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Incidence of Cancer Among Female Flight Attendants: A Meta-Analysis

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Background. Airline flight personnel work in a unique environment with exposure to known or suspected carcinogens and mutagens including ionizing cosmic radiation. A meta-analysis was conducted to study whether the occupational exposure of female flight attendants (FA) increased their relative risk of cancer incidence.

Methods. A bibliographical computer search from 1966 to 2005 of cancer incidence cohort studies of female FA was performed. Combined relative risks (RRc) in cancer incidence were calculated by means of meta-analysis.

Results. RRc and 95% confidence interval (CI) for malignant melanoma and breast cancer in female FA were 2.13 (95% CI: 1.58–2.88) and 1.41 (1.22–1.62) ($p < 0.0001$). Excess risk was not significant for all-site cancer with RRc of 1.10 (0.99–1.21).

Conclusions. The meta-analysis confirmed the significantly increased risks for malignant melanoma and breast cancer in female FA. Increased exposure to cosmic radiation during flight has been suggested as a potential occupational risk factor. Ultraviolet radiation exposure on board seems an unlikely occupational risk, but nonoccupational leisure time sun exposure is a possible risk factor. The etiology of the observed increase in incidence of some cancers remains controversial because assessment of possible confounders, especially nonoccupational exposure factors, has thus far been limited.

Flight personnel work in a unique environment with exposure to known or suspected carcinogens and mutagens such as ionizing radiation, ozone, jet engine emissions, electromagnetic

fields, and cigarette smoke.¹ There is an increased risk of exposure to low-dose cosmic radiation among crew of commercial airlines who fly high-altitude, long-haul flights, especially those with flight paths over or close to the poles. These radiation levels are higher than those found at ground level.^{2,3} Health concerns have been increasing among flight crew.⁴

A large cohort study of flight personnel was recently conducted by a group of European epidemiologists. In their series of papers, they reported cancer mortality for male pilots⁵ and female flight attendants (FA),⁶ as well as cancer incidence in male pilots.⁷ Overall mortality and all-cancer mortality

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were significantly reduced for both male cockpit crew [standardized mortality ratio (SMR) of all-cancer mortality 0.68 (95% CI: 0.63–0.74)]⁵ and female FA [0.78 (0.66–0.95)].⁶ However, SMR from malignant melanoma was significantly increased for male cockpit crew [1.78 (1.15–2.67)].⁵ Although it did not reach statistical significance, the SMR from breast cancer was increased for female FA as well [1.11 (0.82–1.48)].⁶ In male airline pilots, a significant increase in the incidence of skin cancer was also observed.⁷ The study did not report the cancer incidences in female FA.

Ballard and colleagues conducted a meta-analysis of cancer incidence among female FA and reported increased incidences of all cancers, melanoma, and breast cancer.² But since their results were based on only two studies,² the power of their analysis was low. Recently, several papers were published regarding cancer incidence among female FA.^{8–14} Although many of them indicated increased risk for melanoma and breast cancer among female FA, those results were still based on relatively small populations. Thus, the current knowledge still relies on several studies with relatively small populations.

The current study asked whether the occupational exposures of female FA increased their relative risk of cancer incidence. The present study was intended: (1) to update a list of available studies of cancer incidence in female FA, (2) to combine the relative risk estimates of each study by means of meta-analysis, and (3) to discuss the possible etiology for any observed excess risks.

Methods

A computerized literature search from MEDLINE database and ALL EBM Reviews database, including Cochrane Database of Systematic Reviews (CDSR), American College of Physicians (ACP) Journal Club, Database of Abstracts of Reviews of Effectiveness (DARE) was conducted for published studies between 1966 and 2005 (as of September 30, 2005) via the keywords “flight attendant,” “cabin attendant,” “aviator,” “aviation,” “flight,” “cancer,” and “cancer incidence.” A manual review of bibliographies in pertinent articles was also used.

Criterion for selection of published studies for meta-analysis was the ability to extract standardized incidence ratio (SIR) with standard errors or confidence intervals (CI). Only cohort studies of cancer incidence in female commercial airline FA, which compared each incidence with that of a national or state reference population data (ie, SIR), were included. Since the case-control method

estimates relative risks, it was excluded from the present analysis.

The quality of the trials is of obvious relevance to meta-analysis. The critical appraisal of the study is widely recommended.¹⁵ But no standard quality-rating scale is available for a cohort study of an occupational exposure. Thus, the authors used an *a priori* 5-item rating instrument for the quality rating: whether the study contained adequate description of (1) the cohort population, (2) the reference population, (3) extractable SIR and CI, (4) the number of patients and person years at risk, and (5) withdrawal and dropouts. Each item was rated 1 or 0 scale, and the sum of the scores (0–5 points) was regarded as the index of the quality.

The selected studies were then combined by means of meta-analysis in order to integrate the findings and to strengthen the evidence of the risk estimates.¹⁶ If a cancer site was reported in at least three published studies, had an excess risk in at least one study, and had at least five cases in total among eligible studies, its SIRs were combined. The authors used a fixed effects model with inverse variance weighting of the log risk ratios to calculate combined relative risks (RRc).^{17,18} Heterogeneity among the studies was evaluated by the DerSimonian and Laird's Q test.¹⁶ DerSimonian and Laird's Q test is one of the most popular heterogeneity test used in meta-analysis. The test statistic Q consists of a weighted sum of squared deviations around the mean of the effect in each study, and, under the null hypothesis, Q has a chi-square distribution. If the heterogeneity was significant (defined as having a *p* value less than or equal to 0.05), a random effects analysis method was employed.^{16,18} No adjustment for socioeconomic status (SES) was made in the present study (see Discussion).

The authors calculated the attributable risk in cancer incidence for female FA, ie, the proportion of exposed cases for whom the disease was attributable to their occupation as FA.

Results

A MEDLINE search identified six cohort studies of cancer incidence in civilian airline FA^{8–13} and a case-control study of cancer incidence in FA.¹⁴ No study was identified from ALL EBM Reviews. A manual review of bibliographies in pertinent articles added an unpublished cohort study by Wartenberg and colleagues, which was cited in a meta-analysis.²

Table 1 lists the eight identified studies of cancer incidence in female FA and describes the study outcome, study period, reference population, quality

Table 1 Studies on cancer incidence among airline FA

Study author	Study description	Number observed	Person years at risk	Quality rating	Inclusion in analysis
Pukkala et al ⁸	Standardized cancer incidence ratio; FA of Finnish airline companies, Finland, 1967–1992; reference population: whole Finnish population	Female: 1,577; male: 187	Female: 21,974; male: 1,577	5	Yes; no
Lynge ⁹	Standardized cancer incidence ratio; Danish female airline FA registered in the 1970 census, Denmark; reference population: general Danish population	Female: 915	Unreported	2	No
Wartenberg et al., 1998 (in Ballard et al) ²	Standardized cancer incidence ratios; US retired female FA of an airline company; reference population: Surveillance Epidemiology and End Results program of National Cancer Institutes (USA)	Female: 287	Unreported	2	No
Haldorsen et al ¹⁰	Standardized cancer incidence ratio; licensed FA in Norway, 1953–1996; reference population: Norwegian national rates	Female: 3,105; male: 588	Female: 60,401; male: 12,402	5	Yes; no
Rafnsson et al ¹¹	Standardized cancer incidence rates; FA from the Iceland Cabin Crew Association, Iceland, 1955–1997; reference population: population in Iceland	Female: 1,532; male: 158	Female: 27,148; male: 1,114.5	4	Yes; no
Reynolds et al ¹²	Standardized cancer incidence ratios; members of Association of Flight Attendants with California residence, USA, 1988–1995; reference population: California population (non-Hispanic whites, all races combined)	Female: 6,895; male: 1,216	Unreported	4	Yes; no
Linnarsjö et al ¹³	Standardized cancer incidence ratio; FA of Swedish Scandinavian Airline System, Sweden, 1957–1994; reference population: general Swedish population	Female: 2,324; male: 632	Female: 39,135; male: 12,774	5	Yes; no
Rafnsson et al ¹⁴	Case-control study; female member of the union of Icelandic cabin crew, followed up to 2000	Female: 1532		N/A	No
Total included in the meta-analysis		15,433	>148,658		5 studies

FA = flight attendants; N/A = not applicable.

rating, and a decision for inclusion in or exclusion from the meta-analysis. Of these, a case-control study¹⁴ was excluded from the analysis because case control studies do not report SIRs.

Quality of the following two studies was rated relatively poor (scoring 2), and thus they were excluded from the analysis. The study by Lynge⁹ was excluded because it was based on occupational data from the census and provided no way to confirm how long those included had actually served as FA of commercial airlines. There was a possibility that the study population of Wartenberg and colleagues² might have overlapped with that of Reynolds and colleagues.¹² The authors chose to exclude the study by Wartenberg et al because of its lower quality rating and its smaller population size (that of Reynolds and colleagues was more than 20 times larger than that of Wartenberg and colleagues). In addition, their study was not published as an independent paper.

The study by Reynolds and colleagues¹² did not report person years at risk, and the study by

Rafnsson¹¹ did not describe withdrawal and drop-outs (both scoring four). But they were included in the analysis because they provided enough information to estimate the combined risks. In a study by Reynolds and colleagues,¹² SIRs were calculated based on two reference populations: non-Hispanic whites and all races combined. In order to be consistent with other studies, SIRs with reference to all races combined were included in the analysis.

Results from the remaining five cohort studies^{8,10–13} were combined to provide information for both all-site cancers and for 11 specific sites, including breast and malignant melanoma of the skin (Table 2). It was not possible to combine cancer incidence for some sites because of insufficient numbers of patients ($n < 5$) or studies ($n < 3$). Heterogeneity was not significant at any of the cancer sites analyzed. Thus, the results of the random effect model⁸ were not presented here, but they were used to confirm the results of the fixed effects model.

Table 2 RRC for selected cancer incidence (fixed effects model)

Cancer site	ICD-7 code	No. of studies	RRC	95% confidence interval	<i>p</i> Value	Attributable risk
All sites	140–207	5	1.10	0.99–1.21	0.07	0.09
Lung	162	4	0.99	0.53–1.86	0.98	–0.01
Melanoma	190	5	2.13	1.58–2.88	<0.0001	0.53
Breast	170	5	1.41	1.22–1.62	<0.0001	0.29
Cervix uteri	171	4	0.99	0.64–1.53	0.97	–0.01
Uterus	172	4	0.89	0.47–1.69	0.73	–0.12
Ovary	175	5	0.76	0.45–1.31	0.33	–0.32
Bladder	181	3	2.03	0.75–5.43	0.16	0.51
Brain	193	5	0.78	0.40–1.53	0.47	–0.28
Thyroid	194	4	0.94	0.50–1.76	0.84	–0.06
Non-Hodgkin lymphoma	200, 202	3	1.28	0.53–3.09	0.58	0.22
Leukemias	204–208	4	1.93	0.92–4.07	0.08	0.48

RRC in incidence of all-site cancer was slightly increased but not statistically significant [RRC of 1.10 (95% CI: 0.99–1.21) ($p = 0.07$)]. The risks of malignant melanoma and breast cancer were significantly increased with RRC of 2.13 (1.58–2.88) and 1.41 (1.22–1.62), respectively ($p < 0.0001$ for both). These findings suggest that 53% of malignant melanoma and 29% of breast cancer in these FA may be attributable to their occupation. RRs of leukemia was slightly, but not significantly, increased [RRC: 1.93 (0.92–4.07), $p = 0.08$]. Figure 1 shows RRs in incidence of all-site cancer, breast cancer, and melanoma reported in each study included and the calculated RRC by the present study.

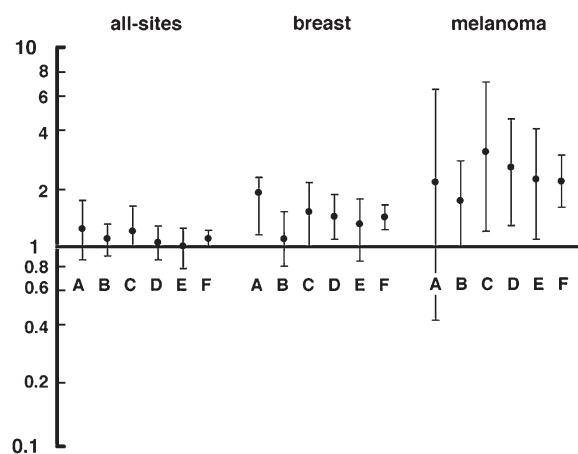


Figure 1 Relative risks in incidence of all-site cancer, breast cancer, and melanoma. Bars indicate 95% confidence intervals. (A) Pukkala et al⁸; (B) Haldorsen et al¹⁰; (C) Rafnsson et al¹¹; (D) Reynolds et al¹²; (E) Linnarsjö et al¹³; (F) the present study.

Conclusions

A meta-analysis of five cohort studies demonstrated significantly increased risks in the incidence of malignant melanoma and breast cancer in female FA. In a large cohort study of cancer incidence in male airline pilots, Pukkala and colleagues reported significantly increased RRs of malignant melanoma (RRC 2.29), squamous cell carcinoma, and basal cell carcinoma.⁷ In a previous meta-analysis by Ballard and colleagues, RRC of malignant melanoma and breast cancer was significantly increased (RRC 2.31 and 1.89, respectively) in female FA.² Heterogeneity of breast cancer was not significant ($p = 0.33$, DerSimonian-Laird's *Q* test) as seen in Figure 1. Heterogeneity of melanoma was not significant, either ($p = 0.80$), but the reported 95% CIs seemed wider than those for breast cancer (Figure 1). This might be because of a relatively small number of patients of melanoma (42 cases of melanoma vs 177 cases of breast cancer). A slight, nonsignificant increase in all-site cancer incidence was observed in the present study. This increase might reflect the significant increases in the incidence of malignant melanoma and breast cancer.

Recently, airline crew have raised concerns about their occupational exposure to suspected carcinogens, such as cosmic ionizing radiation, electromagnetic fields from cockpit instruments, ultraviolet (UV) radiation, ozone, passive smoking, pesticides, jet fuel, volatile substances from aircraft materials, and irregular work hours.^{1,2,19,20} Higher radiation dose rates were reported at higher altitude in the polar area, and cumulative doses have increased as longer flights at higher altitudes have become more frequent.⁴ Airline crew are occupationally exposed to ionizing radiation with doses of 2 to 6 mSv per

year.^{5,21} According to a model calculation, out of 1,000 cabin crew with 20 years of service each, 220 can be expected to die from a non-occupational related cancer, whereas three will die from cancer due to occupational exposure to cosmic radiation.³

Ionizing radiation could contribute to an excess risk of breast cancer in FA,²² but the association may be confounded by reproductive history or other lifestyle factors, such as smoking.⁶ A nested case-control study demonstrated an association between the length of employment and the risk of breast cancer in female FA when it was adjusted for reproductive factors, indicating the women's occupation as FA might be an important factor in the development of breast cancer.¹⁴ However, another study failed to show a similar association between length of employment or cumulative block hours and incidence of melanoma or breast cancer.¹³ The reproductive history of female FA could yield a 10% increase in breast cancer incidence compared with the general population.¹³ This could be an important contributing factor to the increased incidence of breast cancer but would not fully explain the excess risk estimated in the present meta-analysis.

The cause of the increased risk of malignant melanoma of the skin is unclear, and both occupational and nonoccupational causes are likely to be involved. The etiology of melanoma of the skin is multifaceted and complicated with various factors playing a role, including sun exposure, UV radiation exposure, host factors related to skin color, nevi, and genetic predisposition.²³ An association between ionizing radiation and malignant melanoma remains controversial.²⁴ Occupational UV exposure is unlikely to affect FA and pilots because of the effective shielding of aircraft windshield against UV.²⁵ Nonoccupational sun exposure (leisure time exposure) has been suggested as a possible factor,²⁶ but there is no information in the published studies on how often their subjects sunbathed, and thus the influence of recreational leisure time exposure to UV has thus far not been quantified.²¹

Cohort populations included in this study consisted mainly of whites. A previous mortality study reported no deaths from malignant melanoma of the skin among male cockpit crew of Japan Airlines.²⁷ This might indicate a racial factor as a potential confounder, although the small population size might confound the analysis.

RRc of leukemias was nonsignificantly increased among female FA. An association between low-dose exposure to ionizing radiation and the mortality from leukemia was observed in nuclear industry workers;²⁸ this is often considered to be analogous to cosmic radiation exposure among airline crew.

However, the nuclear industry workers studied were predominantly male and were most often exposed to low-dose gamma radiation.²⁹ By contrast, airline crew are exposed to neutrons, which contribute up to 60% of the equivalent dose of cosmic radiation at flight altitude of jet aircraft.³⁰ Thus, nuclear workers might not be an appropriate model for female FA.

SES might be a confounding factor, although no adjustments for it were made in the present study. It is well established that the incidence of some cancers varies with the population's SES. Malignant melanoma and breast cancer are listed among them, with higher SES subjects demonstrating higher incidences.^{31,32} In some studies, FA were classified within the highest class of SES. However, the authors of the present study dispute that categorization. While it is true that FA may have better access to medical service than the general population, there was not enough information available to decide to which socioeconomic class female FA should be classified. Although they are highly educated, their work might not be considered in the same category as other professions classified as Class I (lawyers, physicians, engineers) or II (registered nurses).³³ In addition, the cohort studies included in the present study showed a very high healthy worker effect,¹ which may have as much of an impact as SES level. In the present study, the lack of data prevented SES correction for the FA subjects. The contribution of SES on cancer incidence among airline crew should be investigated further.⁶

This study has several limitations. First, a meta-analysis should include all relevant studies to be complete. Reliance on computer searches and bibliographical review can result in failure to identify studies. Second, the study populations varied among the studies. Some studies analyzed employees of an airline, and others analyzed the members of a union. A study was conducted in the United States and others in Europe. Although the test for the heterogeneity was statistically negative, those potential variability should be noted. Third, there may be a publication bias. Unfortunately, the number of studies included in this study was too small for tests for publication bias such as Begg and Mazumdar.³⁴

In conclusion, significantly increased risks for malignant melanoma and breast cancer were demonstrated among female FA by means of meta-analysis. Although increased exposure to cosmic radiation during flight has been suggested as a potential risk factor, the etiology of the observed increase in incidence of malignant melanoma and breast cancer remains controversial because assessment of possible confounders, such as nonoccupational and socioeconomic factors, has thus far been limited.

Declaration of Interests

The authors state that they have no conflicts of interest.

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