and deficits approaching statistical significance were observed for cancers of the lung and prostate.

With the exception of melanoma, all of the subsequent cancers that occurred significantly in excess of expectation have been linked to medical irradiation in previous

studies, particularly for exposures occurring during childhood (Tucker et al, 1987, 1991; Ron et al, 1988, 1995; NRC, 1990; Neglia et al, 1991; Hawkins et al, 1996; Wong et al, 1997; Karlsson et al, 1998; Little et al, 1998; Schneider et al, 1998; Walter et al, 1998; Bhatia et al, 2002). However, evidence of radiogenic excesses in the present study was mixed. The risks for bone, soft tissue, brain, and thyroid cancer were higher among persons whose baseline treatment included radiation, whereas the risks for leukemia, salivary gland cancer, and melanoma of the skin were not (data not shown). Excess cancer incidence was apparent even within the first 5 years of follow-up, which is shorter than the minimal latent period for most radiation-related solid cancers (NRC, 1990). Although some of the subsequent brain cancers might have been misclassified recurrences rather than new primaries, the excess was greater after the first 5 years of follow-up than during the first 5 years. The relative risk for cancer of the salivary gland increased with time, which is compatible with a radiation effect, but the number of cases was small. The small number of long-term survivors limits the ability to assess late effects of treatment.

Although radiation is a well-established cause of leukemia, it probably was of limited importance in explaining the excess risk in this study cohort. Most patients given radiotherapy for their first cancer would have received radiation only to the skull, which contains a relatively small proportion of the body's active bone marrow after childhood (Cristy, 1981). Chemotherapy, which exposes marrow throughout the body, probably played a greater role. At least 7 of the 12 cases of acute myeloid leukemia received chemotherapy, based on the data covering the initial course of therapy. Nitrosoureas and other chemotherapy agents used in the treatment of brain cancer have been linked with increased occurrence of ANLL (Boice et al, 1983; Greene et al, 1985; Duffner et al, 1998).

Bone and soft tissue sarcoma are known sequelae of irradiation at high doses, typically in excess of 10 Gy

(Tucker et al, 1987; Hawkins et al, 1996; Wong et al, 1997). Risk drops off sharply outside of the irradiated field. Seven of the 12 subsequent bone cancers occurred in the skull or face, and all 7 had received radiotherapy. Chemotherapy with alkylating agents also has been linked to second primary bone sarcoma and might potentiate the effects of radiation or shorten the induction period of radiation-related tumors (Tucker et al, 1987; Hawkins et al, 1996). On the other hand, only 4 of the 13 soft tissue cancers occurred in the head or neck, 3 of which had received baseline radiotherapy. Few cases had chemotherapy recorded in SEER as part of their initial course of therapy. Thus, neither radiotherapy nor chemotherapy can be linked clearly to the excess occurrence of subsequent soft tissue cancers based on these data.

Radiotherapy probably contributed to the moderate excess of thyroid cancer. Brain cancers in children commonly occur in the cerebellum (Russell and Rubenstein, 1989), and radiation directed to the cerebellum can involve sizable incidental doses to the thyroid gland. Susceptibility to radiation-induced thyroid cancer is known to be greater among children than among adults (Ron et al, 1995), and the relative risk of thyroid cancer following brain or other CNS cancer among children was higher than among adults in the present study as well. However, if the increased incidence of thyroid cancer was due entirely to radiotherapy, one would expect the excess to show a stronger inverse association with age at exposure and to appear at least 5 or more years after irradiation. Close medical surveillance of cancer patients might have led to early detection of small thyroid cancers. It is not clear whether the greater relative excess of thyroid cancer among males compared with females reflects differences in radiation exposure to the thyroid gland, chance, or some other factor.

Shared genetic susceptibility might contribute to some of the observed associations (Malkin et al, 1992; Louis and von Deimling, 1995), particularly for sarcomas, leukemia, and new primary cancers of the brain and CNS. Li-Fraumeni syndrome is associated with brain cancer, soft tissue sarcoma, osteosarcoma, and leukemia, among other types of tumors (Hisada et al, 1998; Nichols et al, 2001), while astrocytoma, non-lymphocytic leukemia, and neurofibrosarcoma are associated with neurofibromatosis type 1 (Bader and Miller, 1978). The sarcomas that occurred following a first cancer of the brain and CNS tended to occur at young ages (median of 26 years for soft tissue, 25 years for bone). Five of the 13 cancers of soft tissue were neurofibrosarcomas or malignant schwannomas; the corresponding first cancers included 4 astrocytomas.

The numbers of specific types of subsequent cancers following different histopathologic types of first cancer of the brain and CNS were small, but there were several suggestive associations. Elevated risks following medulloblastoma were seen for leukemia ( $O/E=9.97$ ,  $O=3$ ), brain and CNS cancer ( $O/E=19.62$ ,  $O=5$ ), soft tissue sarcoma ( $O/E=21.61$ ,  $O=2$ ), and cancers of the digestive tract

( $O/E=6.50$ ,  $O=5$ ). The latter might be related to Turcot syndrome, which involves a genetic predisposition to colon polyps and brain tumors (Hamilton et al, 1995; Goldstein et al, 1997). There was a significantly increased risk of stomach cancer following glioblastoma ( $O/E=3.33$ ,  $O=6$ ), and 3 of the 6 cases occurred among blacks ( $O/E=29.48$ ). Subsequent colon cancers occurred more often than expected among persons with mixed glioma ( $O/E=5.53$ ,  $O=5$ ), most of which would be expected to be oligoastrocytoma (Kleihues and Cavenee, 1997). It is noteworthy that astrocytomas and oligodendrogliomas are among the tumors that have been associated with hereditary nonpolyposis colon cancer (Vasen et al, 1996). Contrary to earlier reports (Schoenberg et al, 1975; Malmer et al, 2000; Custer et al, 2002), neither breast cancer ( $O/E=0.72$ ,  $O=5$ ) nor colon cancer risk ( $O/E=0.86$ ,  $O=4$ ) was increased following malignant meningioma.

Cutaneous melanoma occurred more often than expected among brain cancer patients in SEER, which parallels a finding from Finland (Salminen et al, 1999). Melanoma is not established as a late effect of radiotherapy or chemotherapy, although the issue is unsettled. Whether the excess risk might signify a genetic disorder is unclear, but familial clustering of astrocytoma and cutaneous melanoma has been reported (Kaufman et al, 1993; Azizi et al, 1995; Paunu et al, 2002). It also is possible that the excess of melanoma is related to close medical surveillance of cancer patients.

The comparatively low incidence of new primary cancers of the respiratory tract and buccal cavity and other smoking-related cancers probably reflects a low prevalence of smoking in the study cohort, relative to the general population. Smoking does not appear to cause brain cancer, which tends to occur more often among persons of higher social class (Preston-Martin, 1989; Inskip et al, 1995, 2003), who smoke less than the general population.

In summary, excess risk of a new malignancy following a first cancer of the brain and CNS was relatively small for the cohort as a whole, but much larger relative and absolute risks were indicated among persons whose first cancer was diagnosed during childhood. Increases were not seen for the common adult cancers. Instead, cancers of the brain, bone, soft tissue, thyroid, and salivary glands, as well as leukemia, accounted for most of the excess. Radiotherapy for the first cancer appears to be linked to new bone and brain cancers and may have contributed to thyroid and salivary gland cancers as well. Chemotherapy and shared genetic susceptibility likely also played contributory roles, particularly for subsequent leukemias and sarcomas. The very high relative risks following a first cancer of childhood probably reflect a combination of low background risks, effects of treatment during a vulnerable period of life, and genetic predisposition. It will be important to document the cancer experience of childhood brain cancer survivors after they reach the ages at which the usual adult cancers become common. The risk of therapy-related subsequent cancers among glioblastoma patients is not a major clinical issue at this time, given their extremely poor survival.

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## Brain and Other CNS Both Sexes

**Table 14.1.1:** Characteristics of patients with an initial cancer of the brain or other central nervous system, both sexes, SEER 1973-2000.

Characteristics	Males		Females		Total	
	No.	%	No.	%	No.	%
<b>Number of patients with 1st primary cancer</b>						
<b>Total</b>	17,734	100.0	13,602	100.0	31,336	100.0
<b>Initial treatment</b>						
Any radiation	13,162	74.2	9,392	69.0	22,554	72.0
With surgery	9,557	53.9	6,652	48.9	16,209	51.7
Without surgery	3,605	20.3	2,740	20.1	6,345	20.2
No radiation	4,572	25.8	4,210	31.0	8,782	28.0
With surgery	3,048	17.2	2,661	19.6	5,709	18.2
Without surgery	1,524	8.6	1,549	11.4	3,073	9.8
<b>Race</b>						
White	15,948	89.9	12,188	89.6	28,136	89.8
Black	1,007	5.7	823	6.1	1,830	5.8
Other	739	4.2	565	4.2	1,304	4.2
Unknown	40	0.2	26	0.2	66	0.2
<b>Age at 1st primary cancer diagnosis, years</b>						
< 30	4,064	22.9	3,200	23.5	7,264	23.2
30–49	4,379	24.7	2,892	21.3	7,271	23.2
50–69	6,632	37.4	4,583	33.7	11,215	35.8
70–79	2,131	12.0	2,170	16.0	4,301	13.7
≥ 80	528	3.0	757	5.6	1,285	4.1
<b>Number of patients with one or more primary cancers</b>						
One primary cancer only	17,451	98.4	13,421	98.7	30,872	98.5
1st and 2nd cancers	264	1.5	169	1.2	433	1.4
1st, 2nd, and 3rd cancers	18	0.1	12	0.1	30	0.1
1st, 2nd, 3rd, and additional cancers	1	0.0	0	0.0	1	0.0
<b>Other statistics</b>						
Median age at 1st cancer diagnosis	51.5	—	53.7	—	52.3	—
Median year of 1st cancer diagnosis	1988.5	—	1988.6	—	1988.6	—
Median person-years at risk	0.9	—	0.9	—	0.9	—
Percent histologically confirmed*						
Both 1st and 2nd cancers	—	83.4	—	85.6	—	84.3
1st, 2nd, and additional cancers	—	83.0	—	85.6	—	84.1
1st cancer only	—	4.9	—	3.3	—	4.3

\*Percent histologically confirmed among patients who developed a subsequent primary cancer.

**Table 14.1.2:** Risk of subsequent primary cancers after cancer of the brain or other central nervous system, both sexes, SEER 1973-2000.

Subsequent primary cancer	Years after first primary cancer diagnosis											
	<1 year		1-4 years		5-9 years		≥10 years		Total			
	O	O/E	O	O/E	O	O/E	O	O/E	O	E	O/E	EAR
<b>All subsequent cancers</b>	113	0.92	173	1.18*	125	1.36*	85	0.98	496	448.67	1.11*	4.47
All excluding same site	107	0.88	161	1.12	109	1.21	72	0.84	449	441.52	1.02	0.71
<b>Buccal cavity, pharynx</b>	2	0.54	2	0.46	7	2.72*	3	1.36	14	12.88	1.09	0.11
Lip	0	0.00	0	0.00	1	3.37	0	0.00	1	1.61	0.62	-0.06
Tongue	1	1.31	1	1.08	0	0.00	0	0.00	2	2.75	0.73	-0.07
Salivary gland	0	0.00	1	2.55	2	8.09	2	8.55	5	1.17	4.27*	0.36
Mouth	0	0.00	0	0.00	3	4.63	1	1.86	4	3.28	1.22	0.07
Nasopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.67	0.00	-0.06
Tonsil	1	2.59	0	0.00	1	3.43	0	0.00	2	1.41	1.42	0.06
Oropharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.36	0.00	-0.03
Hypopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	1.20	0.00	-0.11
<b>Digestive system</b>	23	0.92	28	1.03	18	1.10	16	1.08	85	83.57	1.02	0.14
Esophagus	0	0.00	0	0.00	1	1.16	1	1.26	2	4.46	0.45	-0.23
Stomach	7	2.79*	3	1.11	3	1.90	0	0.00	13	8.17	1.59	0.46
Small intestine	0	0.00	0	0.00	1	3.39	0	0.00	1	1.43	0.70	-0.04
Colon	13	1.19	15	1.28	5	0.71	9	1.42	42	36.04	1.17	0.56
Rectum, rectosigmoid junction	2	0.43	3	0.59	6	1.99	2	0.75	13	15.39	0.84	-0.23
Anus, anal canal	0	0.00	0	0.00	0	0.00	0	0.00	0	1.11	0.00	-0.10
Liver	0	0.00	1	0.95	0	0.00	1	1.55	2	3.24	0.62	-0.12
Gallbladder	0	0.00	0	0.00	0	0.00	0	0.00	0	1.06	0.00	-0.10
Bile ducts, other biliary	0	0.00	1	1.80	1	2.88	0	0.00	2	1.75	1.14	0.02
Pancreas	1	0.33	5	1.54	1	0.51	2	1.13	9	9.95	0.90	-0.09
<b>Respiratory system</b>	19	0.88	19	0.81	12	0.86	7	0.56	57	71.51	0.80	-1.37
Nose, nasal cavity, ear	0	0.00	1	4.14	1	6.77	0	0.00	2	0.72	2.78	0.12
Larynx	0	0.00	0	0.00	2	1.97	0	0.00	2	5.30	0.38	-0.31
Lung, bronchus	19	0.96	18	0.85	9	0.71	7	0.61	53	65.19	0.81	-1.15
<b>Female breast</b>	8	0.56	24	1.16	10	0.70	5	0.37*	47	62.79	0.75*	-3.28
<b>Female genital system</b>	5	0.74	4	0.42	5	0.82	4	0.70	18	28.01	0.64	-2.08
Cervix uteri	0	0.00	0	0.00	3	2.59	0	0.00	3	5.00	0.60	-0.42
Corpus uteri	3	0.89	3	0.71	1	0.38	1	0.41	8	12.71	0.63	-0.98
Ovary	2	1.03	1	0.36	0	0.00	3	1.68	6	8.42	0.71	-0.50
Vagina	0	0.00	0	0.00	0	0.00	0	0.00	0	0.33	0.00	-0.07
Vulva	0	0.00	0	0.00	1	4.58	0	0.00	1	0.99	1.01	0.00
<b>Male genital system</b>	12	0.57*	18	0.84	17	1.29	11	0.77	58	69.96	0.83	-2.07
Prostate	11	0.54*	16	0.80	17	1.39	10	0.75	54	65.81	0.82	-2.04
Testis	1	1.95	2	1.51	0	0.00	1	1.10	4	3.63	1.10	0.06
<b>Urinary system</b>	8	0.85	12	1.17	5	0.81	7	1.21	32	31.73	1.01	0.03
Urinary bladder	5	0.79	6	0.92	2	0.51	4	1.10	17	20.41	0.83	-0.32
Kidney parenchyma	3	1.16	4	1.27	2	1.02	3	1.62	12	9.55	1.26	0.23
Renal pelvis, other urinary	0	0.00	2	3.45	1	3.00	0	0.00	3	1.78	1.69	0.12
Ureter	0	0.00	0	0.00	0	0.00	0	0.00	0	0.56	0.00	-0.05
<b>Bone, joints</b>	0	0.00	8	23.30*	4	16.55*	0	0.00	12	0.97	12.38*	1.04
<b>Soft tissue including heart</b>	0	0.00	4	4.54*	7	12.39*	2	3.75	13	2.56	5.07*	0.99
<b>Kaposi sarcoma</b>	2	3.98	0	0.00	0	0.00	0	0.00	2	3.33	0.60	-0.13
<b>Melanoma of skin</b>	5	1.38	11	1.93	5	1.31	5	1.31	26	16.95	1.53*	0.85
<b>Eye, orbit</b>	0	0.00	0	0.00	0	0.00	1	6.90	1	0.81	1.23	0.02
<b>Brain, central nervous system</b>	6	3.49*	12	4.76*	16	10.30*	13	9.55*	47	7.15	6.57*	3.76
<b>Thyroid</b>	1	0.89	7	3.21*	5	3.30*	1	0.64	14	6.39	2.19*	0.72
<b>Lymphatic, hematopoietic</b>	8	0.83	21	1.67*	13	1.64	7	0.94	49	37.52	1.31	1.08
Hodgkin lymphoma	0	0.00	1	0.81	0	0.00	0	0.00	1	3.49	0.29	-0.24
Non-Hodgkin lymphoma	4	0.91	5	0.87	1	0.27	3	0.83	13	17.48	0.74	-0.42
Myeloma	2	1.40	1	0.63	2	2.06	1	1.11	6	4.89	1.23	0.11
Leukemia	2	0.62	14	3.55*	10	4.21*	3	1.41	29	11.66	2.49*	1.64
Acute lymphocytic	0	0.00	0	0.00	2	8.03	1	5.82	3	1.10	2.72	0.18
Chronic lymphocytic	1	0.84	2	1.60	3	3.99	1	1.47	7	3.87	1.81	0.30
Acute non-lymphocytic	0	0.00	8	6.02*	4	4.88*	1	1.31	13	3.98	3.27*	0.85
Chronic myeloid	0	0.00	4	7.17*	0	0.00	0	0.00	4	1.66	2.41	0.22

\*P < 0.05. Notes: See Appendices for definitions of cancer sites and "all excluding same site." Abbreviations: O = observed number of subsequent (2nd, 3rd, etc.) primary cancers; E = expected number of subsequent primary cancers; O/E = ratio of observed to expected cancers; PYR = person-years at risk; EAR = excess absolute risk per 10,000 person-years = [(O-E)/PYR] × 10,000. EAR for female cancers is based on 48,074 PYR and for male cancers on 57,847 PYR.

## Brain and Other CNS Females

**Table 14.1.3:** Risk of subsequent primary cancers after cancer of the brain or other central nervous system, females, SEER 1973-2000.

Subsequent primary cancer	Years after first primary cancer diagnosis											
	<1 year		1-4 years		5-9 years		≥10 years		Total			
	Number starting interval	Person-years in interval	O	O/E	O	O/E	O	O/E	O	E	O/E	EAR
	13,602	7,974	7,310	17,614	3,200	11,926	1,732	10,559	13,602	48,074		
<b>All subsequent cancers</b>	37	0.79	64	1.00	49	1.16	43	1.07	193	192.83	1.00	0.04
All excluding same site	37	0.80	59	0.94	44	1.05	33	0.84	173	190.12	0.91	-3.56
<b>Buccal cavity, pharynx</b>	1	1.15	0	0.00	4	5.50*	1	1.53	6	3.39	1.77	0.54
Lip	0	0.00	0	0.00	0	0.00	0	0.00	0	0.19	0.00	-0.04
Tongue	0	0.00	0	0.00	0	0.00	0	0.00	0	0.76	0.00	-0.16
Salivary gland	0	0.00	0	0.00	1	9.69	1	10.02	2	0.46	4.38	0.32
Mouth	0	0.00	0	0.00	2	8.84	0	0.00	2	1.08	1.86	0.19
Nasopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.18	0.00	-0.04
Tonsil	1	11.67	0	0.00	1	14.71	0	0.00	2	0.32	6.23	0.35
Oropharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.08	0.00	-0.02
Hypopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.22	0.00	-0.05
<b>Digestive system</b>	6	0.66	12	1.11	8	1.17	8	1.29	34	33.00	1.03	0.21
Esophagus	0	0.00	0	0.00	1	5.30	1	5.75	2	0.93	2.15	0.22
Stomach	1	1.44	0	0.00	2	3.85	0	0.00	3	2.51	1.20	0.10
Small intestine	0	0.00	0	0.00	0	0.00	0	0.00	0	0.58	0.00	-0.12
Colon	2	0.45	9	1.73	1	0.31	5	1.72	17	15.82	1.07	0.25
Rectum, rectosigmoid junction	2	1.29	1	0.54	3	2.55	1	0.95	7	5.64	1.24	0.28
Rectum	2	1.99	1	0.82	3	3.87	0	0.00	6	3.70	1.62	0.48
Anus, anal canal	0	0.00	0	0.00	0	0.00	0	0.00	0	0.58	0.00	-0.12
Liver	0	0.00	0	0.00	0	0.00	0	0.00	0	0.81	0.00	-0.17
Gallbladder	0	0.00	0	0.00	0	0.00	0	0.00	0	0.70	0.00	-0.15
Bile ducts, other biliary	0	0.00	1	4.40	0	0.00	0	0.00	1	0.71	1.41	0.06
Pancreas	1	0.85	1	0.73	1	1.15	1	1.26	4	4.20	0.95	-0.04
<b>Respiratory system</b>	10	1.68	5	0.67	3	0.61	3	0.63	21	23.00	0.91	-0.42
Nose, nasal cavity, ear	0	0.00	1	11.64	0	0.00	0	0.00	1	0.26	3.92	0.15
Larynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.84	0.00	-0.18
Lung, bronchus	10	1.77	4	0.57	3	0.64	3	0.67	20	21.82	0.92	-0.38
<b>Female breast</b>	8	0.56	24	1.16	10	0.70	5	0.37*	47	62.79	0.75*	-3.28
<b>Female genital system</b>	5	0.74	4	0.42	5	0.82	4	0.70	18	28.01	0.64	-2.08
Cervix uteri	0	0.00	0	0.00	3	2.59	0	0.00	3	5.00	0.60	-0.42
Corpus uteri	3	0.89	3	0.71	1	0.38	1	0.41	8	12.71	0.63	-0.98
Ovary	2	1.03	1	0.36	0	0.00	3	1.68	6	8.42	0.71	-0.50
Vagina	0	0.00	0	0.00	0	0.00	0	0.00	0	0.33	0.00	-0.07
Vulva	0	0.00	0	0.00	1	4.58	0	0.00	1	0.99	1.01	0.00
<b>Urinary system</b>	0	0.00	2	0.80	1	0.61	3	1.93	6	7.71	0.78	-0.36
Urinary bladder	0	0.00	0	0.00	0	0.00	2	2.43	2	4.20	0.48	-0.46
Kidney parenchyma	0	0.00	2	2.08	1	1.55	1	1.58	4	2.96	1.35	0.22
Renal pelvis, other urinary	0	0.00	0	0.00	0	0.00	0	0.00	0	0.55	0.00	-0.11
Ureter	0	0.00	0	0.00	0	0.00	0	0.00	0	0.16	0.00	-0.03
<b>Bone, joints</b>	0	0.00	2	15.53*	2	21.31*	0	0.00	4	0.37	10.85*	0.76
<b>Soft tissue including heart</b>	0	0.00	0	0.00	4	17.10*	0	0.00	4	1.02	3.94*	0.62
<b>Kaposi sarcoma</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.05	0.00	-0.01
<b>Melanoma of skin</b>	1	0.82	2	0.87	1	0.60	3	1.76	7	6.88	1.02	0.02
<b>Eye, orbit</b>	0	0.00	0	0.00	0	0.00	1	15.96	1	0.32	3.08	0.14
<b>Brain, central nervous system</b>	0	0.00	5	5.32*	5	8.14*	10	18.09*	20	2.71	7.39*	3.60
<b>Thyroid</b>	0	0.00	1	0.67	3	2.77	0	0.00	4	4.43	0.90	-0.09
<b>Lymphatic, hematopoietic</b>	3	0.88	6	1.28	2	0.64	4	1.34	15	14.18	1.06	0.17
Hodgkin lymphoma	0	0.00	0	0.00	0	0.00	0	0.00	0	1.37	0.00	-0.29
Non-Hodgkin lymphoma	2	1.24	1	0.46	0	0.00	2	1.40	5	6.66	0.75	-0.35
Myeloma	1	1.88	0	0.00	0	0.00	1	2.65	2	1.95	1.03	0.01
Leukemia	0	0.00	5	3.51*	2	2.21	1	1.23	8	4.20	1.91	0.79
Acute lymphocytic	0	0.00	0	0.00	0	0.00	0	0.00	0	0.40	0.00	-0.08
Chronic lymphocytic	0	0.00	1	2.38	1	3.78	1	4.18	3	1.29	2.32	0.36
Acute non-lymphocytic	0	0.00	3	5.67*	1	2.87	0	0.00	4	1.58	2.53	0.50
Chronic myeloid	0	0.00	1	4.93	0	0.00	0	0.00	1	0.61	1.65	0.08

\*P < 0.05. Notes: See Appendices for definitions of cancer sites and "all excluding same site." Abbreviations: O = observed number of subsequent (2nd, 3rd, etc.) primary cancers; E = expected number of subsequent primary cancers; O/E = ratio of observed to expected cancers; PYR = person-years at risk; EAR = excess absolute risk per 10,000 person-years = [(O-E)/PYR] × 10,000.



**Table 14.1.4:** Risk of subsequent primary cancers after cancer of the brain or other central nervous system, males, SEER 1973-2000.

Subsequent primary cancer	Years after first primary cancer diagnosis											
	<1 year		1-4 years		5-9 years		≥10 years		Total			
	O	O/E	O	O/E	O	O/E	O	O/E	O	E	O/E	EAR
<b>All subsequent cancers</b>	76	0.99	109	1.31*	76	1.54*	42	0.90	303	255.85	1.18*	8.15
All excluding same site	70	0.93	102	1.25*	65	1.34*	39	0.85	276	251.40	1.10	4.25
<b>Buccal cavity, pharynx</b>	1	0.35	2	0.62	3	1.63	2	1.28	8	9.49	0.84	-0.26
Lip	0	0.00	0	0.00	1	3.88	0	0.00	1	1.43	0.70	-0.07
Tongue	1	1.76	1	1.49	0	0.00	0	0.00	2	1.98	1.01	0.00
Salivary gland	0	0.00	1	4.20	1	6.93	1	7.45	3	0.72	4.19	0.39
Mouth	0	0.00	0	0.00	1	2.37	1	2.96	2	2.21	0.91	-0.04
Nasopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.50	0.00	-0.09
Tonsil	0	0.00	0	0.00	0	0.00	0	0.00	0	1.09	0.00	-0.19
Oropharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.27	0.00	-0.05
Hypopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.98	0.00	-0.17
<b>Digestive system</b>	17	1.07	16	0.97	10	1.05	8	0.93	51	50.56	1.01	0.08
Esophagus	0	0.00	0	0.00	0	0.00	0	0.00	0	3.53	0.00	-0.61
Stomach	6	3.31*	3	1.61	1	0.94	0	0.00	10	5.66	1.77	0.75
Small intestine	0	0.00	0	0.00	1	5.87	0	0.00	1	0.85	1.18	0.03
Colon	11	1.69	6	0.92	4	1.06	4	1.17	25	20.22	1.24	0.83
Rectum, rectosigmoid junction	0	0.00	2	0.63	3	1.64	1	0.61	6	9.74	0.62	-0.65
Anus, anal canal	0	0.00	0	0.00	0	0.00	0	0.00	0	0.53	0.00	-0.09
Liver	0	0.00	1	1.26	0	0.00	1	2.10	2	2.44	0.82	-0.08
Gallbladder	0	0.00	0	0.00	0	0.00	0	0.00	0	0.36	0.00	-0.06
Bile ducts, other biliary	0	0.00	0	0.00	1	5.10	0	0.00	1	1.04	0.96	-0.01
Pancreas	0	0.00	4	2.13	0	0.00	1	1.03	5	5.76	0.87	-0.13
<b>Respiratory system</b>	9	0.57	14	0.88	9	1.00	4	0.51	36	48.51	0.74	-2.16
Nose, nasal cavity, ear	0	0.00	0	0.00	1	10.88	0	0.00	1	0.46	2.16	0.09
Larynx	0	0.00	0	0.00	2	2.39	0	0.00	2	4.46	0.45	-0.43
Lung, bronchus	9	0.64	14	0.98	6	0.75	4	0.57	33	43.37	0.76	-1.79
<b>Male breast</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.50	0.00	-0.09
<b>Male genital system</b>	12	0.57*	18	0.84	17	1.29	11	0.77	58	69.96	0.83	-2.07
Prostate	11	0.54*	16	0.80	17	1.39	10	0.75	54	65.81	0.82	-2.04
Testis	1	1.95	2	1.51	0	0.00	1	1.10	4	3.63	1.10	0.06
<b>Urinary system</b>	8	1.07	10	1.29	4	0.88	4	0.94	26	24.02	1.08	0.34
Urinary bladder	5	0.97	6	1.16	2	0.66	2	0.71	15	16.20	0.93	-0.21
Kidney parenchyma	3	1.60	2	0.92	1	0.76	2	1.63	8	6.59	1.21	0.24
Renal pelvis, other urinary	0	0.00	2	5.01	1	4.51	0	0.00	3	1.23	2.44	0.31
Ureter	0	0.00	0	0.00	0	0.00	0	0.00	0	0.40	0.00	-0.07
<b>Bone, joints</b>	0	0.00	6	27.95*	2	13.53*	0	0.00	8	0.60	13.32*	1.28
<b>Soft tissue including heart</b>	0	0.00	4	7.45*	3	9.06*	2	6.53	9	1.55	5.81*	1.29
<b>Kaposi sarcoma</b>	2	4.08	0	0.00	0	0.00	0	0.00	2	3.28	0.61	-0.22
<b>Melanoma of skin</b>	4	1.67	9	2.64*	4	1.85	2	0.95	19	10.07	1.89*	1.54
<b>Eye, orbit</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.49	0.00	-0.08
<b>Brain, central nervous system</b>	6	5.36*	7	4.43*	11	11.72*	3	3.71	27	4.45	6.07*	3.90
<b>Thyroid</b>	1	2.35	6	8.76*	2	4.63	1	2.42	10	1.96	5.11*	1.39
<b>Lymphatic, hematopoietic</b>	5	0.80	15	1.91*	11	2.29*	3	0.67	34	23.34	1.46*	1.84
Hodgkin lymphoma	0	0.00	1	1.31	0	0.00	0	0.00	1	2.12	0.47	-0.19
Non-Hodgkin lymphoma	2	0.72	4	1.11	1	0.44	1	0.46	8	10.82	0.74	-0.49
Myeloma	1	1.11	1	1.05	2	3.56	0	0.00	4	2.94	1.36	0.18
Leukemia	2	0.93	9	3.57*	8	5.44*	2	1.53	21	7.46	2.81*	2.34
Acute lymphocytic	0	0.00	0	0.00	2	12.69*	1	9.25	3	0.70	4.27	0.40
Chronic lymphocytic	1	1.21	1	1.20	2	4.11	0	0.00	4	2.58	1.55	0.24
Acute non-lymphocytic	0	0.00	5	6.25*	3	6.35*	1	2.29	9	2.40	3.75*	1.14
Chronic myeloid	0	0.00	3	8.45*	0	0.00	0	0.00	3	1.06	2.84	0.34

\*P < 0.05. Notes: See Appendices for definitions of cancer sites and "all excluding same site." Abbreviations: O = observed number of subsequent (2nd, 3rd, etc.) primary cancers; E = expected number of subsequent primary cancers; O/E = ratio of observed to expected cancers; PYR = person-years at risk; EAR = excess absolute risk per 10,000 person-years = [(O-E)/PYR] × 10,000.

## Brain and Other CNS Both Sexes, <17 Years of Age

**Table 14.1.5:** Risk of subsequent primary cancers after cancer of the brain or other central nervous system, both sexes, <17 years of age, SEER 1973-2000.

Subsequent primary cancer	Years after first primary cancer diagnosis											
	<1 year		1-4 years		5-9 years		≥10 years		Total			
	O	O/E	O	O/E	O	O/E	O	O/E	O	E	O/E	EAR
<b>All subsequent cancers</b>	4	8.24*	17	10.61*	18	10.77*	15	3.43*	54	8.13	6.64*	14.39
All excluding same site	3	7.77*	11	8.44*	13	8.93*	7	1.70	34	7.25	4.69*	8.39
<b>Buccal cavity, pharynx</b>	0	0.00	0	0.00	2	61.44*	0	0.00	2	0.15	13.53*	0.58
Lip	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Tongue	0	0.00	0	0.00	0	0.00	0	0.00	0	0.02	0.00	-0.01
Salivary gland	0	0.00	0	0.00	1	78.90*	0	0.00	1	0.05	19.77	0.30
Mouth	0	0.00	0	0.00	1	168.74*	0	0.00	1	0.02	40.02	0.31
Nasopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.03	0.00	-0.01
Tonsil	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0.00	0.00
Oropharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0.00	0.00
Hypopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0.00	0.00
<b>Digestive system</b>	1	60.49	1	23.18	2	47.71*	1	4.74	5	0.31	16.00*	1.47
Esophagus	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Stomach	0	0.00	0	0.00	0	0.00	0	0.00	0	0.03	0.00	-0.01
Small intestine	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Colon	1	†	0	0.00	0	0.00	0	0.00	1	0.09	10.57	0.28
Rectum, rectosigmoid junction	0	0.00	0	0.00	2	332.98*	0	0.00	2	0.05	39.45*	0.61
Anus, anal canal	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Liver	0	0.00	0	0.00	0	0.00	0	0.00	0	0.05	0.00	-0.01
Gallbladder	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0.00	0.00
Bile ducts, other biliary	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0.00	0.00
Pancreas	0	0.00	1	†	0	0.00	1	68.70	2	0.02	101.07*	0.62
<b>Respiratory system</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.14	0.00	-0.04
Nose, nasal cavity, ear	0	0.00	0	0.00	0	0.00	0	0.00	0	0.02	0.00	-0.01
Larynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Lung, bronchus	0	0.00	0	0.00	0	0.00	0	0.00	0	0.07	0.00	-0.02
<b>Female breast</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.38	0.00	-0.26
<b>Female genital system</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.60	0.00	-0.41
Cervix uteri	0	0.00	0	0.00	0	0.00	0	0.00	0	0.25	0.00	-0.17
Corpus uteri	0	0.00	0	0.00	0	0.00	0	0.00	0	0.04	0.00	-0.03
Ovary	0	0.00	0	0.00	0	0.00	0	0.00	0	0.27	0.00	-0.18
Vagina	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Vulva	0	0.00	0	0.00	0	0.00	0	0.00	0	0.02	0.00	-0.01
<b>Male genital system</b>	0	0.00	0	0.00	0	0.00	1	2.27	1	0.65	1.53	0.20
Prostate	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Testis	0	0.00	0	0.00	0	0.00	1	2.30	1	0.64	1.57	0.21
<b>Urinary system</b>	0	0.00	0	0.00	1	30.84	0	0.00	1	0.22	4.53	0.24
Urinary bladder	0	0.00	0	0.00	0	0.00	0	0.00	0	0.07	0.00	-0.02
Kidney parenchyma	0	0.00	0	0.00	0	0.00	0	0.00	0	0.15	0.00	-0.05
Renal pelvis, other urinary	0	0.00	0	0.00	1	†	0	0.00	1	0.00	300.22*	0.31
Ureter	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0.00	0.00
<b>Bone, joints</b>	0	0.00	3	30.44*	2	20.20*	0	0.00	5	0.31	15.89*	1.47
<b>Soft tissue including heart</b>	0	0.00	2	22.64*	3	38.93*	1	8.66	6	0.31	19.38*	1.78
<b>Kaposi sarcoma</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.19	0.00	-0.06
<b>Melanoma of skin</b>	1	111.04*	0	0.00	0	0.00	1	1.87	2	0.73	2.74	0.40
<b>Eye, orbit</b>	0	0.00	0	0.00	0	0.00	1	87.21*	1	0.06	17.23	0.30
<b>Brain, central nervous system</b>	1	10.07	6	20.09*	5	23.15*	8	30.76*	20	0.87	22.88*	6.00
<b>Thyroid</b>	0	0.00	0	0.00	1	7.95	1	2.38	2	0.62	3.23	0.43
<b>Lymphatic, hematopoietic</b>	1	5.07	5	7.76*	2	3.41	1	1.02	9	2.41	3.74*	2.07
Hodgkin lymphoma	0	0.00	0	0.00	0	0.00	0	0.00	0	0.84	0.00	-0.26
Non-Hodgkin lymphoma	1	32.45	0	0.00	0	0.00	1	3.12	2	0.60	3.31	0.44
Myeloma	0	0.00	0	0.00	0	0.00	0	0.00	0	0.01	0.00	0.00
Leukemia	0	0.00	5	13.64*	2	9.08*	0	0.00	7	0.96	7.33*	1.90
Acute lymphocytic	0	0.00	0	0.00	2	14.88*	0	0.00	2	0.59	3.37	0.44
Chronic lymphocytic	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0.00	0.00
Acute non-lymphocytic	0	0.00	3	38.78*	0	0.00	0	0.00	3	0.27	11.22*	0.86
Chronic myeloid	0	0.00	2	162.46*	0	0.00	0	0.00	2	0.07	29.57*	0.61

\*P < 0.05. †O/E > 500. Notes: See Appendices for definitions of cancer sites and "all excluding same site." Abbreviations: O = observed number of subsequent (2nd, 3rd, etc.) primary cancers; E = expected number of subsequent primary cancers; O/E = ratio of observed to expected cancers; PYR = person-years at risk; EAR = excess absolute risk per 10,000 person-years = [(O-E)/PYR] × 10,000. EAR for female cancers is based on 14,484 PYR and for male cancers on 17,402 PYR.

**Table 14.1.6:** Risk of subsequent primary cancers after cancer of the brain or other central nervous system, both sexes, ≥17 years of age, SEER 1973-2000.

Subsequent primary cancer	Years after first primary cancer diagnosis											
	<1 year		1-4 years		5-9 years		≥10 years		Total			
	O	O/E	O	O/E	O	O/E	O	O/E	O	E	O/E	EAR
<b>All subsequent cancers</b>	109	0.89	156	1.07	107	1.19	70	0.85	442	440.55	1.00	0.20
All excluding same site	104	0.86	150	1.05	96	1.08	65	0.80	415	434.27	0.96	-2.60
<b>Buccal cavity, pharynx</b>	2	0.54	2	0.46	5	1.97	3	1.41	12	12.73	0.94	-0.10
Lip	0	0.00	0	0.00	1	3.38	0	0.00	1	1.60	0.62	-0.08
Tongue	1	1.31	1	1.09	0	0.00	0	0.00	2	2.72	0.73	-0.10
Salivary gland	0	0.00	1	2.62	1	4.26	2	9.63*	4	1.12	3.57	0.39
Mouth	0	0.00	0	0.00	2	3.11	1	1.91	3	3.26	0.92	-0.04
Nasopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.64	0.00	-0.09
Tonsil	1	2.59	0	0.00	1	3.44	0	0.00	2	1.41	1.42	0.08
Oropharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	0.36	0.00	-0.05
Hypopharynx	0	0.00	0	0.00	0	0.00	0	0.00	0	1.20	0.00	-0.16
<b>Digestive system</b>	22	0.88	27	0.99	16	0.98	15	1.03	80	83.25	0.96	-0.44
Esophagus	0	0.00	0	0.00	1	1.16	1	1.26	2	4.45	0.45	-0.33
Stomach	7	2.79*	3	1.11	3	1.90	0	0.00	13	8.14	1.60	0.66
Small intestine	0	0.00	0	0.00	1	3.40	0	0.00	1	1.41	0.71	-0.06
Colon	12	1.10	15	1.28	5	0.71	9	1.44	41	35.94	1.14	0.68
Rectum, rectosigmoid junction	2	0.43	3	0.60	4	1.33	2	0.76	11	15.34	0.72	-0.59
Anus, anal canal	0	0.00	0	0.00	0	0.00	0	0.00	0	1.10	0.00	-0.15
Liver	0	0.00	1	0.96	0	0.00	1	1.59	2	3.20	0.63	-0.16
Gallbladder	0	0.00	0	0.00	0	0.00	0	0.00	0	1.05	0.00	-0.14
Bile ducts, other biliary	0	0.00	1	1.80	1	2.89	0	0.00	2	1.74	1.15	0.03
Pancreas	1	0.33	4	1.24	1	0.52	1	0.57	7	9.93	0.70	-0.40
<b>Respiratory system</b>	19	0.88	19	0.81	12	0.87	7	0.56	57	71.37	0.80	-1.94
Nose, nasal cavity, ear	0	0.00	1	4.22	1	6.97	0	0.00	2	0.70	2.86	0.18
Larynx	0	0.00	0	0.00	2	1.97	0	0.00	2	5.29	0.38	-0.45
Lung, bronchus	19	0.96	18	0.85	9	0.71	7	0.61	53	65.12	0.81	-1.64
<b>Female breast</b>	8	0.56	24	1.16	10	0.70	5	0.38*	47	62.41	0.75	-4.59
<b>Female genital system</b>	5	0.74	4	0.43	5	0.83	4	0.76	18	27.42	0.66	-2.80
Cervix uteri	0	0.00	0	0.00	3	2.65	0	0.00	3	4.75	0.63	-0.52
Corpus uteri	3	0.89	3	0.71	1	0.38	1	0.42	8	12.67	0.63	-1.39
Ovary	2	1.03	1	0.36	0	0.00	3	1.85	6	8.15	0.74	-0.64
Vagina	0	0.00	0	0.00	0	0.00	0	0.00	0	0.32	0.00	-0.10
Vulva	0	0.00	0	0.00	1	4.63	0	0.00	1	0.98	1.02	0.01
<b>Male genital system</b>	12	0.57	18	0.84	17	1.30	10	0.72	57	69.30	0.82	-3.04
Prostate	11	0.54*	16	0.80	17	1.39	10	0.75	54	65.80	0.82	-2.92
Testis	1	1.99	2	1.57	0	0.00	0	0.00	3	3.00	1.00	0.00
<b>Urinary system</b>	8	0.85	12	1.18	4	0.65	7	1.23	31	31.51	0.98	-0.07
Urinary bladder	5	0.79	6	0.92	2	0.51	4	1.11	17	20.34	0.84	-0.45
Kidney parenchyma	3	1.17	4	1.30	2	1.03	3	1.66	12	9.40	1.28	0.35
Renal pelvis, other urinary	0	0.00	2	3.46	0	0.00	0	0.00	2	1.77	1.13	0.03
Ureter	0	0.00	0	0.00	0	0.00	0	0.00	0	0.56	0.00	-0.08
<b>Bone, joints</b>	0	0.00	5	20.42*	2	14.02*	0	0.00	7	0.65	10.70*	0.86
<b>Soft tissue including heart</b>	0	0.00	2	2.52	4	8.20*	1	2.39	7	2.26	3.10*	0.64
<b>Kaposi sarcoma</b>	2	3.98	0	0.00	0	0.00	0	0.00	2	3.14	0.64	-0.15
<b>Melanoma of skin</b>	4	1.11	11	1.95	5	1.36	4	1.22	24	16.22	1.48	1.05
<b>Eye, orbit</b>	0	0.00	0	0.00	0	0.00	0	0.00	0	0.76	0.00	-0.10
<b>Brain, central nervous system</b>	5	3.09	6	2.70	11	8.23*	5	4.54*	27	6.28	4.30*	2.80
<b>Thyroid</b>	1	0.89	7	3.31*	4	2.88	0	0.00	12	5.77	2.08*	0.84
<b>Lymphatic, hematopoietic</b>	7	0.74	16	1.35	11	1.50	6	0.93	40	35.12	1.14	0.66
Hodgkin lymphoma	0	0.00	1	0.93	0	0.00	0	0.00	1	2.66	0.38	-0.22
Non-Hodgkin lymphoma	3	0.69	5	0.88	1	0.28	2	0.61	11	16.88	0.65	-0.79
Myeloma	2	1.40	1	0.63	2	2.06	1	1.12	6	4.88	1.23	0.15
Leukemia	2	0.65	9	2.51*	8	3.71*	3	1.59	22	10.71	2.06*	1.53
Acute lymphocytic	0	0.00	0	0.00	0	0.00	1	11.37	1	0.51	1.96	0.07
Chronic lymphocytic	1	0.84	2	1.60	3	4.00	1	1.48	7	3.87	1.81	0.42
Acute non-lymphocytic	0	0.00	5	3.99*	4	5.31*	1	1.50	10	3.71	2.70*	0.85
Chronic myeloid	0	0.00	2	3.67	0	0.00	0	0.00	2	1.59	1.25	0.05

\*P < 0.05. Notes: See Appendices for definitions of cancer sites and "all excluding same site." Abbreviations: O = observed number of subsequent (2nd, 3rd, etc.) primary cancers; E = expected number of subsequent primary cancers; O/E = ratio of observed to expected cancers; PYR = person-years at risk; EAR = excess absolute risk per 10,000 person-years = [(O-E)/PYR] × 10,000. EAR for female cancers is based on 33,590 PYR and for male cancers on 40,445 PYR.

