ORIGINAL ARTICLE

Mortality from cancer and other causes in commercial airline crews: a joint analysis of cohorts from 10 countries

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ABSTRACT

Background Commercial airline crew is one of the occupational groups with the highest exposures to ionising radiation. Crew members are also exposed to other physical risk factors and subject to potential disruption of circadian rhythms.

Methods This study analyses mortality in a pooled cohort of 93 771 crew members from 10 countries. The cohort was followed for a mean of 21.7 years (2.0 million person-years), during which 5508 deaths occurred.

Results The overall mortality was strongly reduced in male cockpit (SMR 0.56) and female cabin crews (SMR 0.73). The mortality from radiation-related cancers was also reduced in male cockpit crew (SMR 0.73), but not in female or male cabin crews (SMR 1.01 and 1.00, respectively). The mortality from female breast cancer (SMR 1.06), leukaemia and brain cancer was similar to that of the general population. The mortality from malignant melanoma was elevated, and significantly so in male cockpit crew (SMR 1.57). The mortality from cardiovascular diseases was strongly reduced (SMR 0.46). On the other hand, the mortality from aircraft accidents was exceedingly high (SMR 33.9), as was that from AIDS in male cabin crew (SMR 14.0).

Conclusions This large study with highly complete follow-up shows a reduced overall mortality in male cockpit and female cabin crews, an increased mortality of aircraft accidents and an increased mortality in malignant skin melanoma in cockpit crew. Further analysis after longer follow-up is recommended.

What this paper adds

- Through their occupation, commercial airline crew are exposed to ionising radiation of cosmic origin as well as other risk factors. They are subject to disruption of circadian rhythms.
- The overall mortality in male cockpit and female cabin crew is strongly reduced compared with the general population; the mortality from cancer is reduced with few exceptions, notably malignant skin melanoma in cockpit crew.
- The mortality from female breast cancer, leukaemia and brain cancer is similar to that of the general population.
- The mortality from cardiovascular diseases is considerably reduced; the one from aircraft accidents is remarkably high, as is that of AIDS in male cabin crew.

BACKGROUND

Through their occupation, commercial airline crew are exposed to ionising radiation of cosmic origin, as well as other risk factors, including electromagnetic fields from wiring and appliances, circadian rhythm disruption, ozone and noise.[1–3] Airline crew is one of the occupational groups with the highest radiation exposures, typically an excess dose of approximately 2 milliSievert (mSv) annually, roughly the dose from natural background radiation.[4–8] Cumulative occupational lifetime doses of ionising radiation generally remain below 100 mSv.[9]

The first reports on cancer incidence and mortality of civil and military aircraft crew were published in the early 1990s.[10–16] Additionally, data were combined in pooled analyses of cancer incidence and mortality.[17–21] A low overall and cardiovascular mortality of aircrew was consistently observed, indicating a strong effect of selection.[22] Another finding was a twofold increased incidence of skin melanoma.[17 18] There is limited evidence that ionising radiation is a risk factor for malignant melanoma, while the risk factor with the highest attributable fraction is ultraviolet (UV) radiation.[23 24]

In pooled analyses of male cockpit crew, decreasing mortality rates for all causes and all cancers with increasing estimated doses of ionising radiation were observed.[21] An increased risk for cancers of the central nervous system (CNS) has been observed in some cohorts.[25] A risk increase of about 20% was found for the incidence of prostate cancer, which was associated with the number of long-haul flight hours in pooled analyses of studies from the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden).[17] Shift work associated with a disruption of the circadian rhythm is one potential risk factor for breast and possibly prostate cancer.[2]

For male cabin crew, the overall and cancer mortality is similar to that of the general population, with few exceptions. In a recent pooled analysis of cancer incidence, significant excesses in melanoma and non-melanoma skin cancer, Kaposi sarcoma and alcohol-related cancers were observed, confirming previous results on mortality.[18 20] Additionally, increased mortality from leukaemia has been reported.[19 20]

In female cabin crew, an increased risk of breast cancer was observed both in incidence and mortality studies, as was a non-significantly increased risk of leukaemia.[18 20]

Findings from a pooled mortality analysis of 10 national cohorts of commercial airline crew are presented here. These include six cohorts with a prolonged observation period compared to previous publications and two new cohorts. This is the first publication where European and US data are combined. With an increase of 30% in the size of the study population and 69% in the number of person-years of observation compared to previous analyses, this study has a much greater statistical power and, thereby, precision for quantifying mortality risks. The cohorts are still young and it is important to track increases in cause-specific mortality as the cohort ages, especially if preventive measures may be deduced. The present publication reports standardised mortality ratio (SMR) analyses of the pooled cohorts separately for cockpit and cabin crew.

METHODS

Study population

The study population consists of cohorts of commercial airline crew from Denmark, Finland, Germany, Greece, Iceland, Italy, Norway, Sweden, UK and the USA. Individual cohort studies with similar protocols were set up so that data could be delivered in a common format for pooled analyses, following a long collaboration between eight of the study groups.[19 20] The UK and US cohorts were included ex novo, while the follow-up of cohort members from six out of eight other countries (with the exception of Greece and Italy) was extended for these new analyses. The national cohorts were compiled from varying sources in the participating countries (see online supplementary table S6). Procedures were described previously in more detail.[18 26–39] Briefly, airline crews were identified from personnel files of generally one airline in Finland, Germany, Greece, Iceland, Italy, Sweden and the USA. These data were supplemented by data from airline pilot associations in Finland and Iceland. In the UK, Iceland and Norway, license data of the national aviation authority were used for cockpit cohort identification and enumeration. In Denmark, all commercial cockpit crew on file in the National Clinic of Aviation Medicine in Copenhagen were included. Cabin crew had to be employed or licensed for at least 6 months (1 year in the USA) to be included in the cohort, while no such limit applied to cockpit crew. For simplicity, the pooled cohort will be termed 'multinational cohort' hereafter.

The data collected included sex, year of birth and employment or license dates. Information on occupational history was recorded wherever possible. The start of employment was available for each cohort member, except in the UK, where information obtained by questionnaire was available for about 50% of the cohort. The date for end of service as a crew member for retired crew members was available in the initial follow-up of the original eight cohorts. The employment status at end of follow-up for the current study was known for study subjects from Germany, Greece, Italy and the USA.

Vital status follow-up

The individual period of observation started at the first date of employment (at the date of the first valid license during the period 1 January 1989–31 December 1999 in the case of the UK cohort), at immigration, or at the country-specific start of follow-up, whichever was latest. It ended at the date of death, emigration, loss to follow-up, or at the end of the study period (2004 or later, depending on the country, except 1996 for Italy and 1997 for Greece), whichever came first. Ascertainments of vital status and causes of death were carried out according to country-specific procedures.[18 26–39]

Mortality endpoints

All causes of death were coded according to the International Classification of Diseases (ICD) revision in use at the date of death (ICD 7-10), and additionally recoded to the groups of causes used in previous analyses.[19 20] As the study focused on potential effects of exposure to ionising radiation of cosmic origin, these groups include single cancer sites as well as three combined group of neoplasms. A first group, herein termed 'radiation-related cancers', consists of cancers of the oesophagus, stomach, large intestine, female breast, bladder/urinary tract, thyroid gland and leukaemia excluding chronic lymphocytic leukaemia (CLL). This original categorisation was based on Boice *et al*[40] and the 2000 United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) Report. [41] Lung cancer, although known to be associated with ionising radiation, is not included due to its strong link with smoking. A second group of 'alcohol-related cancers' was considered, including cancers of the oral cavity, pharynx, larynx, oesophagus and liver (as in Dreyer *et al* [42]). Finally, cancers of the lung, oral cavity, pharynx, larynx, nasal cavities or sinuses, oesophagus, pancreas, urinary bladder, renal pelvis, stomach, liver, kidney, uterine cervix and myeloid leukaemia are subsumed as 'smoking-related cancers'.[43] A list of all causes of death and corresponding ICD codes can be found in online supplementary table S7.

Mortality rates for the general population

Sex, age-group, and calendar-period-specific mortality rates for the general population of each participating country were obtained from WHO Mortality Database, or from the national statistical offices (Finland, Norway, the UK and the USA).

STATISTICAL METHODS

For the analyses, data were transferred to the Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI) at the University Medical Center, Mainz, Germany. A complete analysis plan was laid down in writing and approved by the study group prior to the statistical analysis. Persons with missing or implausible data were excluded from the dataset. Similarly, records relating to 752 female cockpit crew members were not further analysed, as the size of this subcohort was very small and only eight deaths were observed.

Person-years at risk were dynamically allocated to 5-year age and calendar-period intervals and, additionally, to categories of employment/licensing duration (>0–9.9, 10–19.9, 20–29.9, 30+ years). A latency period for cancer development after the beginning of radiation exposure (ie, start of employment) of 2 years was assumed for leukaemia, and of 10 years for solid tumours.[44]

SMRs and associated 95% CI were computed using the mortality rates described above. To account for missing causes of

Table 1 Number of persons, follow-up time and mean age at end of follow-up in cohorts included in the multinational cohort of commercial airline crew

	Persons				Person-years				Mean duration of observation (in years)				Mean age at end of follow-up			
	Cockpit	Cabin crew			Cockpit	Cabin crew			Cockpit	Cabin crew			Cockpit	Cabin crew		
	Men	Men	Women	All	Men	Men	Women	All	Men	Men	Women	All	Men	Men	Women	All
Denmark	3757	1286	4889	9932	95 923	34 571	132 998	263 491	25.5	26.9	27.2	26.5	51.9	52.8	51.0	51.6
Finland	800	188	1576	2564	20 545	4983	43 588	69 116	25.7	26.5	27.7	27.0	54.1	52.3	53.9	53.8
Germany	6013	3731	17 019	26 763	141 539	72 575	303 945	518 059	23.5	19.5	17.9	19.4	51.6	45.2	42.5	44.9
Greece	843	627	1226	2696	18 923	12 203	22 830	53 956	22.4	19.5	18.6	20.0	53.0	46.9	42.1	46.6
Iceland	438	153	1531	2122	11 922	2325	38 442	52 689	27.2	15.2	25.1	24.8	54.2	39.0	47.8	48.5
Italy	3020	3415	3429	9864	54 024	47 902	51 700	153 626	17.9	14.0	15.1	15.6	50.7	42.9	39.1	44.0
Norway	3659	570	3068	7297	99 657	16 524	90 364	206 545	27.2	29.0	29.5	28.3	56.3	56.8	54.4	55.6
Sweden	1478	631	2323	4432	45 710	20 406	69 816	135 932	30.9	32.3	30.1	30.7	61.1	59.1	55.5	57.9
UK	16 808	0	0	16 808	258 881	0	0	258 881	15.4	0	0	15.4	53.3	0	0	53.3
USA	0	1687	9606	11 293	0	40 520	279 463	319 983	0	24.0	29.1	28.3	0	53.8	54.8	54.7
Total	36 816	12 288	44 667	93 771	747 123	252 010	1 033 146	2 032 279	20.3	20.5	23.1	21.7	53.3	47.9	47.9	50.0

death, the method proposed by Rittgen and Becker was used.[45] Following this method, the 'corrected' number of deaths, O_C, corresponds to the ratio O/p, where O is the number of observed deaths from a known cause and p is the proportion of known causes among all causes. Similarly, a corrected SMR is computed as $SMR_C=SMR/p=Oc/E$. Corresponding corrected confidence limits are computed by taking the variance of p into account. SMRs are reported only for single causes of death or groups with three or more observed cases. The heterogeneity between countries was analysed by χ^2 tests.[46]

To investigate a potential effect of employment duration, SMRs stratified by employment duration were computed for single causes of death or groups with 100 or more observed cases in any of the three subcohorts of male cockpit crew and male or female cabin crew. As there is a high collinearity of employment duration with age and work-related exposures, this must be interpreted with caution and not simply as dose-response analysis. No trend analyses of mortality with increasing employment duration were done.

All analyses were performed using SAS V.9.3.[47]

RESULTS

The cohort consisted of 93 918 persons, 147 of whom were excluded from the analyses for one of the following reasons: missing birth date (1), missing date of vital status (1), death or emigration before the beginning of the study period (23), date of death before the beginning of employment (18), deceased more than a month before the end of recorded employment (16), beginning of employment at age 65 years or later (5), and end of employment at age 66 years or later (83).

The final analysis dataset included 36 816 male cockpit crew, 12 288 male, and 44 667 female cabin crew (table 1). The cohort was quite young: the mean age at the end of follow-up was 53.3 for male cockpit crew, 47.9 for male and 47.9 for female cabin crew. The mean (and median) duration of follow-up were 20.3 (17.3), 20.5 (19.7) and 23.1 (22.9) years, respectively. At the end of follow-up, most cohort members were alive, 80 290 (85.6%), 5508 (5.9%) were deceased, and 6390 (6.8%) had emigrated (table 2). Few were lost to follow-up (1.7%). Person-years tabulated by age and duration of employment are shown in online supplementary table S8.

In the male cockpit crew subcohort, most person-years of observation are contributed by individuals from the Nordic countries (37%), the UK (35%) and Germany (19%). In the male and female cabin crew subcohorts, most person-years are contributed by persons from the Nordic countries (31% and 36%), Germany (29% and 29%), and the USA (16% and 27%).

Male cockpit crew

Among male cockpit crew, a total of 2703 deaths was observed, including 135 (5.0%) from unknown causes (table 3).

The mortality from all causes (SMR=0.56, 95% CI 0.54 to 0.58), and all cancers (SMR=0.69, 95% CI 0.64 to 0.76) were significantly reduced compared to the general population. The mortality from 'radiation-related cancers' was also reduced (SMR=0.73, 95% CI 0.62 to 0.85); that due to non-CLL leukaemia was SMR=0.92 (95% CI 0.59 to 1.39).

The mortality from smoking-related cancers was low: it was significantly reduced for cancers of the buccal cavity and pharynx (SMR=0.27, 95% CI 0.16 to 0.44), as well as for lung cancer (SMR=0.43, 95% CI 0.36 to 0.52).

The mortality from malignant melanoma was significantly increased (SMR=1.57, 95% CI 1.06 to 2.25). Mortality from

Table 2 Results of mortality follow-up in the multinational cohort of commercial airline crew

	Cockpit crew	Cabin crew		
	Men	Men	Women	All
Total persons	36 816	12 288	44 667	93 771
Vital status				
Alive	31 383	9940	38 967	80 290
Dead	2703	1360	1445	5508
Emigrated	2157	762	3471	6390
Lost to follow-up	573	226	784	1583
Employment status				
Not employed*	4532	5618	21 241	31 391
Still active	6144	4030	11 615	21 789
Unknown	26 140	2640	11 811	40 591

*Retired or left the company (where applicable).

Table 3 Standardised mortality ratios for male cockpit crew in the multinational cohort of commercial airline crew

Cause of death	Observed cases	$Observed_C$	Expected cases	SMR_C	95% CI
All causes	2703	2703.00	4806.42	0.56	0.54 to 0.58
All known causes except aircraft accidents	2342	2465.12	4801.22	0.51	0.49 to 0.54
All cancers	933	982.05	1414.27	0.69	0.64 to 0.76
Radiation-related	234	246.30	337.24	0.73	0.62 to 0.85
Other	699	735.75	1076.95	0.68	0.62 to 0.75
Cancer subtypes					
Buccal cavity/pharynx	22	23.16	85.27	0.27	0.16 to 0.44
Oesophagus	28	29.47	58.55	0.50	0.31 to 0.77
Stomach	45	47.37	83.10	0.57	0.39 to 0.80
Large intestine	85	89.47	97.66	0.92	0.70 to 1.18
Rectum	39	41.05	49.55	0.83	0.55 to 1.19
Bilary tree/liver	41	43.16	45.10	0.96	0.65 to 1.36
Pancreas	57	60.00	71.55	0.84	0.60 to 1.14
Larynx	12	12.63	18.41	0.69	0.32 to 1.29
Bronchial tree and lung	161	169.46	390.40	0.43	0.36 to 0.52
Bone	2	2.11	4.94		
Malignant melanoma	40	42.10	26.75	1.57	1.06 to 2.25
Other skin	3	3.16	3.40	0.93	0.15 to 3.04
Breast	0	0.00	1.60		
Prostate	114	119.99	97.62	1.23	0.98 to 1.53
Testis/other male genital organ	4	4.21	8.29	0.51	0.11 to 1.45
Kidney	28	29.47	38.25	0.77	0.48 to 1.18
Bladder/other urinary tract	33	34.73	47.19	0.74	0.47 to 1.09
Eye	3	3.16	1.38	2.28	0.36 to 7.48
CNS (includes brain)	59	62.10	54.50	1.14	0.83 to 1.54
Thyroid gland/other endocrine	5	5.26	4.99	1.06	0.28 to 2.72
All lymphoma	33	34.73	52.71	0.66	0.43 to 0.98
Non-Hodgkin lymphoma	28	29.47	44.82	0.66	0.41 to 1.01
Hodgkin lymphoma	5	5.26	7.89	0.67	0.18 to 1.72
All leukaemia*	38	40.00	44.15	0.91	0.60 to 1.31
Leukaemia CLL	6	6.32	8.85	0.71	0.22 to 1.71
Leukaemia non-CLL	31	32.63	35.30	0.92	0.59 to 1.39
Kaposi sarcoma	0	0.00	0.09		
All other cancer	81	85.26	128.82	0.66	0.50 to 0.86
Benign neoplasms	11	11.58	25.85	0.45	0.20 to 0.87
Non-cancer causes					
Diabetes	22	23.16	71.52	0.32	0.19 to 0.52
Cerebrovascular disease	132	138.94	275.99	0.50	0.41 to 0.62
All cardiovascular disease	530	557.86	1343.66	0.42	0.37 to 0.46
Rheumatic heart disease	3	3.16	29.26	0.11	0.02 to 0.35
Other ischaemic heart disease	139	146.31	405.98	0.36	0.29 to 0.44
Acute myocardial infarction	270	284.19	638.56	0.45	0.38 to 0.52
Hypertension	15	15.79	37.95	0.42	0.21 to 0.74
All other cardiovascular disease	103	108.41	231.91	0.47	0.37 to 0.59
Non-malignant respiratory disease	58	61.05	208.23	0.29	0.21 to 0.40
Ulcer of stomach+duodenum	12	12.63	26.30	0.48	0.22 to 0.91
Liver cirrhosis	54	56.84	150.60	0.38	0.27 to 0.52
Nephritis and nephrosis	1	1.05	13.99		
Influenza and pneumonia	23	24.21	97.23	0.25	0.15 to 0.40
All other infectious diseases (except AIDS)	18	18.95	45.32	0.42	0.23 to 0.71
AIDS	5	5.26	11.93	0.44	0.12 to 1.14
Aircraft accidents	226	237.88	5.20	45.74	38.83 to 53.62
All external except aircraft	289	304.19	488.11	0.62	0.54 to 0.72
Motor vehicle accidents	71	74.73	102.29	0.73	0.55 to 0.96
Suicides	114	119.99	186.12	0.64	0.51 to 0.80
Homicides, except unclear accidents	2	2.11	16.63		
Unclear accidental deaths	6	6.32	14.20	0.44	0.14 to 1.06
All other external causes	96	101.05	168.86	0.60	0.47 to 0.76

Continued

Table 3 Continued

Cause of death	Observed cases	$Observed_C$	Expected cases	SMR_C	95% CI
Ill-defined cause of death	51	53.68	109.38	0.49	0.35 to 0.68
All other causes	203	213.67	518.85	0.41	0.35 to 0.49
Unknown cause	135				

*Including one case that could neither be classified as CLL or non-CLL.
CLL, chronic lymphocytic leukaemia; CNS, central nervous system; $Observed_C$, numbers of death corrected for missing causes using the method proposed by Rittgen and Becker (see Methods); SMR_C, standardised mortality ratio, using numbers of death corrected for missing causes.

prostate cancer was elevated (SMR=1.23, 95% CI 0.98 to 1.53), albeit not significantly. The mortality rates for cancers of the brain and CNS (SMR=1.14, 95% CI 0.83 to 1.54), and thyroid/other endocrine glands (SMR=1.06, 95% CI 0.28 to 2.72) did not differ from those of the general population.

The mortality from most non-cancer causes was markedly lower than in the reference population; the observed number of cardiovascular deaths, in particular, was less than half the expected (SMR=0.42; 95% CI 0.37 to 0.46). Aircraft accidents accounted for 8.4% of all recorded deaths among cockpit crew (SMR=45.74; 95% CI 38.83 to 53.62), while mortality from other external causes, including accidents, was significantly decreased (SMR=0.62; 95% CI 0.54 to 0.72). In contrast with cabin crew (see below), the mortality due to suicide was significantly reduced in cockpit crew, with an SMR of 0.64 (95% CI 0.51 to 0.80).

In the analyses of mortality by employment duration, cockpit crew who had worked less than 10 years had the highest SMR for aircraft accidents, while the SMRs for other causes did not show strong variations according to employment duration (see online supplementary table S9).

Male cabin crew

In male cabin crew, a total of 1360 deaths were observed, including 85 (6.3%) from unknown causes (table 4).

In contrast with cockpit crew, mortality rates from all causes (SMR=1.07, 95% CI 1.02 to 1.13) were significantly higher than those of the reference population. Many (n=216, 15.9%) died of AIDS. The mortality from all cancers (SMR=0.97, 95% CI 0.84 to 1.13) and ‘radiation-related cancers’ (SMR=1.00, 95% CI 0.74 to 1.33) did not differ from those of the reference population. The mortality from malignant melanoma was non-significantly elevated (SMR=1.20, 95% CI 0.45 to 2.59), while the mortality from prostate cancer was below its expectation (SMR=0.75, 95% CI 0.40 to 1.29).

As in cockpit crew, the mortality from cancers of the brain and CNS (SMR=1.25, 95% CI 0.64 to 2.18), and that due to non-CLL leukaemia (SMR=1.33, 95% CI 0.63 to 2.47), did not differ significantly from that of the general population.

On the contrary, the mortality from AIDS (SMR=16.47, 95% CI 13.86 to 19.51), infectious diseases except AIDS (SMR=3.69, 95% CI 2.55 to 5.18), non-melanoma skin cancer (SMR=8.01, 95% CI 2.98 to 17.33), and non-Hodgkin lymphoma (SMR=2.37, 95% CI 1.41 to 3.73) was significantly elevated.

The mortality from ‘alcohol-related’ cancers (47 cases in total) was elevated, but not significantly different from that of the general population.

The SMRs from most non-cancer causes, other than those mentioned above and aircraft accidents, were below 1.

Female cabin crew

In female cabin crew, 1445 deaths were observed, including 91 (6.3%) from unknown causes (table 5).

The mortality from all causes (SMR=0.73, 95% CI 0.69 to 0.77) and all cancers (SMR=0.85, 95% CI 0.77 to 0.95) was significantly reduced. However, as in male cabin crew, the mortality from ‘radiation-related-cancer’ was close to its expectation (SMR=1.01, 95% CI 0.88 to 1.15). In contrast to male cabin crew, the mortality from alcohol-related cancers was reduced (SMR=0.68, 95% CI 0.46 to 0.98).

The mortality from breast cancer (SMR=1.06, 95% CI 0.89 to 1.27), malignant melanoma (SMR=1.17, 95% CI 0.64 to 1.97), and cancer of the thyroid/other endocrine glands (n=6, SMR=1.53, 95% CI 0.47 to 3.69) did not differ from that of the reference population.

The SMRs for most non-cancer causes, except aircraft accidents, were below 1. The SMR for suicide was 1.23 (95% CI 0.96 to 1.55).

No difference in mortality rates between strata with different duration of employment was noted (see online supplementary table S10).

DISCUSSION

This study of nearly 94 000 commercial airline crew members followed for an average of 21.7 years, including cohorts from nine European countries and the USA, is the largest study of this occupational group to date. Compared to previous pooled analyses of European aircrew and the analysis of the US cohort taken together, 28.8% more cases (20.5%, 27.9% and 48.8% more cases among male cockpit and male and female cabin crews, respectively), corresponding to 68.8% more person-years, were included.[19 20 38]

In male cockpit and female cabin crews, a markedly reduced overall cardiovascular mortality and decreased cancer mortality were observed, consistent with other aircrew cohorts not included here.[10–13 48 49] Similar patterns are often observed in occupational cohorts. The overall mortality does not appear to increase with increasing duration of employment in this cohort. The high social status and strict health requirements may concur to explain the low overall mortality among cockpit crew. The low mortality from smoking-related cancers, especially in cockpit crew, indicates that smoking was probably less common in aircrew members than in the general population.

When comparing results of the current study with those of previous pooled analyses, including the analyses of cancer incidence in Nordic countries, it is important to keep in mind that these cohorts are part of the current analyses.[17 18] Consistent results are hence to be expected.

The mortality experience of the US and European cohorts is very similar in general, with significant differences in SMR for all causes in female cabin crew (US SMR: 0.59, current pooled SMR: 0.73), all cancer in female cabin crew (US SMR: 0.85, current pooled SMR: 0.71).[38]

Compared to previous analyses of European crew only, the all-cause mortality of male pilots is significantly lower than in

Table 4 Standardised mortality ratios for male cabin crew in a multinational cohort study of commercial airline crew

Cause of death	Observed cases	Observed$_C$	Expected cases	SMR$_C$	95% CI
All causes	1360	1360	1266.97	1.07	1.02 to 1.13
All known causes except aircraft accidents	1254	1337.60	1265.05	1.06	0.98 to 1.15
All cancers	306	326.40	334.93	0.97	0.84 to 1.13
Radiation-related	71	75.73	75.45	1.00	0.74 to 1.33
Other	235	250.67	259.46	0.97	0.82 to 1.14
Cancer subtypes					
Buccal cavity/pharynx	18	19.20	11.96	1.61	0.87 to 2.73
Oesophagus	14	14.93	10.54	1.42	0.70 to 2.57
Stomach	8	8.53	17.01	0.50	0.19 to 1.09
Large intestine	22	23.47	23.88	0.98	0.57 to 1.59
Rectum	8	8.53	11.02	0.77	0.29 to 1.68
Biliary tree/liver	13	13.87	12.08	1.15	0.55 to 2.13
Pancreas	12	12.8	17.37	0.74	0.34 to 1.40
Larynx	2	2.13	5.04		
Bronchial tree and lung	73	77.87	96.49	0.81	0.60 to 1.06
Bone	0	0	1.50		
Malignant melanoma	8	8.53	7.14	1.20	0.45 to 2.59
Other skin	8	8.53	1.07	8.01	2.98 to 17.33
Breast	1	1.07	0.40		
Cervix uteri					
All other uterine					
Ovary					
Prostate	17	18.13	24.18	0.75	0.40 to 1.29
Testis/other male genital organ	4	4.27	2.82	1.51	0.33 to 4.34
Kidney	6	6.40	9.93	0.64	0.20 to 1.55
Bladder/other urinary tract	11	11.73	9.63	1.22	0.54 to 2.37
Eye	0	0	0.31		
CNS (includes brain)	16	17.07	13.69	1.25	0.64 to 2.18
Thyroid gland/other endocrine	0	0	1.36		
All lymphoma	27	28.80	14.12	2.04	1.24 to 3.17
Non- Hodgkin lymphoma	25	26.67	11.26	2.37	1.41 to 3.73
Hodgkin lymphoma	2	2.13	2.86		
All leukaemia*	15	16.00	12.62	1.27	0.64 to 2.26
Leukaemia CLL	1	1.07	2.22		
Leukaemia non-CLL	13	13.87	10.40	1.33	0.63 to 2.47
Kaposi sarcoma	0	0	0.01		
All other cancer	23	24.53	30.74	0.80	0.47 to 1.28
Benign neoplasms	3	3.20	6.42	0.50	0.08 to 1.65
Non-cancer causes					
Diabetes	5	5.33	22.13	0.24	0.06 to 0.63
Cerebrovascular disease	45	48.00	62.06	0.77	0.53 to 1.09
All cardiovascular disease	221	235.73	329.54	0.72	0.60 to 0.85
Rheumatic heart disease	2	2.13	3.81		
Other ischaemic heart disease	76	81.07	94.49	0.86	0.64 to 1.13
Acute myocardial infarction	82	87.47	149.62	0.58	0.44 to 0.76
Hypertension	11	11.73	11.45	1.03	0.45 to 2.00
All other cardiovascular disease	50	53.33	70.17	0.76	0.53 to 1.06
Non-malignant respiratory disease	35	37.33	48.33	0.77	0.50 to 1.14
Ulcer of stomach+duodenum	4	4.27	5.31	0.80	0.17 to 2.31
Liver cirrhosis	42	44.80	46.50	0.96	0.65 to 1.38
Nephritis and nephrosis	5	5.33	4.81	1.11	0.30 to 2.88
Influenza and pneumonia	16	17.07	19.71	0.87	0.45 to 1.52
All other infectious diseases (except AIDS)	47	50.13	13.58	3.69	2.55 to 5.18
AIDS	216	230. 40	13.99	16.47	13.86 to 19.51
Aircraft accidents	21	22.40	1.92	11.66	6.62 to 19.11
All external except aircraft	155	165.33	186.02	0.89	0.73 to 1.08
Motor vehicle accidents	37	39.47	50.65	0.78	0.51 to 1.14
Suicides	65	69.33	60.03	1.16	0.85 to 1.55
Homicides, except unclear accidents	5	5.33	12.31	0.43	0.12 to 1.13

Continued

Table 4 Continued

Cause of death	Observed cases	Observed$_C$	Expected cases	SMR$_C$	95% CI
Unclear accidental deaths	1	1.07	5.86		
All other external causes	47	50.13	57.41	0.87	0.60 to 1.23
Ill-defined cause of death	24	25.60	34.66	0.74	0.44 to 1.18
All other causes	130	138.67	137.06	1.01	0.81 to 1.25
Unknown cause	85				

*Including one male case that could not be classified as CLL or non-CLL.
CLL, chronic lymphocytic leukaemia; CNS, central nervous system; Observed$_C$, numbers of death corrected for missing causes using the method proposed by Rittgen and Becker (see Methods); SMR$_C$, standardised mortality ratio, using numbers of death corrected for missing causes.

Table 5 Standardised mortality ratios for female cabin crew in a multinational cohort study of commercial airline crew

Cause of death	Observed cases	Observed$_C$	Expected cases	SMR$_C$	95% CI
All causes	1445	1445.00	1988.70	0.73	0.69 to 0.77
All known causes except aircraft accidents	1319	1407.65	1987.05	0.71	0.66 to 0.77
All cancers	653	696.89	816.34	0.85	0.77 to 0.95
Radiation-related	353	376.72	374.45	1.01	0.88 to 1.15
Other	300	320.16	441.86	0.72	0.63 to 0.84
Cancer subtypes					
Buccal cavity/pharynx	7	7.47	9.13	0.82	0.28 to 1.86
Oesophagus	6	6.40	6.87	0.93	0.29 to 2.25
Stomach	23	24.55	23.44	1.05	0.61 to 1.68
Large intestine	40	42.69	50.47	0.85	0.57 to 1.22
Rectum	15	16.01	17.98	0.89	0.45 to 1.59
Biliary tree/liver	9	9.60	18.90	0.51	0.20 to 1.06
Pancreas	33	35.22	33.87	1.04	0.67 to 1.55
Larynx	1	1.07	2.05		
Bronchial tree and lung	89	94.98	145.28	0.65	0.50 to 0.84
Bone	3	3.20	2.52	1.27	0.20 to 4.20
Malignant melanoma	19	20.28	17.30	1.17	0.64 to 1.97
Other skin	1	1.07	1.17		
Breast	196	209.17	196.93	1.06	0.89 to 1.27
Cervix uteri	15	16.01	33.72	0.47	0.24 to 0.85
All other uterine	11	11.74	17.91	0.66	0.29 to 1.28
Ovary	52	55.49	58.98	0.94	0.66 to 1.30
Prostate					
Testis/other male genital organ					
Kidney	7	7.47	13.67	0.55	0.19 to 1.24
Bladder/other urinary tract	5	5.34	7.31	0.73	0.19 to 1.90
Eye	0	0.00	0.75		
CNS (includes brain)	29	30.95	32.41	0.95	0.59 to 1.46
Thyroid gland/other endocrine	6	6.40	4.18	1.53	0.47 to 3.69
All lymphoma	19	20.28	27.29	0.74	0.41 to 1.25
Non-Hodgkin lymphoma	13	13.87	21.80	0.64	0.30 to 1.18
Hodgkin lymphoma	6	6.40	5.49	1.17	0.36 to 2.81
All leukaemia	25	26.68	26.28	1.02	0.61 to 1.60
Leukemia CLL	1	1.07	2.36		
Leukaemia non-CLL	24	25.61	23.91	1.07	0.63 to 1.70
Kaposi sarcoma	0	0.00	0.03		
All other cancer	42	44.82	67.92	0.66	0.45 to 0.94
Benign neoplasms	8	8.54	13.18	0.65	0.24 to 1.40
Non-cancer causes					
Diabetes	8	8.54	41.16	0.21	0.08 to 0.45
Cerebrovascular disease	45	48.02	101.17	0.47	0.33 to 0.67
All cardiovascular disease	94	100.32	269.22	0.37	0.29 to 0.48
Rheumatic heart disease	2	2.13	6.95		
Other ischaemic heart disease	18	19.21	64.77	0.30	0.16 to 0.50

Continued

Table 5 Continued

Cause of death	Observed cases	$Observed_C$	Expected cases	SMR_C	95% CI
Acute myocardial infarction	24	25.61	94.30	0.27	0.16 to 0.43
Hypertension	6	6.40	16.87	0.38	0.12 to 0.91
All other cardiovascular disease	44	46.96	86.33	0.54	0.37 to 0.77
Non-malignant respiratory disease	32	34.15	77.85	0.44	0.28 to 0.66
Ulcer of stomach+duodenum	2	2.13	6.17		
Liver cirrhosis	58	61.90	60.72	1.02	0.73 to 1.39
Nephritis and nephrosis	2	2.13	6.03		
Influenza and pneumonia	5	5.34	24.71	0.22	0.06 to 0.56
All other infectious diseases (except AIDS)	12	12.81	26.75	0.48	0.22 to 0.91
AIDS	6	6.40	9.89	0.65	0.20 to 1.56
Aircraft accidents	35	37.35	1.65	22.60	14.70 to 33.34
All external except aircraft	227	242.26	243.03	1.00	0.84 to 1.18
Motor vehicle accidents	43	45.89	61.58	0.75	0.51 to 1.06
Suicides	103	109.92	89.63	1.23	0.96 to 1.55
Homicides, except unclear accidents	10	10.67	21.42	0.50	0.21 to 1.00
Unclear accidental deaths	6	6.40	10.43	0.61	0.19 to 1.48
All other external causes	65	69.37	60.72	1.14	0.84 to 1.53
Ill-defined cause of death	42	44.82	45.44	0.99	0.67 to 1.41
All other causes	125	133.40	245.39	0.54	0.43 to 0.67
Unknown cause	91				

CLL, chronic lymphocytic leukaemia; CNS, central nervous system; $Observed_C$, numbers of death corrected for missing causes using the method proposed by Rittgen and Becker (see Methods); SMR_C, standardized mortality ratio, using numbers of death corrected for missing causes.

previous analyses (previous SMR: 0.64, current pooled SMR: 0.54), and much lower for cancer of the buccal cavity and pharynx, lungs, cardiovascular diseases and liver cirrhosis.[19] The all-cause mortality of female cabin crew is lower than previously observed (previous SMR: 0.80, current pooled SMR: 0.73).[20]

Heterogeneity is most present in those causes of death for which confounding factors may play a major role, such as lung cancer, buccal cancer, liver cirrhosis, or causes for which national mortality rates differ substantially, such as suicide rates. No obvious pattern of higher or lower SMRs per cause emerges, as was exemplified by Zeeb *et al*.[20]

Mortality from non-cancer causes

The low mortality from cardiovascular causes and most other non-cancer causes in respect to the general population persists in the current prolonged follow-up.

Mortality from aircraft accidents is elevated in all subcohorts, and particularly high in cockpit crew where it accounts for 44% of all deaths from external causes. Young pilots seem to have the highest risk. While occupational and private accidents could not be differentiated here, a study of Norwegian pilots suggested that a large proportion of these deaths are related to leisure-time flying.[50]

An elevated mortality of male cabin crew from AIDS and related causes was already observed in previous analyses.

Self-perceived mental health in female aircrew was investigated earlier, and the authors found that several work-related factors, possibly implying anxiety or depressed mood, were of concern.[51–54] In the current analyses, suicide rates in cabin crew were higher than in the general population, but significantly lower in cockpit crew.

Skin melanoma

An elevated incidence of, and mortality from, malignant melanoma has been reported by previous studies, including studies not included in the current analyses.[12 15 55] An excess mortality was observed here for cockpit crew. The major risk factors for malignant melanoma of the skin include host factors related to skin colour and nevi, sunburn at an early age, and intermittent sun exposure, with exposure to solar UV radiation representing an overwhelming etiologic fraction in the general population.[24 56] As aircraft windows provide effective shielding against such radiation, occupational exposures on board are unlikely.[57] UV exposures among airlines crew may be recreational or occur during stopovers. Among Nordic cabin crew, a non-significant elevated incidence of skin melanoma of the trunk was observed 20 years after first employment, and a positive dose-response relationship was observed between estimated radiation exposure and melanoma incidence in Nordic pilots.[17 18] The authors concluded that the excess incidence may be attributed to UV radiation.[17] In a recent study comparing UK flight crew and air traffic controllers, no differences in skin melanoma rates were observed. The strongest risk predictors of skin melanoma in both occupations were light skin and sunbathing.[58] The similar site-specific cancer risks between the two occupational groups suggest that risks are not directly related to occupational exposures.

Leukaemia

Ionising radiation is a well-established risk factor for non-CLL leukaemia.[59] Assuming a strength of association similar to that reported elsewhere, the expected SMR would not exceed 1.08.[18 59 60] The SMRs for cockpit crew, male and female cabin crews, were inconclusive due to a relatively small number of cases.

Cancers of the brain and CNS

In a recent analysis of the German aircrew cohort (that contributes 14 of the 51 CNS cancer deaths in cockpit crew in the present study), a statistically significant increased mortality from CNS cancers was observed (SMR=2.13), while no increase in incidence was found in Nordic pilots or in male or female cabin crew of Nordic countries.[17 18 25] In the current analyses, the

SMR for brain cancers was not significantly different from the general population in any of the subcohorts.

Breast cancer

Breast cancer is one of the cancers most consistently increased in female cabin crew when incidence is considered. No elevation was found in the present study with focus on mortality. Note that for breast cancer, the mortality estimate is a weak measure and affected by the good survival.[20 61 62]

A statistically significantly elevated incidence of breast cancer was observed in Nordic crew (standardised incidence ratio (SIR) =1.50), with an increased SIR at 20 years since first employment compared to shorter latency periods.[18] However, in a nested case-control analysis within that cohort with adjustment for parity and age at first childbirth, an OR of 0.98 per 10 mSv cumulative effective dose was observed. No known risk factors seemed to explain the excess in breast cancer, though residual confounding remains an issue. The authors also considered screening bias unlikely.

Health effects of circadian rhythm disruptions are currently investigated by several research groups, many of which focus on breast cancer as a health outcome.[63 64] In a recent monograph, the International Agency for Research on Cancer (IARC) classified shift-work involving circadian rhythm disruption as probably carcinogenic to humans (Group 2A).[2] Human data supporting this classification are strongest for breast cancer.[54 63–65] While there are plausible biological mechanisms for cancer development, notably the involvement of the melatonin pathway, the issue is still unresolved.

Prostate cancer

An increased mortality from cancers of the prostate was observed in cockpit crew (SMR=1.23), but not in cabin crew. In previous pooled mortality analyses, no increases were observed.[19] In the Nordic studies, prostate cancer incidence was non-significantly raised in cockpit crew (SIR=1.21), with a significant trend of increasing risk with increasing cumulative effective dose in pilots below age 60 years (but not beyond this age).[18 29]

Methodological issues

This study reports on mortality, an outcome affected by disease incidence, screening activities and treatment. For cancer, studies of disease incidence provide a better picture of risks, but such data were available only in Nordic countries.

Details of flight history (flight hours per aircraft type per year) were available for certain subcohorts only, and usually only for cockpit crew. These data were therefore not used here.

The list of cancers considered being radiation-related, and the lack of distinction between cancers with much, fair, little or no evidence for causation may be criticised. Several additional cancers were included in a list developed as part of the IARC re-evaluation of ionising radiation as a group 1 carcinogen: cancers of the salivary glands, bone, skin (basal cell carcinoma), brain and CNS, thyroid and kidney.[66] As a sensitivity analysis, SMRs were computed for this extended definition. All SMRs were qualitatively unchanged.

Aircrew are exposed to a number of potential risk factors for cancer, such as ionising radiation, circadian rhythm disruptions (jet lag), pesticides, jet fuel, electromagnetic fields, and other exposures, such as leisure-time UV radiation, nutritional factors and stress. Such factors were not assessed in the current study. A good correlation between employment duration and occupational exposure to ionising radiation of aircrew was shown in Germany, although employment duration and ionising radiation exposure have not been as well correlated in US pilots.[8 9]

Finally, despite the large number of subjects, the cohort is still relatively young; only 5.9% of cohort members died during the observation period, resulting in small numbers of deaths and large risk uncertainty for many cancers. The overall mortality in male cockpit and female cabin crew is strongly reduced; the mortality from cancer was reduced with few exceptions, notably malignant skin melanoma in cockpit crew. Further analysis after a longer follow-up is recommended.

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