Mortality Among Aerial Pesticide Applicators and Flight Instructors: Follow-up From 1965–1988

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Background *Vital status followup for a retrospective cohort mortality study of 9,961 male aerial pesticide applicators was extended beyond a previous study (1965–1979) (Cantor et al. 1991), through December 31, 1988.*
Methods *Rate ratios (RR) were used to compare directly adjusted mortality rates between applicators and a comparison cohort of 9,969 flight instructors. Standardized mortality ratios (SMR) were calculated for comparisons with the U.S. white male population.*
Results *Among applicator pilots, there were 1,441 deaths, and among instructors, 1,045. In both groups, aircraft accidents were the major cause of death (446 applicators; 234 instructors). Compared with flight instructors, aerial applicator pilots were at significantly elevated risk for all causes of death (risk ratio = 1.34) and for malignant neoplasms (1.18), non-motor vehicle accidents (1.71), motor vehicle accidents (1.69), and stroke (1.91). Pancreatic cancer (2.71) and leukemia (3.35) were significantly elevated. Applicators were at lower risk of colon cancer (0.51) and multiple myeloma (0.23) mortality. Based on U.S. rates, the SMR for all causes of death among applicators was 111 (95% confidence interval (CI) = 105–117) and among instructors, 81 (CI = 76–85).*
Conclusions *Aircraft accidents were a major cause of mortality in both applicator and flight instructor cohorts. Several other causes of death, some possibly related to pesticide exposure, were also elevated among pesticide applicator pilots.* Am. J. Ind. Med. 36: 239–247, 1999. *Published 1999 Wiley-Liss, Inc.*†

KEY WORDS: pesticides; cancer; leukemia; prostate cancer; retrospective cohort; pesticide applicators

INTRODUCTION

Pilots who spray agricultural chemicals are at a higher risk of death than other aviators because of flying under more hazardous conditions [Cantor and Booze Jr., 1991]. This includes the challenge of flying small planes at low altitudes, stresses due to heat, vibration, and noise [Richter et al., 1981], and the possibility of exposure to neurotoxic pesticides that impair coordination, balance, and other neuromotor functions that can interfere with crucial flying skills. In addition to the ever-present dangers of traumatic injury, are the additional hazards associated with chronic pesticide exposure.

We earlier presented results from a followup study from 1965 through 1979 of a cohort of aerial pesticide applicators and a comparison group of flight instructors in the U.S. [Cantor and Booze Jr., 1991]. We found excesses of mortality from aircraft accidents and deficits from most

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chronic diseases, including all cancers. A limitation was that the vital status closing date was 15 years after establishment of the computerized database from which the cohort was identified. This period was only marginally adequate to identify excess cancer risk that may have been associated with pesticide or other exposures common to aerial applicators. Here we report findings from a nine-year extension of vital status followup that provides greater potential for detecting carcinogenic risks experienced by this occupational group.

METHODS

Cohort Definition and Identification

The Federal Aviation Administration (FAA) requires an annual qualifying medical examination for all commercial pilots (semi-annual for passenger-carrying pilots) [FAA, 1996], and has maintained a digitized file of data collected from these examinations since 1965 in the Aeromedical Certification Divison of the Office of Aviation Medicine. Using these records, we identified and selected 9,961 men who reported their occupation as "aerial applicator" at least once in the period 1965–1980. In addition, we randomly selected 9,969 male flight instructors, to serve as a comparison group, from a pool of more than 41,000 individuals from the same database. The comparison cohort was matched to the aerial applicator group on 5-year birth date group and the U.S. geographic region of their most recent address. Date of entry into the study was the medical examination date when the cohort member first reported an occupation as applicator or flight instructor. The FAA medical examination record does not include information on race. Of 1,379 deceased applicators with information from death certificates on race, 1,375 (99.7%) were Caucasian. Among instructors, 978 of 987 (99.1%) were Caucasian. Further details on the FAA database and methods of cohort selection are published elsewhere [Cantor and Booze Jr., 1991].

Followup Procedures

In a previous followup of this cohort (through 12/31/79), we used a variety of resources to determine vital status [Cantor and Booze Jr., 1991]. Because the National Death Index (NDI) was available as a followup resource during the additional period covered by this study, and this resource is relatively complete [Boyle and Decoufle, 1990; Curb et al., 1985; Wentworth et al., 1983], we used the NDI as the sole followup resource for the period 1/1/80 through 12/31/88. We requested death certificates from state vital statistics offices. Certificates were coded by a trained nosologist who used the rubrics of the International Classification of Diseases, Eighth Revision. Subjects lost to followup, and subjects reported deceased but with no date of death available, were considered alive at the study closing date. When no death certificate was available but the date of death was known, subjects were considered deceased and cause of death was grouped in the "other" cause category.

Data Analysis

We calculated cause-specific rate ratios (RR) by dividing the directly adjusted mortality rate among applicators by the rate among instructors, and 95% confidence intervals calculated were based on a chi-square test. The population of the combined cohorts, divided into 10-year age groups and 5-year calendar year strata, was used for calculating adjusted rates.

In addition, we calculated standardized mortality ratios (SMRs) by cause, using U.S. white males as the referent population [Monson, 1974]. Expected numbers of deaths were estimated by applying cause-specific 5-year age and 5-year calendar time U.S. mortality rates to the appropriate stratum in the cohort of interest, and summing over all strata. The SMR was computed by dividing the observed by the expected number of deaths, and multiplying by 100.

As an index of "exposure" for applicators, we estimated the number of flight hours as an applicator (pre-1980), based on self-reported information from the computerized FAA medical examination record abstract. This estimate did not include aerial application activity prior to the first FAA computerized record of a medical examination because the data were not available to us. Estimation procedures are described in detail in a previous report from this study [Cantor and Booze Jr., 1991]. Flight hour data were sometimes lacking in consistency or missing entirely from medical examination records. Where possible, we made assumptions to permit derivation of reasonable estimates for missing or improbable numbers. When reasonable flight hour estimates could not be derived, the individual was excluded from analyses which used flight hours as a surrogate exposure measure. After exclusions, 8,524 aerial applicators were included in these analyses, with 139,075.5 person-years and 1,195 (total) deaths. To estimate dose effects, applicator pilots were grouped in one of three applicator flight hour strata, with total person-years divided more or less evenly among them: <455 flight hours, 455–1,897 hours, and 1,898+ hours. (median level $= 250.2$, 1,361.5, and 4,031.3, respectively). Cause-specific adjusted mortality rates were calculated by this flight-hour grouping. Standard methods were used to calculate tests of trend for these adjusted rates [Breslow et al., 1983]. The trend test used the correlation coefficient between the log-transformed adjusted mortality rate and the log-transformed median number of flight hours in each exposure group. The correlation was weighted by person-years. In calculating trend tests, flight instructors served as the unexposed

TABLE I. Numbers of Aerial Applicators and Flight Instructors in Study Cohorts, Grouped by Age at Entry and Year of Entry[a]

	Year of entry					
Age at entry	1965–1969	1970–1974	1975–1979	1980–1984	Total	Percentage
15–24	510/579	380/546	518/529	55/48	1463/1702	14.7/17.1
25–34	1456/1456	1021/1049	1302/914	123/89	3902/3508	39.2/35.2
35–44	1679/1164	436/569	598/628	67/38	2780/2399	27.9/24.1
45–54	899/742	276/446	264/525	28/44	1467/1757	14.7/17.6
55–64	151/160	56/121	91/237	10/19	308/537	3.1/5.4
65+	19/26	9/14	12/23	1/3	41/66	0.4/0.7
Total	4714/4127	2178/2745	2785/2856	284/241	9961/9969	
(Percentage)	(47.3/41.4)	(21.9/27.5)	(28.0/28.7)	(2.8/2.4)		(100.0/100.1)

[a]Data are presented as # applicators/# instructors.

referent group (a nominal low level of 10 flight hours was assigned to instructors to facilitate the log-transformation calculation).

RESULTS

The numbers of persons in the aerial applicator and flight instructor cohorts, by 5-year age group at entry and 5-year date of entry, are shown in Table I. There was a reasonably good age match between the two cohorts, even though matching was on year of birth and not year of entry. Included in this study, but not in the previous followup [Cantor and Booze Jr., 1991], were 284 applicators and 241 instructors who were first entered in FAA records as applicators or instructors in 1980.

We show summary statistics for the two cohorts in Table II. The number of person-years of followup (164,271.1 for applicators) was approximately twice that of the earlier followup [Cantor and Booze Jr., 1991]. We identified 1,471 deaths among applicators and 1,080 among flight instructors. Death certificates were located for 1,380 applicators (94%) and 988 instructors (91%). Among decedents with no death certificate, the date of death was available for 61 applicators and 57 instructors. We considered these persons as deceased in our analysis (cause listed as "other and ill-defined conditions"). The 30 applicators and 35 instructors whose deaths were reported, but with no date of death, were considered alive at the end of the study. In the earlier followup, 438 persons were "lost-to-followup" (241 applicators, 197 instructors). Forty-seven (47) of these pilots died prior to the close of this update (25 applicators, 22 instructors). Individuals in this group with no report of death were considered alive at the study closing date.

Table III shows the number of decedents and the mortality rate per 100,000 person-years for major causes of death in each cohort, adjusted to the joint population distribution of age and year of death in the two cohorts. Also shown is the applicator-to-instructor ratio of the adjusted rates, and 95% confidence limits for the ratio. Aerial applicators suffered higher mortality rates than flight instructors for each major cause listed, except suicide. The 95% confidence interval excluded 1.0 for all causes combined (rate ratio (RR) = 1.34), all malignant neoplasms (RR = 1.18), stroke (RR = 1.91), accidents other than motor vehicle (RR = 1.71), and motor vehicle accidents (RR = 1.69). Among the 491 aerial applicator deaths from "accidents other than motor vehicle" were 446 aircraft accidents (90.8%). For instructors, 234 of 268 deaths in this category were due to aircraft accidents (87.7%).

TABLE II. Characteristics of Aerial Pesticide Applicators and Flight Instructor Cohorts, Including Vital Status at the Study Closing Date (31 December 1988)

	Aerial pesticide applicators	Flight instructors
Cohort size	9961	9969
Total person-years	164,271.1	159,920.1
Mean age at entry	35.37	36.21
Mean followup (y)	16.49	16.04
Vital status at closing date (1/1/89)		
Assumed alive	8520	8924
Death reported (but no date or death certificate available)	30	35
Lost to followup in previous study	216	175
No other information	8274	8714
Dead	1441	1045
Death certificate	1380	988
No certificate (date of death available)	61	57

TABLE III. Observed Number of Deaths, Adjusted Mortality Rates, and Rate Ratios for Major Causes of Death Among Aerial Pesticide Applicators and Flight Instructors Followed Through 31 December 1988[a]

	Aerial applicators		Flight instructors			
Cause of death	**Obs no.**	**Rate (adj.)**	**Obs no.**	**Rate (adj.)**	**Rate ratio**	**Confidence limits for ratio**
All causes	1,441	883.5	1,045	657.1	1.34	1.26–1.4
All malignant neoplasms	263	163.0	225	138.6	1.18	1.01–1.4
Arteriosclerotic heart disease	275	170.1	244	151.7	1.12	0.97–1.3
Stroke	29	17.9	15	9.4	1.91	1.1–3.2
Diseases of nervous system and sense organs	7	4.3	3	1.9	2.30	0.7–7.2
Respiratory disease	34	21.4	28	17.0	1.25	0.8–1.9
Liver cirrhosis	26	15.7	20	12.6	1.24	0.8–2.0
Accidents other than motor vehicle	491	298.6	268	174.6	1.71	1.5–1.9
Motor vehicle accidents	71	43.0	41	25.4	1.69	1.2–2.3
Suicide	35	20.9	38	23.4	0.89	0.6–1.3

[a]Mortality rates per 100,000 person-years of experience, adjusted to the age distribution of the combined aerial applicator and flight instructor cohorts.

TABLE IV. Observed Number of Deaths, Adjusted Mortality Rates, and Rate Ratios for Malignant Neoplasm Deaths Among Aerial Pesticide Applicators and Flight Instructors Followed Through 31 December 1988[a]

	Aerial applicators		Flight instructors			
Cause of death	**Obs no.**	**Rate (adj.)**	**Obs no.**	**Rate (adj.)**	**Rate ratio**	**Confidence limits for ratio**
All malignant neoplasms	263	163.0	225	138.6	1.18	1.01–1.37
Buccal cavity & pharynx	6	3.8	6	3.6	1.05	0.4–2.7
Esophagus	5	3.1	4	2.4	1.28	0.4–3.9
Stomach	9	5.6	4	2.4	2.31	0.9–6.2
Colon	15	9.5	31	18.8	0.51	0.3–0.9
Rectum	4	2.4	6	3.6	0.68	0.2–2.0
Liver	3	1.9	5	3.1	0.60	0.2–2.0
Pancreas	22	13.6	8	5.0	2.71	1.4–5.3
Larynx	6	3.7	1	0.8	4.79	0.8–28.3
Lung	79	49.0	79	49.1	1.00	0.8–1.3
All Skin	15	9.2	11	6.8	1.35	0.7–2.6
Melanoma	11	6.7	8	5.0	1.33	0.6–2.9
Other skin	4	2.5	3	1.8	1.40	0.4–4.9
Prostate	21	13.8	17	10.4	1.32	0.8–2.3
Testis	2	1.3	0	–	–	–
Bladder	6	3.5	3	1.8	1.90	0.6–6.1
Kidney	9	5.5	5	3.0	1.82	0.7–4.6
Eye	1	0.6	0	–	–	–
Brain	9	5.5	8	5.0	1.11	0.5–2.5
Lymphosarcoma/ reticulum cell sarcoma	3	1.8	4	2.6	0.70	0.2–2.5
Hodgkin's disease	2	1.2	1	0.6	1.99	0.3–14.9
Multiple myeloma	2	1.1	8	4.9	0.23	0.1–0.8
Leukemia	14	8.3	4	2.5	3.35	1.3–8.5
All lymphopoietic	32	19.1	22	13.6	1.41	0.9–2.2

[1]Mortality rates per 100,000 person-years of experience, adjusted to the age distribution of the combined aerial applicator and flight instructor cohorts.

TABLE V. Standardized Mortality Ratios (SMR) and Their 95% Confidence Intervals (CI) for Major Causes of Death and Selected Malignancies Among Aerial Pesticide Applicators and Flight Instructors Followed Through 31 December 1988[a,b]

	Aerial applicators		Flight instructors	
Cause of death	SMR	CI	SMR	CI
All causes	111	(105–117)	81	(76–85)
Malignant neoplasms:				
Total	83	(74–94)	71	(62–81)
Stomach	83	(38–158)	37	(10–95)
Colon	55	(31–91)	112	(76–160)
Pancreas	140	(88–212)	51	(22–100)
Larynx	138	(50–300)	23	(0–129)
Lung	67	(53–84)	67	(53–83)
Melanoma	167	(83–299)	124	(53–243)
Prostate	140	(87–214)	107	(62–171)
Brain	82	(37–155)	75	(32–147)
Leukemia	118	(64–198)	34	(9–86)
Arteriosclerotic heart disease	66	(58–74)	59	(52–67)
Stroke	54	(36–77)	28	(16–46)
Respiratory disease	46	(32–65)	38	(25–54)
Liver cirrhosis	60	(39–88)	48	(29–75)
Accidents other than motor vehicle	984	(899–1075)	557	(492–627)
Motor vehicle accidents	141	(110–178)	84	(60–114)
Suicide	82	(57–114)	91	(65–126)

[a] Standardized mortality ratios based on U.S. mortality rates for white males.
[b] See Tables III and IV for numbers of deaths by cause.

Rate and RR data for specific cancers are shown in Table IV. As compared with flight instructors, the cancer mortality rate among aerial applicators was elevated for all cancers combined, and for some individual cancer sites. Notable were cancers of the stomach (RR = 2.31, CI = 0.9–6.2), pancreas (RR = 2.71, CI = 1.4–5.3), larynx (RR = 4.79, CI = 0.8–28.3), and leukemia (RR = 3.35, CI = 1.3–8.5). Other malignancies with elevated rates among applicators included cancers of the skin (15 applicator cases, RR = 1.35, CI = 0.7–2.6), bladder (6 cases, RR = 1.90, CI = 0.6–6.1), and kidney (9 cases, RR = 1.82, CI = 0.7–4.6). For this last group of tumors, risk ratios were less than 2.0 and confidence intervals were wide. Applicators experienced lower mortality than instructors for colon cancer (RR = 0.51, CI = 0.3–0.9) and multiple myeloma (RR = 0.23, CI = 0.1–0.8). The RR for lung cancer mortality was at the null (RR = 1.00, CI = 0.8–1.3).

In addition to comparing aerial applicators with flight instructors, we also calculated standardized mortality ratios (SMRs) for each group, using U.S. national mortality rates for white males as the comparison. Table V shows findings for major causes of death and for selected cancer sites. Notable were the very high SMRs, in both cohorts, for death from accidents other than motor vehicle accidents, with applicators experiencing almost 10 times the expected number of accidental deaths (SMR = 934), and instructors about 5.6 times (SMR = 557). Accidental deaths, excluding motor vehicle accidents, comprised the largest single cause of death among applicators (491) and instructors (268). Among applicators, this cause was the major contributor to the all-cause SMR of 111 (CI = 105–117). Smoking- and alcohol-related causes of death were significantly lower than expected in both groups. Among applicators and instructors, respectively, the SMRs for lung cancer were 67 and 67; for arteriosclerotic heart disease, 66 and 59; for stroke, 54 and 28; and for respiratory disease, 46 and 38. SMRs for cirrhosis of the liver were 60 and 48. The overall SMRs for all malignant neoplasms were significantly below 100 for both cohorts (applicators: SMR = 83, instructors: SMR = 71), due, in large part, to deficits in lung cancer. In the context of generally low SMR's for most smoking-related cancer sites, it is notable among applicators that the SMR for pancreas cancer was 140, and for larynx cancer, 138. Both have been linked to cigarette smoking. Mortality due to motor vehicle accidents may be a general indicator of risk-taking behaviors in these populations. The motor vehicle SMR among applicators (but not flight instructors) was elevated (SMR = 141, CI = 110–178).

Fourteen applicators died of leukemia, with an overall SMR of 118 (95% CI = 64–198). Of these, one was acute lymphatic, five were acute myeloid (SMR = 142, CI = 46–332), three were chronic lymphatic (SMR = 171, CI = 34–500), three were chronic myeloid (SMR = 168, CI = 34–492), and one each of acute erythremia and unspecified lymphatic leukemia. Of the four leukemia deaths among flight instructors, one was chronic lymphatic, two were chronic myeloid (SMR = 111, CI = 13–403), and one was unspecified type.

Table VI shows the mortality RRs for pesticide applicators by their total accrued number of flight hours. Mortality rates for all 9,969 flight instructors were used as the comparison. This analysis was restricted to the 8,524 applicators with usable information on self-reported flight hours in their medical examination records. There were 47,502.1 person-years at risk in the lowest flight hour group (< 455 h), 46,628.1 person-years at risk in the intermediate group (455–1,897 h), and 44,945.4 person-years in the highest flight hour group (1,898+h). Rate ratios for all causes combined increased with flight hours, with non-motor vehicle accident the single major contributor. Rate ratios for accidents involving motor vehicles also increased significantly with aerial applicator flight hours. In addition, increases in RRs for stroke, all respiratory diseases, and diseases of the nervous system were found with increasing flight hours. SMRs for malignant neoplasms as a group did

TABLE VI. Relative Risks and Observed Number of Deaths (in parentheses) for Selected Causes of Death, by Self-reported Number of Flight Hours Among Aerial Pesticide Applicators[a]

	Flight hours of applicators			
Cause of death	<455 (47,502)[b]	455–1897 (46,628)[b]	1898+ (44,945)[b]	p (trend)[c]
All causes	1.15 (387)	1.49[d] (393)	1.49[d] (397)	0.03
Arteriosclerotic heart disease	1.06 (86)	1.24 (64)	1.09 (64)	0.19
Vascular lesions of CNS (stroke)	1.10 (6)	3.73[d] (11)	1.47 (7)	0.30
All resp. disease	0.86 (8)	1.20[d] (7)	1.97[d] (11)	0.30
Dis. of nervous syst./sense organs	— (0)	— (1)	2.51 (3)	0.43
Motor veh. accid.	1.32 (18)	1.59[d] (19)	1.91[d] (23)	0.005
Other accidents	1.40 (119)	1.84[d] (160)	2.26[d] (154)	0.006
Malignant neoplasms:				
Total	1.15 (83)	1.17 (57)	1.06 (66)	0.23
Stomach	— (1)	— (1)	6.29[d] (6)	0.30
Colon	0.56 (5)	0.48 (4)	0.49 (3)	0.02
Pancreas	2.62 (7)	1.64 (3)	3.45[d] (8)	0.11
Larynx	— (1)	11.7[d] (3)	— (1)	0.22
Lung	0.88 (23)	1.21 (20)	0.81 (20)	0.80
Skin melanoma	1.14 (3)	— (1)	1.36 (3)	0.96
Prostate	1.26 (7)	1.82 (6)	0.48 (2)	0.87
Bladder	2.11 (2)	3.60 (3)	— (1)	0.45
Kidney	2.17 (4)	— (0)	2.80 (3)	0.56
Brain	1.89 (4)	— (1)	0.86 (2)	0.65
Lymphosarcoma-reticulum cell sarcoma	1.67 (2)	— (0)	— (1)	0.68
Leukemia	5.27[d] (8)	— (0)	3.47[d] (4)	0.49

[a]For the 8,426 aerial applicators (139,075 person-years at risk, 1177 deaths) with valid flight hour data.
[b]Person-years among applicators in the flight-hour category.
[c]p (trend) of the log-transformed adjusted mortality rate, from the regression coefficient with the corresponding log-transformed median number of flight hours in each group. The correlation was weighted by person-years. The mortality rate among flight instructors was included in the calculation of p(trend) as the no-exposure referent level (Rel. risk = 1.0).
[d]95 % confidence interval excludes 1.0.

not vary. However, the patterns of SMRs for several specific cancers were notable. Gastric cancer SMRs increased with flight hours, and an increase was also seen for pancreas cancer. The SMRs for colon cancer and leukemia decreased with increasing flight hours as an applicator.

DISCUSSION

In this study, we continued vital status followup for nine additional years of a previously reported cohort of aerial pesticide applicators identified from the computerized medical examination data base maintained by the FAA [Cantor and Booze Jr., 1991]. With a doubling of person-years of observation, and identification of 772 additional deaths among applicators and 626 among a comparison group of flight instructors, we confirmed many previously-observed mortality patterns, and made new observations. The current followup, through 1988, permitted observation of mortality over a 24-year period since the start of computerization of FAA records. Potentially important exposures for many applicators identified in the first years of registration likely predated the 1965 starting date.

We relied primarily on the National Death Index (NDI), established by the U.S. National Center for Health Statistics in 1979, for vital status followup. In our earlier followup of this group, prior to the NDI, we used a variety of other resources. The high quality of the NDI in identifying deaths in the U.S. population, especially among white males, is well established. In tests where lists of known deaths were submitted to the NDI, the proportion identified correctly was greater than 95% [Curb et al., 1985; Boyle and Decoufle, 1990; Wentworth et al., 1983]. However, it is likely that we did not identify all deaths. In internal comparisons, comparable deficits in the exposed and unexposed groups should not affect point estimates of risk. However, in our comparisons with the mortality experience of the U.S. male population, undercounting of deaths would underestimate the true risk.

We used flight instructors as the primary comparison group, although we also made limited comparisons with the mortality experience of the white male U.S. population. While our analysis using U.S. population rates is of interest, comparison with flight instructors is more appropriate in assessing risk to applicators, because pilots differ from the general population in important respects. All commercial pilots in the U.S. must qualify medically and meet a set of minimal health standards for cardiopulmonary, vascular, neuromuscular, and other physiologic systems [FAA, 1996]. This was apparent in the low SMRs that we observed in both cohorts for mortality due to arteriosclerotic heart disease, stroke, and respiratory disease. In addition, low SMRs for lung cancer, other respiratory disease, and liver cirrhosis among these and other commercial aircraft pilots indicate low levels of smoking and alcohol consumption [Band et al., 1996; Irvine and Davies, 1992; Salisbury et al., 1991]. Alcohol consumption among general aviation pilots may resemble more closely that of the general population [Modell and Mountz, 1990].

In contrast to the low mortality from most major chronic diseases was the high death rate associated with aircraft accidents. In addition to low-altitude flying with the ever-present danger of striking obstacles, agricultural pilots are subject to high occupational stress from heat [Froom et al., 1993; Gribetz et al., 1980], noise, G forces, vibration, and heavy work schedules [Richter et al., 1981]. Exacerbating these hazards is the potential for exposure to organophosphate, carbamate, and other pesticides that can decrease cholinesterase levels and compromise the high level neurologic performance required for precision flying [Quantick and Perry, 1981; Reich and Berner, 1968; Richter et al., 1981]. Such exposure has been documented in studies that measured pesticide levels in cockpit air [Atallah et al., 1982; Richter et al., 1980], on aircraft surfaces [Yoshida et al., 1990], in blood or urine of pilots [Driskell et al., 1991; Knopp and Glass, 1991], and in studies that detected decrements in cholinesterase levels [Dellinger, 1985; Richter et al., 1980; Smith et al., 1968] or documented poisoning episodes [Roan et al., 1982; Shapiro, 1990]. Improvements in aircraft design have decreased risk of exposure and improved crashworthiness [Bruggink et al., 1964]. A common observation in surveys that estimated pesticide exposures to pilots, loader-mixers, flaggers, and/or aircraft mechanics, is that ground support personnel have higher exposures and/or body burdens than pilots [Atallah et al., 1982; Knopp and Glass, 1991; McConnell et al., 1990; Yoshida et al., 1990]. If the cancer excess that we found among applicators is causally linked to pesticide exposure, then exposed ground crew may be at higher risk.

Deaths due to motor vehicle accidents were in excess among applicators and were also associated with number of flying hours as an applicator. This may indicate a propensity for risk-taking among applicators, or result from impaired neurologic function following acute or chronic pesticide exposure. The excess may also reflect a requirement to drive at dawn and dusk, in poor driving conditions before and after long flight days. An investigation of the timing of motor vehicle accidents relative to pesticide application activity is warranted to further evaluate this observation.

Relative to flight instructors, mortality from all cancer combined, and some specific cancer sites, was elevated among aerial applicators. Excess risk of pancreatic cancer was a new observation in this cohort, suggesting a link with pesticides or other exposures common to aerial applicators. Most studies of farmers and other pest-control workers have not observed elevated risk of pancreatic cancer [Blair and Zahm, 1991]. However, there are some indications of risk. A large study of mortality patterns among farmers in 23 states of the U.S. for 1984–1988 found elevated risk [Blair et al., 1993]. In addition, DDT-exposed manufacturing workers [Garabrant et al., 1992], flour industry workers with likely pesticide exposures [Alavanja et al., 1990], licensed agricultural pesticide users in Italy [Forastiere et al., 1993], and pancreatic cancer cases with self-reported exposure to pesticides [Falk et al., 1990] have elevated risk.

Stomach cancer deaths were twice as common among pesticide applicators as flight instructors. Among applicators with available measures of flight hours, six of eight gastric cancer deaths among applicators occurred in the highest flight-hour exposure group. However, the trend with flight-hours was not significant. It should be noted that overall SMRs for both applicators and instructors, based on comparison with U.S. rates, were below expectation. Elevated stomach cancer among farmers and others with exposure to pesticides has been found in many studies [Blair and Zahm, 1991]. The suggestive elevation of laryngeal cancer among applicators was unexpected. Both stomach [Olsen and Sabroe, 1984; Ward et al., 1997] and laryngeal cancers [Chow et al., 1994; Parent et al., 1998] have been linked with dusty working environments.

Leukemia deaths were elevated among applicators in this followup, as they were previously [Cantor and Booze Jr., 1991], and exposures to agriculture chemicals are suspect. Leukemia has been associated with farming [Blair and Zahm, 1991], other agricultural occupations [Amadori et al., 1995; Johnson et al., 1986; Pearce et al., 1986], and pesticide exposures [Blair et al., 1983; Brown et al., 1990] in numerous studies, with different subtypes at excess in varying exposure circumstances. The leukemia excesses in this study were observed across all major subtypes, although numbers for any single subtype did not reach a statistically meaningful level. Excess incidence of acute myeloid leukemia was found in a cohort study of Air Canada pilots [Band et al., 1996], suggesting that aviation-related exposures other than pesticide application may also be implicated.

The low overall chronic disease mortality among both aerial applicator and flight instructor cohorts was counterbalanced by excessive aircraft fatalities, resulting in an overall SMR of 111 for applicators and 81 for flight instructors. Cancer mortality of applicators was significantly above that of flight instructors (RR = 118), as in our previous followup [Cantor and Booze Jr., 1991]. However, the cancer experience of both was below expectation when compared with the U.S. standard. At the close of followup, the mean age in both cohorts was about 52 years, an age at which cancer in most populations starts to contribute substantially to overall mortality. Thus, future followup of this cohort will be of interest.

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