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Cohort Study of Air Canada Pilots: Mortality, Cancer Incidence, and Leukemia Risk

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Despite the special working environment and exposures of airline pilots, data on risk of death and cancer incidence in this occupational group are limited. The authors investigated a cohort of 2,740 Air Canada pilots who contributed 62,449 person-years of observation. All male pilots employed for at least 1 year on and since January 1, 1950, were studied. The cutoff date for outcome information was December 31, 1992. Standardized mortality ratio (SMR) and standardized incidence ratio (SIR) were used to compare mortality rates and cancer incidence rates of the cohort with the respective Canadian population rates. Ninety percent confidence intervals of the SMR and SIR were calculated. Statistically significant decreased mortality was observed for all causes (SMR = 0.63, 90% confidence interval (CI) 0.56–0.70), for all cancers (SMR = 0.61, 90% CI 0.48–0.76), and for all noncancer diseases (SMR = 0.53, 90% CI 0.45–0.62). Mortality from aircraft accidents was significantly raised (SMR = 26.57, 90% CI 19.3–35.9). Significantly decreased cancer incidence was observed for all cancers (SIR = 0.71, 90% CI 0.61–0.82), rectal cancer (SIR = 0.42, 90% CI 0.14–0.96), lung cancer (SIR = 0.28, 90% CI 0.16–0.46), and bladder cancer (SIR = 0.36, 90% CI 0.12–0.82). Prostate cancer (SIR = 1.87, 90% CI 1.38–2.49) and acute myeloid leukemia (SIR = 4.72, 90% CI 2.05–9.31) were significantly increased. The preferred relative risk model for radiation-induced nonchronic lymphoid leukemia (Beir V report) was applied to the cohort by using published estimates of in-flight radiation exposures. The estimated relative risk ranged from 1.001 to 1.06 and did not differ significantly from the observed SIR (SIR = 1.88, 90% CI 0.80–3.53). However, the incidence rate of acute myeloid leukemia was significantly increased. Monitoring of in-flight radiation exposure and long-term follow-up of civil aviation crew members is needed to further assess cancer incidence and leukemia risk in this special occupational group. *Am J Epidemiol* 1996;143:137–43.

aviation; leukemia; mortality; neoplasms; risk

Civil aviation crew members are exposed to known or suspected physical and chemical carcinogens or mutagens, particularly ionizing radiation, ozone, and jet engine emissions (1–4). Despite the special working environment and exposures of airline pilots, data on risk of death and cancer incidence in this occupational group are limited. Death certificate studies have reported increased proportional mortality ratios for deaths due to aircraft accidents (5–8); for rectal (5), colon (8), prostate (8), and brain cancers (8); and for malignant melanoma (8) and decreased proportional mortality ratios for deaths due to atherosclerotic heart (5–8) and respiratory (5, 7, 8) diseases. Proportional mortality studies are limited by inaccuracies of cause of death certification (9), and within a single occupational group, markedly high or low proportional mortality ratios for common causes of death may affect these ratios for less common causes including cancer (5).

In the first published cohort study of airline pilots of which we are aware, we reported excess relative rates for mortality due to aircraft accidents and rectal and brain cancers and decreased mortality risks from atherosclerotic heart diseases, as well as increased relative incidence rates for brain cancer and Hodgkin's disease (10). These results were based on a small cohort; few incident cancer cases were observed, risk estimates showed wide confidence intervals, and it was concluded that caution needed to be exercised in interpreting the data. In this paper, we report mortality and cancer incidence rates in a different and larger cohort of airline pilots.

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Abbreviations: AML, acute myeloid leukemia; CI, confidence interval; CLL, chronic lymphoid leukemia; SIR, standardized incidence ratio; SMR, standardized mortality ratio.

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MATERIALS AND METHODS

Subject characteristics and data collection

All male pilots employed by Air Canada for 1 year or more on and since January 1, 1950, were included in this study. Completeness of the cohort enumeration was ensured by a thorough search of the company's employee records. The following information was obtained from the company records: full name, date of birth, social insurance number, date of first hire, date of termination of employment, and current or last known address and telephone number. For pilots no longer employed whose current addresses were unknown to the company, information was sought from active pilots, the Canadian Air Line Pilots Association, government authorities responsible for issuing driver's licenses, the Ministry of Transport of Canada, and various other sources. Cause and date of death and cancer incidence information, including date of diagnosis, site, and histology, were ascertained through the Divisions of Vital Statistics and the Cancer Registries of the Canadian Provinces, the Canadian Mortality Data Base, Air Canada medical records, the pilots' pension plan, hospitals, and physicians' offices. The cutoff date for outcome information was December 31, 1992.

Statistical procedure

Analyses for mortality and cancer incidence were carried out separately. For mortality rates, person-years at risk were calculated from 1 year after the date of hire to December 31, 1992, or to the year of death, whichever came first. For cancer incidence rates, person-years at risk were calculated from 1 year after the date of hire to December 31, 1992, to the year of cancer diagnosis, or to the year of death from noncancer causes, whichever came first. For pilots lost to follow-up, observations were censored at the date when last known to be alive.

Standardized mortality ratios (SMRs) and standardized cancer incidence ratios (SIRs) were used to compare the mortality and cancer incidence of the cohort with those of the Canadian male population. Canadian population mortality rates, obtained from the Laboratory Centre for Disease Control, Health Canada, were calculated by 5-year age groups and 5-year calendar periods dating back to 1950, with the rates for 1985–1989 being used for the period 1990–1992. Similarly, Canadian cancer incidence rates were obtained from the Laboratory Centre for Disease Control by the same 5-year age groups and calendar periods for the years 1969–1988. Incidence rates for the years prior to 1969 were estimated by the 1969–1973 incidence rates, and rates for 1989–1992 by the incidence rates for 1984–1988. Tests of significance and of the SMRs and SIRs were calculated assuming the observed number of events followed a Poisson distribution with mean given by the expected number of events (11). To facilitate data comparison with our previous study (10), one-sided t test and 90 percent confidence intervals corresponding to a 5 percent significance level were used. Incidence ratios for nonmelanoma skin cancer could not be calculated since national rates for this cancer are not available. During the study period, causes of death were coded according to four versions of the *International Classification of Diseases*, Sixth, Seventh, Eighth, and Ninth Revisions. All codes for both causes of death and cancer incidence were reconciled to the Ninth Revision (12).

Estimation of leukemia risk due to in-flight radiation exposure

The number of leukemia cases in the cohort expected to be due to ionizing radiation exposure was calculated by using exposure estimates from Friedberg et al. (13). Friedberg et al. estimated the radiation doses to the bone marrow during conditions of average solar activity received by aircraft crew members for various flight paths originating or terminating in the United States. These authors estimated exposures ranging between 0.2 milliSievert (mSv) to 9.1 mSv per working year for crew members flying these paths. Data on current flight patterns for Air Canada pilots, obtained from Air Canada, showed the following breakdown of proportional flight hours for the overall pilot cohort: 1) within Canada, 53 percent; 2) Canada-United States, 18 percent; 3) Canada-Europe, 16 percent; 4) elsewhere and charter flights: 13 percent. Taking a New York-to-Chicago flight (13) to be representative of categories 1 and 2 gave an estimated annual dose of 5 mSv for flights in these categories. Taking a Chicago to London flight to be representative of categories 3 and 4 yielded an estimated annual dose of 7 mSv. Weighting these estimates by the overall proportion of time spent flying in categories 1–4 gave a mean exposure of 5.6 mSv per year per pilot in the cohort. Since it is expected that exposures for Canadian pilots would be slightly higher because of the more northerly latitude and probable longer average flight duration, this number was rounded up to 6.0 mSv per year. Data from in-flight measurements made in Lufthansa airplanes at altitudes ranging between 10 km (33,000 feet) and 11.1 km (37,000 feet) (14) led to similar estimates of exposures, ranging between 3 and 5 mSv per working year. For each pilot, total doses of ionizing radiation by age were calculated by using the person-years method for the period of employment. The preferred relative risk model for radiation-induced

leukemia mortality from the BEIR V report (15) was then applied to the cohort by using the estimated exposures to obtain the expected number of cases of leukemia excluding chronic lymphoid leukemia (CLL) (15). It was assumed that the relative risks for radiation-induced leukemia mortality applied to leukemia incidence. To derive an estimated range of risks, we also used the lowest and highest amounts of annual radiation exposure reported by Friedberg et al., 0.2 and 9.1 mSv, respectively (13).

RESULTS

A total of 2,740 eligible pilots were identified, of whom 2,680 were successfully traced (97.8 percent). The characteristics and person-year distribution of the cohort are shown in tables 1 and 2, respectively. As of December 31, 1992, 219 pilots had died, 81 (37 percent) from cardiovascular conditions, 56 (26 percent) from cancer, 31 (14 percent) from aircraft accidents, and 51 (23 percent) from other causes (table 3). All causes of death were confirmed. A total of 125 cancer incident cases, excluding 106 cases of nonmelanoma skin cancer, were ascertained (table 4); one pilot had two synchronous cancers (a transitional cell carcinoma of the bladder and an adenocarcinoma of the kidney). All cancers were histologically confirmed and, except for three (one brain tumor, one colon cancer, and one acute myeloid leukemia diagnosed in 1952, 1960, and 1964, respectively), were diagnosed in 1969 or later. All brain tumors were astrocytomas (three grade II; four grades III and IV). Seven of the nine leukemias were myeloid leukemias, and of these, six were acute myeloid leukemias (AML). SMRs and SIRs for diseases with two or more deaths or cancer incident cases are shown in tables 3 and 4, respectively. SMRs (table 3) were significantly decreased statistically for all causes of death; for all cancers combined; and for deaths due to cardiovascular, respiratory, and digestive diseases, nonaircraft accidents, and lung cancer and were significantly increased for deaths due to aircraft accidents. Elevated SMRs were observed for malignant melanoma of the skin and for prostate and brain cancers. SIRs (table 4) were significantly decreased statistically for all cancers and for rectal, lung, and bladder cancers and were significantly increased for prostate cancer, all myeloid leukemias, and AML. Elevated SIRs were observed for malignant melanoma of the skin, brain cancer, astrocytomas and glioblastomas (astrocytomas grades III and IV) combined, and for all leukemias including and excluding CLL.

TABLE 1. Cohort characteristics of Air Canada pilots, Canada, 1950–1992

	No.	%
Total eligible	2,740	100
Employed	1,906	69.6
Terminated	834	30.4
Lost to follow-up	60	2.2
Successfully traced	2,680	97.8
Age at first hire (years)		
Mean (SD)	26.3 (3.7)	
Median	25.8	
Age at study termination (years)		
Mean (SD)	50.5 (12.4)	
Median	50.1	
Years worked		
Mean (SD)	20.8 (10.1)	
Median	20.2	
Person-years (mortality)*	62,449	
Person-years (incidence)†	61,856	

* Person-years for mortality rate calculation (see text).
† Person-years for incidence rate calculation (see text).

SIRs for prostate cancer, brain cancer, and AML were further examined using time-dependent exposure categories defined as time since first employment and duration of employment. No time-related effects were observed for prostate or brain cancers. For AML, SIRs were, respectively, 3.77 (90 percent confidence interval (CI) 0.65–11.86) for two cases with less than 20 years since first employed and 5.41 (90 percent CI 1.84–12.36) for four cases with over 20 years since first employed. Similarly, SIRs were 1.67 (90 percent CI 0.07–7.88) for one case with less than 20 years of duration of employment and 7.46 (90 percent CI 2.93–15.68) for five cases with over 20 years of duration of employment.

The preferred leukemia model from the BEIR V report (15), which excludes CLL, applied to the cohort gave an estimated expected number of cases of 3.87 for all non-CLL, assuming a mean annual dose of 6 mSv per pilot in the cohort and expected numbers of cases of 3.73 and 3.94 assuming mean annual doses of 0.2 mSv and 9.1 mSv, respectively. In the absence of radiation exposure, the expected number of cases of non-CLL was 3.72 (table 4); the estimated expected excess of non-CLL cases attributed to in-flight radiation exposure is therefore 0.01, 0.15, and 0.22 for the mean annual dose estimates of 0.2, 6.0, and 9.1 mSv, respectively. The estimated average relative risks of the cohort for non-CLL due to radiation exposure corresponding to these mean annual doses are 1.001, 1.04, and 1.06. These relative risks fall within the 90 percent confidence interval for non-CLL (table 4).

DISCUSSION

The cohort of Air Canada pilots described in this report comprises over three times the numbers and person-years of follow-up of a different cohort of Canadian Pacific Airlines pilots previously published

TABLE 2. Person-years distribution of Air Canada pilots, Canada, 1950–1992

Age group (years)	Calendar period					Total
	1950–1959	1960–1969	1970–1979	1980–1989	1990–1992	
20–29	1,919	1,808	1,990	2,175	154	8,046
30–39	2,616	4,585	6,580	6,843	1,921	22,545
40–49	705	2,661	5,027	6,597	1,812	16,802
50–59	38	680	2,562	4,836	2,127	10,243
60–69		35	606	2,314	831	3,786
70–79			23	467	494	984
80–89				12	31	43
Total	5,278	9,769	16,788	23,244	7,370	62,449

TABLE 3. Standardized mortality ratio for diseases with two or more deaths and for deaths due to accidents, Air Canada pilots, Canada, 1950–1992

Cause of death	ICD-9* code	Observed	Expected	SMR*	90% CI*	*p* value
All causes of death	001–999	219	350.18	0.63	0.56–0.70	<0.001
Cancer						
Mouth	143–145	2	0.55	3.63	0.63–11.40	0.11
Esophagus	150	2	2.32	0.86	0.15–2.70	0.59
Stomach	151	3	5.27	0.57	0.15–1.47	0.23
Colon	153	10	8.16	1.23	0.67–2.09	0.30
Trachea, bronchus, lung	162	8	31.59	0.25	0.12–0.45	<0.001
Malignant melanoma of skin	172	2	1.34	1.49	0.26–4.68	0.40
Prostate	185	7	4.62	1.52	0.71–2.85	0.18
Kidney	189	3	2.47	1.22	0.33–3.15	0.45
Brain	191	5	3.52	1.42	0.56–2.98	0.28
Lymphatic and hematopoietic	200–208	6	9.08	0.66	0.29–1.30	0.20
Non-Hodgkin's lymphoma	200, 202	2	3.23	0.62	0.11–1.95	0.37
Leukemia	204–208	3	3.50	0.86	0.23–2.22	0.54
Myeloid leukemia	205	2	1.51	1.32	0.23–4.15	0.44
All cancers	140–208	56	92.24	0.61	0.48–0.76	<0.001
Noncancer diseases	001–139, 240–799	105	199.59	0.53	0.45–0.62	<0.001
Circulatory system	390–459	81	134.03	0.60	0.49–0.72	<0.001
Ischemic heart disease	410–414, 429.2	56	98.00	0.57	0.45–0.71	<0.001
Acute myocardial infarction	410	37	60.79	0.61	0.45–0.80	<0.001
Cerebrovascular disease	430–438	8	14.55	0.55	0.27–0.99	0.05
Aortic aneurysm	441	3	3.15	0.95	0.26–2.45	0.61
Respiratory system	460–519	5	17.60	0.28	0.11–0.59	<0.001
Pneumonia	480–486	4	5.10	0.78	0.27–1.78	0.42
Digestive system	520–579	6	17.09	0.35	0.15–0.69	<0.001
Chronic liver disease and cirrhosis	571	3	10.15	0.30	0.08–0.77	0.01
Central nervous system	320–389	4	5.45	0.73	0.25–1.67	0.36
Accidents	E800–E999	58	58.36	0.99	0.79–1.23	0.52
Aircraft	E840–E845	31	1.17	26.57	19.3–35.9	<0.001
Nonaircraft	E800–E838, E846–E999	27	57.18	0.47	0.33–0.65	<0.001

* ICD-9, *International Classification of Diseases*, Ninth Revision; SMR, standardized mortality ratio; CI, confidence interval.

(10). This study confirms our previous findings of statistically significant decreased death rates from all causes and from cardiovascular and respiratory diseases. These results are consistent with those from mortality studies (5–8) and reflect the healthy worker effect of this occupational group highly selected for their health and physical fitness. The marked increased mortality from aircraft accidents noted in this study is comparable in magnitude with previously reported observations from different commercial airlines (8, 10) and from mortality studies (5–7) and likely represents a hazard specific to the occupation. Our study

TABLE 4. Standardized incidence ratio for incident cancer with two or more cases, Air Canada pilots, Canada, 1950–1992

Cancer site	ICD-9* code	Observed	Expected	SIR*	90% CI*	p value
All cancers†	140–208	125	175.77	0.71	0.61–0.82	<0.001
Lip	140	2	3.18	0.63	0.11–1.98	0.38
Mouth	143–145	2	1.98	1.01	0.17–3.17	0.59
Esophagus	150	2	2.42	0.83	0.14–2.61	0.56
Stomach	151	5	7.09	0.70	0.28–1.47	0.29
Colon	153	13	14.86	0.87	0.51–1.38	0.38
Rectum	154	4	9.58	0.42	0.14–0.96	0.04
Lung	162.2–162.9	11	38.89	0.28	0.16–0.46	<0.001
Malignant melanoma of skin	172	8	5.27	1.52	0.76–2.74	0.16
Prostate	185	34	18.16	1.87	1.38–2.49	0.001
Testis	186	2	3.19	0.63	0.11–1.98	0.38
Bladder	188	4	11.12	0.36	0.12–0.82	0.01
Kidney	189	3	5.92	0.51	0.14–1.32	0.16
Brain	191	7	4.57	1.53	0.72–2.87	0.18
Astrocytomas	9400–9421§	7	3.55	1.97	0.92–3.70	0.07
Glioblastomas‡	9440–9441§					
Non-Hodgkin's lymphoma	200, 202	4	7.71	0.52	0.18–1.19	0.12
All leukemias	204–208	9	5.47	1.65	0.86–2.88	0.10
Nonchronic lymphoid leukemias	204–208, except 204.1	7	3.72	1.88	0.80–3.53	0.08
Chronic lymphoid leukemia	204.1	2	1.75	1.15	0.20–3.61	0.52
Myeloid leukemia	205	7	2.39	2.93	1.37–5.50	0.01
Acute myeloid leukemia	205.0	6	1.27	4.72	2.05–9.31	0.002

* ICD-9, *International Classification of Diseases*, Ninth Revision; SIR, standardized incidence ratio; CI, confidence interval.
† Nonmelanoma skin cancer excluded.
‡ Astrocytomas grades III and IV.
§ *International Classification of Diseases for Oncology.*

also confirms the statistically significant decreased incidence of all cancers, mostly attributable to the markedly reduced lung and bladder cancer rates, which strongly suggests that pilots smoke less than does the general population. The increased SMR and SIR noted for brain cancer, calculated on mortality and incidence rates for all malignant brain tumors, did not reach statistical significance as previously observed (10), although the confidence interval from both studies overlapped and did not show any time-related effects. All brain tumors reported in this study and in our previous study were astrocytomas. SIR based on astrocytoma- and glioblastoma- (astrocytomas grades III and IV) specific rates showed an almost twofold excess (table 4). The elevated rectal cancer mortality rate (10) was not corroborated in this study; excess risk for rectal cancer had also been reported in one mortality study (5), but not in others (6–8). Reasons for these discrepancies are not readily apparent but may be related to chance variation due to small numbers. Similarly, the increased Hodgkin's disease incidence rate seen in the Canadian Pacific Airlines cohort (relative risk = 4.54 based on three observed cases) was not confirmed.

The main new findings of this study are the statistically significant increased relative incidence rates of prostate cancer and AML. The etiology of prostate cancer is unknown; aside from certain occupational risks, notably farming, a high intake of animal fat has been suggested as the main potential risk factor (16). The latter possibility seems unlikely in our study, since one would not expect an increased consumption of animal fat to be associated with a markedly reduced mortality from atherosclerotic heart disease. Detection bias might be a more likely explanation, since throughout their career pilots must undergo yearly physical examinations, including a digital rectal examination. However, the mortality rate from prostate cancer was elevated, but not significantly so, and in a study of British Airways pilots excess deaths from prostate cancer were observed (8).

The epidemiology of acute leukemias has been addressed in several recent reviews (17–19). Among the risk factors associated with these diseases, exposures to ionizing and nonionizing radiation and benzene require special consideration. Benzene is a known human leukemogen, predominantly causing AML (19, 20), and is present in low concentrations in jet fuel (21) and jet fuel vapors (22). However, evidence of the carcinogenicity to humans of jet fuel is inadequate (21), and a recent cohort of workers exposed to jet fuel did not reveal any increased leukemia risk (23). Epi-

demiologic studies have provided some evidence of an association between acute leukemia, particularly AML, and exposure to 50/60 Hz electromagnetic field (19, 24–26) . Airline pilots are exposed to electromagnetic fields ranging from 400 Hz to several thousand gigahertz. Whether such exposures may play a role in the elevated AML risk observed in our study remains hypothetical.

Exposure to ionizing radiation is a well-known cause of all types of leukemia except CLL (15, 18, 19). Pilots are exposed to cosmic radiation, to periodic solar flares during which cosmic dose rates are substantially increased (27–30), and to radioactive material that may be transported as cargo (27). This occupational exposure may exceed the radiation dose limits recommended for the general population and has led to the suggestion that commercial aviation crew members be considered as radiation workers (28–30).

By applying the preferred leukemia mortality relative risk model to leukemia incidence, we estimated that the expected excess of non-CLL experienced in the cohort is between 0.01 and 0.22 cases over the entire study period. Application of this model involves the assumption that survival for radiation-induced leukemia is similar to that for leukemia not induced by radiation. Uncertainties also exist in the way in which we have estimated cumulative radiation doses. First, the radiation doses reported by Friedberg et al. (13) do not take into account solar proton events during which radiation dose rates may be considerably increased or exposure from transportation of radioactive material. In addition, radiation doses received by pilots would show great variation, but data on individual exposures are not available. The change from propeller-driven aircraft to jets in the early 1960s, with the concomitant gain in cruising altitude and radiation exposure and the assumption that pilots were flying the same number of hours annually in the past as currently would suggest that we may have overestimated past exposure; such overestimate is unlikely to be large since only 9 percent of the cohort's total person-year distribution accumulated prior to 1960.

Our study found no statistically significant excess for non-CLL, and not all subtypes of leukemias associated with radiation exposure were observed. However, the incidence rate for AML, the leukemia type most strongly associated with radiation exposure (15, 18), significantly exceeded the expected number. It is of interest to note that AML was also the main type of non-CLL found among British Airways (8) and Canadian Pacific Airlines (10) pilots. The SIRs observed in our study for AML increased with time since first employment and with duration of employment; because of small numbers, these time-related effects should be interpreted with caution. No definite explanation for this excess risk can be provided at this time. Although a chance occurrence cannot be excluded, a synergistic effect between known or suspected leukemogens remains a possibility (31). Monitoring of in-flight radiation exposure as well as long-term follow-up of cohorts of civil aviation crew members is needed to further assess cancer incidence, particularly brain cancer (8, 10) and leukemia risk, in this special occupational group.

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