Risk Factors for Skin Cancer among Finnish Airline Cabin Crew

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Increased incidence of skin cancers among airline cabin crew has been reported in several studies. We evaluated whether the difference in risk factor prevalence between Finnish airline cabin crew and the general population could explain the increased incidence of skin cancers among cabin crew, and the possible contribution of estimated occupational cosmic radiation exposure. A self-administered questionnaire survey on occupational, host, and ultraviolet radiation exposure factors was conducted among female cabin crew members and females presenting the general population. The impact of occupational cosmic radiation dose was estimated in a separate nested case-control analysis among the participating cabin crew (with 9 melanoma and 35 basal cell carcinoma cases). No considerable difference in the prevalence of risk factors of skin cancer was found between the cabin crew (N = 702) and the general population subjects (N = 1007) participating the study. The mean risk score based on all the conventional skin cancer risk factors was 1.43 for cabin crew and 1.44 for general population (P = 0.24). Among the cabin crew, the estimated cumulative cosmic radiation dose was not related to the increased skin cancer risk [adjusted odds ratio (OR) = 0.75, 95% confidence interval (CI): 0.57-1.00]. The highest plausible risk of skin cancer for estimated cosmic radiation dose was estimated as 9% per 10 mSy. The skin cancer cases had higher host characteristics scores than the noncases among cabin crew (adjusted OR = 1.43, 95% CI: 1.01–2.04). Our results indicate no difference between the female cabin crew and the general female population in the prevalence of factors generally associated with incidence of skin cancer. Exposure to cosmic radiation did not explain the excess of skin cancer among the studied cabin crew in this study.

Keywords: case-control studies; cosmic radiation; occupational exposure; skin neoplasms; ultraviolet rays

INTRODUCTION

Increased incidence of skin cancer among airline cabin crew has been reported in several studies. Excess of cutaneous malignant melanoma (CMM) was found in all published studies on skin cancer incidence (Pukkala *et al.*, 1995; Haldorsen *et al.*, 2001; Rafnsson *et al.*, 2001; Reynolds *et al.*, 2002; Linnersjö *et al.*, 2003). An increased incidence of squamous cell carcinoma (SCC) was observed in three studies (Haldorsen *et al.*, 2001; Rafnsson *et al.*, 2001; Linnersjö *et al.*, 2003). A meta-analysis suggested a metastandardized incidence ratio (SIR) = 2.15 [95% posterior interval (PI): 1.56–2.88] for CMM and meta-SIR = 1.91 (95% PI: 0.71–3.73) for SCC for female cabin crew (Buja *et al.*, 2006). Among the Finnish female cabin crew, SIR for CMM is 1.80

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[95% confidence interval (CI): 0.72–3.71], for SCC 2.65 (95% CI: 0.53–7.76), and for BCC 2.46 (95% CI: 1.76–3.35) (Pukkala *et al.*, 2012).

Exposure to ultraviolet radiation (UVR) is the most important risk factor for all types of skin cancers (Solar and Ultraviolet Radiation, 1992). The exposure pattern of risk however vary according to the skin cancer type. Epidemiological studies have shown that in most cases cumulative UVR exposure seems to be a risk factor for SCC, whereas intermittent exposure is related to higher risk of BCC and CMM (Karagas et al., 2006). Approximately 50-90% of the skin cancer incidence worldwide is estimated to be attributable to UVR exposure, depending on the skin cancer type (Lucas et al., 2006). Therefore, UVR exposure is a potential explanation for the increased skin cancer risk among cabin crew. The cabin crew is not exposed to UVR in the aircraft cabin but the crew may possibly spend more time at sun resorts due to their work than the general population, e.g. during stopovers between work shifts and free or discounted holiday flights. In an Norwegian study, an increasing trend in CMM incidence by duration of employment was observed (Haldorsen et al., 2001). This might indicate a relation between exposure to cosmic radiation and CMM. However, due to lack of studies with information on exposure to both cosmic radiation and UVR and strong collinearity of age and cumulative exposure, the issue has remained unsolved.

There is little information on aircrew exposure to UVR. One study has evaluated the UVR exposure of cabin crew compared to the general population (Rafnsson *et al.*, 2003). We conducted a comparative survey of risk factors for skin cancers among Finnish cabin crew and a random sample of the Finnish population. In order to assess the contribution of occupational exposure to cosmic radiation, we carried out a nested case–control study among the cabin crew.

METHODS

Study population and exposure information

The source population consisted of Finnish female cabin crew workers identified from the files of Finnair (Finnish airline company established in 1923) and the Finnish Cabin Crew Union. The subjects (N = 1342) had started their work in 1999 or before and were residents of Finland at the time of the survey (2004). However, women born in 1960 or later and still working in 2000 were

excluded because Finnair could not supply any updated information on its staff due to a recent restrictive privacy protection policy. In the source population, 7.2% of the women (N = 97) could not be contacted because of unknown current address. Thus, the final number of female cabin crew in the study was 1245. A random sample of females (N = 2000) was selected as a reference group from the Finnish Population Register Centre with similar age distribution. Of the reference group, one thousand subjects were selected from the Uusimaa district (including the Helsinki metropolitan area) and another thousand were selected from other regions in Finland in order to take into account regional differences in skin cancer incidence.

Both the cabin crew and the reference population were sent a self-administered questionnaire (followed by two reminder letters for nonrespondents). Information was collected from both groups on UVR exposure indicators including (i) skin burns in childhood, i.e. before the age of 15, (ii) skin burns in adulthood, i.e. after the age of 15, (iii) solarium use, (iv) use of topical sunscreens, (v) sunbathing habits, (vi) outdoor activities in Finland during summertime, (vii) residence in southern countries with higher UVR exposure, and (viii) the average annual number of vacation weeks spent at sun resorts by decade. Further, information was collected on host risk factors for skin cancer including natural hair, eve and skin colour, family history of skin cancer (among first-degree relatives), and phototype (Fitzpatrick, 1975). Phototype means the tendency to burn or tan in response to sun exposure is divided into four (or six) categories where I = 'always burns, does not tan', II = 'burns easily, tans poorly', III = 'tans after initial burn', and IV = 'burns minimally, tans easily' (categories V and VI are for very dark natural skin colours and are not used among Caucasians). Among the cabin crew, information was collected on UVR-related occupational factors, i.e. average annual number of days spent at sun resorts due to work, such as, waiting for the next work shift or having days off between work shifts, by decade. The Pirkanmaa hospital district ethics committee approved the study protocol. All study subjects gave a written informed consent prior to participation.

Cumulative occupational cosmic radiation dose estimation was based on the number of work years and on the average annual dose for a cabin crew member (Kojo *et al.*, 2007). Information on frequency of flights and aircraft type on each route at 5-year intervals (from 1960 to 1995) was collected from Finnair timetables. The cosmic radiation dose for every route was calculated using the European Program package for the Calculation of Aviation Route Doses developed by GSF-National Research Center for Environment and Health, Germany. The package estimates effective dose rates by altitude, latitude, and solar cycle phase. Information on number of cabin crew in each aircraft and the total number of cabin crew employed by Finnair at different time periods was collected. Combining this information, the average annual dose for one cabin crew member employed during a given calendar year was calculated. Based on the individual information from Finnair and the Finnish Cabin Crew Union on number of work years and absences from work during the career, the cumulative dose was estimated.

Analyses for risk factor comparison

We obtained risk estimates for both host and UVR-related behavioural factors from recently published meta-analyses for CMM summarizing the research evidence on skin cancer (Nelemans et al., 1995; Huncharek and Kupelnic, 2002; Gefeller and Pfahlberg, 2002; Dennis et al., 2003; Gallagher et al., 2005; Gandini et al., 2005a,b; Caini et al., 2009; Olsen et al., 2010). For example, a pooled relative risk (RR) estimate of 2.6 was used for red, 2.0 for blonde, and 1.5 for light brown hair compared to dark natural hair colour (Table 1) (Olsen et al., 2010). The exposure information collected in this study was coded to be consistent with the groupings in the meta-analyses utilized in this study (Nelemans et al., 1995; Huncharek and Kupelnic, 2002; Gefeller and Pfahlberg, 2002; Dennis et al., 2003; Gallagher et al., 2005; Gandini et al., 2005a,b; Caini et al., 2009; Olsen et al., 2010). A subject was considered to have had intermittent exposure if she reported (i) sunbathing at a sun resort at least once a year or (ii) sunbathing in Finland during summertime at least once a week or (iii) spending time outdoors in Finland during summertime at least 2h daily, or (iv) living in a sunny country at least for 1 year but no >5 years.

For each risk factor, we calculated a risk factorspecific mean score, i.e. a stratified average of the risk estimate, for both the cabin crew and the reference group. To account for regional differences, a mean was first calculated separately for the two reference groups from different areas (Uusimaa district versus the rest of the country), after which the means were combined with weighting based on the area distribution among cabin crew (86%) in Uusimaa district). To compare the cabin crew and the reference group, an overall mean risk score was calculated combining all the risk factorspecific mean scores to represent the overall risk of skin cancer given the distribution of different exposures. Also the mean risk scores were calculated combining (i) only the host risk factorspecific scores and (ii) only the UVR behaviour risk factor-specific scores. The scores were not normally distributed (e.g. skewness-kurtosis test for normality for overall mean risk score for all risk factors, P < 0.001). Therefore, the statistical significance of the differences of the overall mean risk scores between the cabin crew and the reference group was assessed with a non-parametric Mann-Whitney U-test.

Nested case-control analyses among cabin crew

The skin cancer cases diagnosed since 1 January 1953 among the participated cabin crew and registered in the Finnish Cancer Registry database before 26 September 2011 were identified by a record linkage using the unique personal identity code. For every skin cancer case, all cabin crew members free of skin cancer at the time of the diagnosis of the case and with the same year of birth and the same residential area (Uusimaa district versus the rest of the country) were used as controls. The number of controls per case varied from 3 to 32. The exposure information was taken into account until the year of diagnosis for cases and controls. Both the CMMs and BCCs were included in the analysis, whereas the SCCs (two cases) were excluded. This is because BCC shares an UVR exposure pattern of risk that is more similar to CMM than SCC.

The association between skin cancer and cumulative radiation dose was analysed with conditional logistic regression methods per 10 mSv (milliSievert) increment in dose, assuming a linear dose-response relationship without a threshold. The dose received within 10 years prior to diagnosis (for both cases and their controls) was excluded to allow for a lag period of 10 years. Multivariable analysis with both estimated cosmic radiation dose and conventional risk factors for skin cancer, i.e. factors related to host and UVR exposure, in the Model 1 was used to evaluate the effects of these exposures simultaneously. Variable selection for modelling was based on strong previous evidence of the relation to CMM and BCC risk. In addition, all the cabin crew members were assigned an individual summary risk estimate,

$ \frac{1}{N^{a}} (\%) $ 366 (52.4) 187 (26.8) 139 (19.9) 6 (0.9) 1.35 93 (13.6) 2(5 (52.5))	N ^a (%) 548 (54.7) 258 (25.8) 172 (17.2) 23 (2.3) 1.35	1.0 1.5 2.0 2.6	
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6 (0.9) 1.35 93 (13.6)	23 (2.3)		
1.35 93 (13.6)		2.6	
93 (13.6)	1.35		
			$P = 0.06^{\circ}$
265 (52.5)	113 (11.6)	1.0	
365 (53.5)	557 (57.0)	1.5	
224 (32.8)	307 (31.4)	1.6	
1.46	1.48		$P = 0.22^{\circ}$
188 (26.9)	166 (16.6)	1.0	
510 (73.1)	836 (83.4)	1.9	
1.66	1.75		$P < 0.001^{\circ}$
153 (24.4)	158 (18.7)	1.0	
319 (50.8)	386 (45.6)	1.4	
103 (16.4)	186 (22.0)	2.0	
53 (8.4)	116 (13.7)	2.3	
1.48	1.58		$P = 0.001^{\circ}$
639 (91.9)	905 (91.9)	1.0	
56 (8.1)	80 (8.1)	1.7	
1.06	1.06		$P = 0.96^{\circ}$
1.40	1.44		$P < 0.001^{\circ}$
191 (28.2)	201 (20.5)	1.0	
	780 (79.5)	2.2	
1.86	1.96		$P < 0.001^{\circ}$
49 (7.1)	79 (8.0)	1.0	
1.84	1.84		$P = 0.88^{\circ}$
421 (63 7)	757 (77 7)	1.0	
1.25	1.17	1.,	$P < 0.001^{\circ}$
291 (81-5)	549 (83 4)	1.0	
			$P = 0.80^{\circ}$
	365 (53.5) 224 (32.8) 1.46 188 (26.9) 510 (73.1) 1.66 153 (24.4) 319 (50.8) 103 (16.4) 53 (8.4) 1.48 639 (91.9) 56 (8.1) 1.06 1.40 191 (28.2) 486 (71.8) 1.86 49 (7.1) 645 (92.9) 1.84 421 (63.7) 240 (36.3)	365 (53.5) $557 (57.0)$ $224 (32.8)$ $307 (31.4)$ 1.46 1.48 $188 (26.9)$ $166 (16.6)$ $510 (73.1)$ $836 (83.4)$ 1.66 1.75 $153 (24.4)$ $158 (18.7)$ $319 (50.8)$ $386 (45.6)$ $103 (16.4)$ $186 (22.0)$ $53 (8.4)$ $116 (13.7)$ 1.48 1.58 $639 (91.9)$ $905 (91.9)$ $56 (8.1)$ $80 (8.1)$ 1.06 1.06 1.40 1.44 $191 (28.2)$ $201 (20.5)$ $486 (71.8)$ $780 (79.5)$ 1.86 1.96 $49 (7.1)$ $79 (8.0)$ $645 (92.9)$ $909 (92.0)$ 1.84 1.84 $421 (63.7)$ $757 (77.7)$ $240 (36.3)$ $217 (22.3)$ 1.25 1.17 $291 (81.5)$ $549 (83.4)$ $66 (18.5)$ $109 (16.6)$	365 (53.5) $557 (57.0)$ 1.5 $224 (32.8)$ $307 (31.4)$ 1.6 1.46 1.48 $188 (26.9)$ $166 (16.6)$ 1.0 $510 (73.1)$ $836 (83.4)$ 1.9 1.66 1.75 $153 (24.4)$ $158 (18.7)$ 1.0 $319 (50.8)$ $386 (45.6)$ 1.4 $103 (16.4)$ $186 (22.0)$ 2.0 $53 (8.4)$ $116 (13.7)$ 2.3 1.48 1.58 $639 (91.9)$ $905 (91.9)$ 1.0 $56 (8.1)$ $80 (8.1)$ 1.7 1.06 1.06 1.44 $191 (28.2)$ $201 (20.5)$ 1.0 $486 (71.8)$ $780 (79.5)$ 2.2 1.86 1.96 1.96 $49 (7.1)$ $79 (8.0)$ 1.0 $645 (92.9)$ $909 (92.0)$ 1.9 1.84 1.84 1.7 $421 (63.7)$ $277 (77.7)$ 1.0 $240 (36.3)$ $217 (22.3)$ 1.7 1.25 1.17 1.6

Table 1. Skin cancer risk factor distribution, risk estimates, risk factor-specific mean scores, and overall mean risk scores among cabin crew and reference population.

Table 1. Continued

Risk factor	Cabin crew	Reference population	Relative risk estimate	Statistical significance
	N^{a} (%)	N ^a (%)		
Sunscreen use				
Yes	639 (91.4)	826 (82.4)	1.0	
No	60 (8.6)	176 (17.6)	1.1	
Mean risk score ^b	1.01	1.02		$P < 0.001^{\circ}$
Intermittent UVR exposure				
No	103 (14.8)	237 (23.6)	1.0	
Yes ^f	594 (85.2)	766 (76.4)	1.6	
Mean risk score ^b	1.51	1.46		$P < 0.001^{\circ}$
Overall score _{UVR-related behaviour factors}	1.46	1.44		$P = 0.130^{\circ}$
Overall score _{all risk factors}	1.43	1.44		$P = 0.237^{\circ}$

^aTotals differ in some cases because of missing data on specific characteristics.

^bStratified average by residential area, with weighting based on cabin crew.

°Statistical significance assessed from comparison of differences with Pearson's chi-square test.

 ^{d}I = 'always burns, does not tan', II = 'burns easily, tans poorly', III = 'tans after initial burn', and IV = 'burns minimally, tans easily'.

eStatistical significance assessed from comparison of differences with non-parametric Mann-Whitney U-test.

^fIf (i) sunbathing at a sun resort at least once a year or (ii) sunbathing in Finland during summertime at least once a week or (iii) spending time outdoors in Finland during summertime at least 2h daily, or (iv) living in a sunny country at least for 1 year but no >5 years.

The overall scores and their statistical significance for (i) only all the host factors or (ii) only all the UVR-related behaviour factors, or (iii) all risk factors are bolded

which was calculated using the risk factor-specific estimates obtained from the meta-analyses as

UVR behaviour (Model 2) was used to evaluate the effects of these exposures simultaneously.

$$1 + \sum_{i=1}^{11} (RE_i - 1),$$

where RE is risk estimate for each risk factor.

The summary risk estimate represents the sum of excess risk for each risk factor reported by the crew, reflecting the effects of conventional risk factors for skin cancers. If the estimate for a risk factor was missing (approximately 8% for cases and 6% for controls, two-sample test of proportions P = 0.11), imputation with a variable mean of nonmissing observations was used. The highest proportion of non-response was in phototype (10% of all respondents) and the lowest in sunscreen use (<1%). Two separate summary risk estimates were calculated (i) for host factors and (ii) for UVR behaviour factors. In the UVR behaviour factors, spending time at sun resorts due to work was included to the previously defined intermittent UVR exposure variable. A cabin crew member was considered to have had intermittent UVR exposure if she spent on average >1 day per week at a sun resort due to work. Multivariable analysis with both radiation dose and the summary risk estimates for host factors and

RESULTS

A total of 702 cabin crew members returned a completed questionnaire, corresponding to a response rate of 56%. In the reference group, 1007 (50%) responded to the survey. At the time of the survey, the mean age of the respondents among the cabin crew was 51.4 years and among the reference population 51.6 years. The corresponding ages for those who did not participate were 52.9 and 54.0 years, respectively. Of the respondents among the cabin crew, 85.8% and of the reference population 65.0% lived in the Uusimaa area. The corresponding figures for nonparticipants were 80.8 and 62.5%, respectively.

The overall mean risk score for skin cancer based on host factors only was slightly higher in the reference group (1.44 versus 1.40, P < 0.001) than among the cabin crew (Table 1). The overall mean risk score based on UVR behavioural factors did not differ between the cabin crew and the reference population (1.46 versus 1.44, P = 0.13). There was no difference in skin burns in adulthood between the cabin crew and the reference

Table 2. Average number of days spent in a year at sun resorts due to work among all cabin crew by decade.

Decade	Median (95% CI)
1960s	10 (8–14)
1970s	19 (14–20)
1980s	25 (20–30)
1990s	20 (19–30)
2000s	12 (0–30)

population. However, the mean risk score based on skin burns in childhood was lower (1.86 versus 1.96, P < 0.001), whereas score for solarium use (1.17 versus 1.25, P < 0.001) was higher for the cabin crew. Also the score for intermittent UVR exposure was higher among the cabin crew (1.51 versus 1.46, P < 0.001) than among the reference group. The overall mean risk scores, calculated based on all the conventional skin cancer risk factors, were similar for the cabin crew and for the reference population (1.43 versus 1.44, P = 0.24).

Among the participated cabin crew, a total of 44 skin cancer cases (9 CMM and 35 BCC) with 692 matched controls were included in the casecontrol analysis. The estimated cumulative cosmic radiation doses were lower among the cases than among the controls, with medians 10.7 (95% CI: 4.1-14.6) mSv and 18.2 (95% CI: 16.1-19.9) mSv, respectively. The cases had higher summary risk estimates based on host factors than the controls, with means 2.26 and 1.90 (P = 0.01 with Mann-Whitney U-test), respectively. A fairly similar difference was found in the summary risk estimates based on the UVR behaviour factors where the mean was 2.20 among the cases and 1.96 among the controls (P = 0.12). Table 2 shows the average time spent in a year at sun resorts due to work reported by all cabin crew.

In the multivariable conditional logistic regression analysis, the estimated cosmic radiation dose was not associated with an increased risk of skin cancer [odds ratio (OR) = 0.82 per 10 mSv, 95% CI: 0.62–1.09] when adjusted for natural hair colour, natural skin colour, and skin burns in childhood. An adjustment for summary risk factors, i.e. including all host and UVR behaviour risk factors in the model, further reduced the risk estimate for the estimated cosmic radiation dose resulting in a point estimate below unity of borderline significance (OR = 0.75, 95% CI: 0.57–1.00). The host factors (OR = 1.43, 95% CI: 1.01–2.04) showed statistically significant association with skin cancer, whereas the point estimate for UVR behaviour

cabili ciew.			
Risk factor	Adjusted ^a OR (95% CI)		
Model 1 $(N = 651)^{b}$			
Cumulative radiation dose	0.82 (0.62–1.09)		
(per 10 mSv)	41\610		
Natural hair colour			
Brown or black	1.00 (ref)		
	30\513		
Red or blonde	1.69 (0.78-3.66)		
	11\97		
Natural skin colour			
Dark	1.00 (ref)		
	9\201		
Fair	1.38 (0.61-3.10)		
	32\409		
Skin burns in childhood			
No	1.00 (ref)		
	7\183		
Yes	2.02 (0.83-4.93)		
	34\427		
Model 2 ($N = 736$) ^c			
Cumulative radiation dose	0.75 (0.57-1.00)		
(per 10 mSv)	44\692		
Host risk factors	1.43 (1.01–2.04)		
UVR exposure risk factors	1.52 (0.91–2.52)		

Number of cases\controls in each exposure category are given below the respective OR.

^aMutually adjusted for all other variables within the model.

^bA multivariate analysis with skin cancer as a dependent variable and estimated cosmic radiation dose and conventional risk factors for skin cancer as independent variables in the model.

^cA multivariate analysis with skin cancer as a dependent variable and estimated cosmic radiation dose and the summary risk estimates for host factors and UVR behaviour factors as independent variables in the model.

factors (OR = 1.52, 95% CI: 0.91-2.52) was slightly higher but statistically non-significant (Table 3).

DISCUSSION

No substantial differences were found in host factors or behavioural factors related to UVR exposure between the female cabin crew and the population-based reference group. In fact, the reference population had a higher risk score of skin cancers related to host factors. However, the cabin crew did report more solarium use than the reference population. Also, intermittent UVR exposure was slightly more common among the cabin

Table 3. ORs with 95% CIs of skin cancer risk among cabin crew.

crew. The average number of days spent at sunny resorts due to work among the cabin crew was highest during the 1980s and lowest during the 1960s. There is no information on how the cabin crew spend its time at the sun resorts (e.g. sunbathing or resting inside). Nevertheless, it is possible that these days at sun resorts increase the cabin crew's total amount of UVR exposure. Among the cabin crew that participated the survey, the estimated cosmic radiation dose was not associated with the increased risk of skin cancers in the case–control analysis, whereas the host-related factors showed statistically significant association but the UVR-related behavioural factors did not.

The skin cancer cases were identified by a record linkage from Finnish Cancer Registry, a nationwide, population-based registry. The completeness of registration of the Finnish Cancer Registry has been shown to be >99% for most solid cancers, including CMM and SCC, but the coverage for BCC registration is probably lower (Teppo *et al.*, 1994). We did not assess incidence of BCC, and therefore undercount may result in misclassification of outcome in the sampling of cases and controls among the cabin crew for case-control analysis. Reduced sensitivity of disease status ascertainment has been shown to mainly lower precision in case-control studies (Brenner and Savitz, 1990).

We estimated the cumulative exposure to cosmic radiation for those who participated the survey based on work years and average annual doses for the skin cancer cases and controls among the crew. The calculation method of the cosmic radiation dose has been previously described in detail and its validity has been fully evaluated (Kojo et al., 2007). This method eliminates recall bias since it is based on timetable information on flight patterns. However, the approach does not fully take into account the individual variation due to differences in flight patterns. Rather, radiation dose is determined by the year of employment and length of the career. In this study, the effect of estimated cosmic radiation dose was analysed using the case-control approach with individual matching on the year of birth because age is a strong determinant of skin cancer risk and also correlates with the cumulative radiation dose. However, as the year of birth notably defines the year of first employment (Pearson correlation coefficient = 0.96), overmatching is possible and may result in underestimation of the association between skin cancer and estimated cumulative cosmic radiation dose. Yet, we found that only 12% of the cumulative dose was explained by the year of first employment, whereas 83% of the dose was explained by the length of the career, suggesting that overmatching is not a major concern. Birth year was not strongly related to the length of the career (Pearson correlation coefficient = -0.34).

We used risk estimates from meta-analyses to quantify the contribution of previously established, conventional risk factors for skin cancers since meta-analyses provide a quantitative synthesis of the research evidence. The outcome in all meta-analyses was CMM, whereas meta-analyses on the risk factors of SCC and BCC have not been published. In general, intermittent exposure to UVR, such as skin burns, is associated with both CMM and BCC, whereas cumulative exposure is considered a risk factor for SCC and BCC (Green and Trichopoulos, 2002; Almahroos and Kurban, 2004; Karagas et al., 2006). The exposure information collected was grouped to be consistent with the categories in the meta-analyses. This resulted in a rather crude exposure estimated, which might have caused losing some information on the variation of the variables,

A limitation of this study was the relatively low participation rate despite two reminders. The response proportion was similar to previous questionnaire studies among cabin crew (Rafnsson et al., 2003; Kojo et al., 2005). A low participation rate can lead to selection bias if the exposure distribution differs between participants and nonparticipants. Such bias may distort the estimates towards either direction. In the reference population, non-participation was associated with higher age, whereas such difference was not found among the cabin crew. However, the age distribution was similar among the participating cabin crew and the reference group and, therefore, selection bias is unlikely to affect our results. Further, there is a possibility of information bias, in case the quality of the exposure information supplied by the subjects differs between the cabin crew and the reference population or between the cases and non-cases. It is possible that the cabin crew with skin cancer is more likely to report UVR exposure or host factors with a higher sensitivity than the cabin crew without the diagnosis. This kind of recall bias would overestimate the true association. In addition, the case ascertainment was retrospective and, thus, deceased cases were not available for the study.

Another limitation was the small number of skin cancer cases restricting the statistical power. Due to the small number of cases, the effect of cosmic radiation could not be studied by skin

cancer type but the skin cancers had to be combined as one outcome category. As the source population consisted of all eligible Finnish female cabin attendants, the constraint could not be overcome. The highest plausible risk of skin cancer for estimated cosmic radiation dose can be estimated as the upper limit of the CI (1.09), i.e. 9% per 10 mSv. The median cumulative career dose for Finnair cabin crew cohort (N = 1289) estimated in our previous study was 20.8 mSv (Kojo et al., 2007). Thus, the highest contribution of radiation exposure consistent with our results is 20.8%, given the dose distribution. Using the upper limits of the CIs from the adjusted model, the maximal fraction of skin cancer incidence among cabin crew attributable to host risk factors is 51%, and to UVR exposure 60%. The estimated cosmic radiation dose showed a borderline significant protective effect.

Only one previous study has assessed the UVR exposure of cabin crew (Rafnsson *et al.*, 2003). These Icelandic results were similar to our study, i.e. there were no substantial differences in host or behavioural risk factors between the aircrew and population sample. Similar to our study, the cabin crew reported more solarium use, more sunscreen use, and more sun vacations than the reference females also in the Icelandic study. However, past skin burns were more frequent among the cabin crew than the reference females, which contradicts our results.

In our study, the estimated occupational exposure to cosmic radiation among airline cabin crew was not related to an increased skin cancer risk. A number of earlier studies have evaluated the relation between skin cancers and occupational exposure to repeated low doses of ionizing radiation. For example, among the US radiologic technologists, an increased but statistically nonsignificant risk of CMM (RR = 1.8, 95% CI: 0.6-5.5) was found among those who began their work before 1950, i.e. when the exposure was likely to be highest (Freedman et al., 2003). The results were similar for BCC; the risk was increased among those technologists who worked during the high radiation exposure period (Yoshinaga et al., 2005). The results were not modified by UVR exposure but the effect of early work periods was stronger among subjects with lighter hair or eye colour. Both studies among radiologic technologists were limited by the lack of radiation dose estimates. A population-based case-control study conducted by the American Cancer Society suggested that occupational exposure to X-rays

increases the risk of CMM (Pion et al., 1995). A case-control study among Lawrence Livermore National Laboratory workers reported an association between CMM and ionizing radiation, but this finding could not be confirmed by a subsequent study (Austin and Reynolds, 1997; Moore et al., 1997). In a Canadian cohort study of cancer incidence in radiation-exposed workers, statistically significantly elevated incidence of CMM was found among men, but not among women (Sont et al., 2001). The excess relative risk (ERR) for CMM was estimated as 4.3 (90% CI: <0-19.6)per Sv for both genders combined. In a study among radiation workers in the UK, increasing incidence trends with dose for all skin cancers (P = 0.01) and non-melanoma skin cancers only (P = 0.02) were observed (Muirhead *et al.*, 2009). A recent large cohort study of nuclear industry workers with individual dose monitoring in 15 countries found no association between radiation dose and CMM mortality (ERR/Sv 0.15, 90% CI: <0-5.44) (Cardis et al., 2007). Thus, on the basis of the previous studies, the evidence on the relation between low-dose radiation and skin cancers remains inconclusive. However, results of studies on low-linear energy transfer (LET) radiation such as X- and gamma rays on skin cancer risk are not straightforwardly generalizable to the cosmic radiation consisting of high-LET neutrons.

Very little knowledge is available on the joint effect of ionizing radiation and UVR on skin cancer risk. In a study of patients irradiated for tinea capitis in New York, a higher risk of BCC was found on the areas exposed to UVR compared to shielded areas (Shore *et al.*, 2002). However, studies among atomic bomb survivors in Japan do not support this finding (Ron *et al.*, 1998; Kishikawa *et al.*, 2005).

CONCLUSION

The prevalence of risk factors for skin cancer did not differ between the female cabin crew and the general female population. The nested case–control study among cabin crew showed no association between the estimated cosmic radiation dose and the increased risk of skin cancer but this might be due to the study not encompassing enough statistical power to reveal the relation. The highest plausible risk of skin cancer for estimated cosmic radiation dose was 9% per 10 mSv, based on the upper limit of CI of adjusted logistic regression model. At present, there seems to be no undisputed evidence on the relation between cosmic radiation exposure and skin cancers. This is the first study assessing the contribution of cosmic radiation and UVR to the skin cancer risk among cabin crew and, clearly, more studies with robust cosmic radiation and UVR exposure estimations and a larger sample size are needed.

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ETHICAL ASPECTS

The Pirkanmaa hospital district ethics committee reviewed and approved the study protocol. All study subjects gave a written informed consent prior to participation.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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