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The Risk of Melanoma in Airline Pilots and Cabin Crew A Meta-analysis

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Abstract

Importance—Airline pilots and cabin crew are occupationally exposed to higher levels of cosmic and UV radiation than the general population, but their risk of developing melanoma is not yet established.

Objective—To assess the risk of melanoma in pilots and airline crew.

Data Sources—PubMed (1966 to October 30, 2013), Web of Science (1898 to January 27, 2014), and Scopus (1823 to January 27, 2014).

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Author Contributions: Drs Sanlorenzo and Ortiz-Urda had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Sanlorenzo, Wehner, Linos, Vujic, Ortiz-Urda.
Acquisition, analysis, or interpretation of data: Sanlorenzo, Wehner, Linos, Kornak, Kainz, Posch, Johnston, Gho, Monico, McGrath, Osella-Abate, Quaglino, Cleaver.
Drafting of the manuscript: Sanlorenzo, Wehner, Kainz, Johnston, Gho, Monico.
Critical revision of the manuscript for important intellectual content: Sanlorenzo, Wehner, Linos, Kornak, Kainz, Posch, Vujic, McGrath, Osella-Abate, Quaglino, Cleaver, Ortiz-Urda.
Statistical analysis: Sanlorenzo, Wehner, Linos, Kornak, Vujic, McGrath, Quaglino.
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Study supervision: Ortiz-Urda.

Conflict of Interest Disclosures: None reported.

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Study Selection—All studies were included that reported a standardized incidence ratio (SIR), standardized mortality ratio (SMR), or data on expected and observed cases of melanoma or death caused by melanoma that could be used to calculate an SIR or SMR in any flight-based occupation.

Data Extraction and Synthesis—Primary random-effect meta-analyses were used to summarize SIR and SMR for melanoma in any flight-based occupation. Heterogeneity was assessed using the χ^2 test and I^2 statistic. To assess the potential bias of small studies, we used funnel plots, the Begg rank correlation test, and the Egger weighted linear regression test.

Main Outcomes and Measures—Summary SIR and SMR of melanoma in pilots and cabin crew.

Results—Of the 3527 citations retrieved, 19 studies were included, with more than 266 431 participants. The overall summary SIR of participants in any flight-based occupation was 2.21 (95% CI, 1.76-2.77; $P < .001$; 14 records). The summary SIR for pilots was 2.22 (95% CI, 1.67-2.93; $P = .001$; 12 records). The summary SIR for cabin crew was 2.09 (95% CI, 1.67-2.62; $P = .45$; 2 records). The overall summary SMR of participants in any flight-based occupation was 1.42 (95% CI, 0.89-2.26; $P = .002$; 6 records). The summary SMR for pilots was 1.83 (95% CI, 1.27-2.63, $P = .33$; 4 records). The summary SMR for cabin crew was 0.90 (95% CI, 0.80-1.01; $P = .97$; 2 records).

Conclusions and Relevance—Pilots and cabin crew have approximately twice the incidence of melanoma compared with the general population. Further research on mechanisms and optimal occupational protection is needed.

Cutaneous melanoma is one of the 5 most common cancers in the United States and is the most common fatal malignant neoplasm in young adults. Melanoma rates are consistently rising; in 2014, 76 100 individuals will be diagnosed with melanoma of the skin, and 9710 cases will result in death.[1] Several cohort studies have suggested a higher incidence of melanoma in pilots and flight crew.[2,3] Flight-based workers are thought to have a greater occupational hazard risk of melanoma owing to increased altitude-related exposure to UV and cosmic radiation. Although the risks of exposure to ionizing radiation for pilots and cabin crew are known and levels are regularly monitored, UV exposure is not a well-recognized occupational risk factor for the flight crew.

The aim of this study was to contrast and establish the statistical significance among available studies regarding the occupational risk of melanoma for pilots and cabin crew.

Methods

We carried out this review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.[4] The study was approved by the Committee on Human Research of the University of California, San Francisco (IRB No. 12-09483).

Identification of Articles

We identified suitable studies by searching electronic databases and scanning reference lists of articles. We searched PubMed (1966 to present), Web of Science (1898 to present), and

Scopus (1823 to present). The last PubMed search was run on October 30, 2013. Search terms included 12 terms for flight crew or air travel and 8 terms for skin cancer. The specific search strategies for each are detailed in the eAppendix in the Supplement. In addition, we reviewed journal articles and relevant reviews to locate publications missed by the database searches.

Study Selection

All articles that reported a standardized incidence ratio (SIR) or standardized mortality ratio (SMR) of melanoma or evaluated melanoma risk in populations of flight crew or pilots were eligible for inclusion. The SIR is a measure of the incidence and SMR is a measure of the mortality in a study population (in this study, flight crew or pilots) compared with the general population. Both are typically standardized by age and sex. Values for SIR and SMR greater than 1 indicate higher incidence or mortality in the study population compared with the general population.

Two authors (M.S. and M.R.W.) independently assessed the eligibility of studies. Any disagreements were settled by consensus, including a third and fourth investigator (E.L. and S.O.-U.). The article title and abstract were used for initial screening, followed by review of the full text or equivalent. Studies published in languages other than English were assessed for eligibility after translation. Inclusion criteria for quantitative meta-analysis were studies that reported an SIR or SMR or data on expected and observed cases of melanoma or confirmed melanoma that could be used to calculate an SIR or SMR.[5] We excluded articles that presented no data, such as review articles and editorials. If duplicate data were present in separate publications, we included the publication with the larger amount of data, obtained either through a longer follow-up period or greater number of participants.

Data Extraction

We used a data extraction form based on the Cochrane Consumers and Communication Review Group's data extraction template.[6] We extracted the following data items from each study: characteristics of study participants (including age, sex, and relevant occupation), inclusion and exclusion criteria, characteristics of the study design, outcomes (effect estimates SIR and SMR), and statistical methods (including age and sex standardization).

Statistical Analysis

For our primary analyses, we summarized the SIR and SMR of any flight-based occupations. Later, we performed secondary analyses stratified by sex and specific occupation. The included studies had different definitions of flight-based occupations, and we decided to divide our population into 2 groups: (1) workers who are in the cockpit (pilots and cockpit crew) and (2) workers who are in the cabin (cabin crew and flight attendants).

Stata, version 12, statistical software (StataCorp) was used to perform random-effects model meta-analyses, yielding summary relative risks and 95% CIs. We chose conservative random-effects methods that take heterogeneity into account. All statistical tests were 2-sided. To investigate variability (heterogeneity) in study outcomes, we used a χ^2 test for heterogeneity (considered significant at $P = .10$) and an I^2 statistic.

To assess potential small-study effects and publication bias across studies, we created funnel plots by plotting the effect found by each study against the inverse of its standard error. We reviewed the funnel plot visually and used the Begg rank correlation test and Egger weighted linear regression test for formal testing. This was done to investigate the possibility that small studies showing no effects may not be published and that small studies are more likely to be conducted with less methodologic rigor, leading to inaccurate effect estimates.

Results

Our search yielded 2450 results on PubMed, 2253 on Scopus, and 1555 on Web of Science. After duplicates were removed, there were 3527 unique results. A search by hand through reference lists, review articles, and publicly available data yielded 2 additional publications. We screened the 3529 unique records by titles and abstracts. After exclusions, 83 records were assessed for eligibility in full text or the equivalent; 19 records met inclusion criteria and were included (Figure 1). Six records were available only in German or French, and these were assessed for eligibility after translation.[7-12] Thirteen records were found to have duplicate study cohorts,[13-25] and in these cases, we included the records with the largest amount of data. In several cases, the study cohorts were the same but the reported measure was different (SIR[16,17,23-25] vs SMR[13,26]). Because these would not be included in the same analysis, these records with duplicate study cohorts were included. Six studies were excluded because the full text was not available.[27-32]

The 19 records included in this review were published between 1990 and 2013, reported data from 1943 to 2008 from 11 countries, and included more than 266 431 participants (Table). Fifteen reported data on pilots and 4 on cabin crew.

The overall summary SIR for participants in any flight-based occupation was 2.21 (95% CI, 1.76-2.77; $P < .001$; 14 records). The summary SIR for pilots was 2.22 (95% CI, 1.67-2.93; $P = .001$; 12 records). The summary SIR for cabin crew was 2.09 (95% CI, 1.67-2.62; $P = .45$; 2 records) (Figure 2A).

The overall summary SMR for participants in any flight-based occupation was 1.42 (95% CI, 0.89-2.26; $P = .002$; 6 records). The summary SMR for pilots was 1.83 (95% CI, 1.27-2.63; $P = .33$; 4 records). The summary SMR for cabin crew was 0.90 (95% CI, 0.80-1.01; $P = .97$; 2 records) (Figure 2B).

When results were separated by sex, the overall summary SIR for female participants in a flight-based occupation was 1.93 (95% CI, 1.50-2.48; $P = .41$; 2 records), and the overall summary SIR for male participants in a flight-based occupation was 2.38 (95% CI, 1.75-3.23; $P = .001$; 12 records). The overall summary SMR for women in any flight-based occupation was 0.61 (95% CI, 0.13-2.85; $P = .51$; 2 records), and the overall summary SMR for men was 1.87 (95% CI, 1.32-2.65; $P = .39$; 5 records) (Figure 3).

Heterogeneity, Small Study Effects, and Publication Bias

Heterogeneity was observed in several of the main analyses. The I^2 statistics and the *P* values of the χ^2 test for heterogeneity are shown in Figures 2 and 3.

Funnel plots were created for both SIR and SMR overall calculations for melanoma (Figure 4). The results of the Begg rank correlation test were $P = .19$ for SIR and $P > .99$ for SMR. The results of the Egger weighted linear regression test were $P = .70$ for SIR and $P = .12$ for SMR. No test was at or below the significance level of $P = .10$; thus, there was no evidence of publication bias.

Discussion

In this systematic review and meta-analysis including 19 studies and more than a quarter of a million participants, we found that the combined and separate SIRs for pilots and cabin crew were greater than 2, indicating that pilots and air crew have twice the incidence of melanoma compared with the general population. In the general population, the number of new melanomas per year is 21.3 per 100 000.[1] Therefore, the calculated number needed to harm is 4695. Furthermore, we found that the combined SMR for pilots and air crew was 1.42. This indicates an approximately 42% higher melanoma mortality rate compared with the general population, for whom the number of deaths by melanoma is 2.7 per 100 000 per year.[1] Therefore, the calculated number needed to harm for mortality is 88 183.

Limitations

Significant heterogeneity was observed in the overall summary SIR but, when analyzed separately for pilots and cabin crew and separately for men and women, significant heterogeneity remained in the pilots and male groups, while no heterogeneity was observed in the cabin crew or female groups. Significant heterogeneity was observed in the overall summary SMR but was not present when SMR was analyzed separately for pilots and cabin crew and separately for men and women, indicating that these differences between groups may have caused the heterogeneity in the overall summary analysis.

This study is limited by the fact that it included only observational and mostly retrospective studies. While they standardized to age and sex when applicable, they could not adjust for confounders. Another potential limitation is that the included studies may have had different definitions of flight-based occupations (cabin crew, flight deck, airline crew, and pilot), which may result in exposure heterogeneity. For example, although we grouped all flight-based occupations together, the actual time spent in the air for participants of each study may have varied significantly (eg, typical flight duration and frequency or years working as a pilot). These may account for some of the study heterogeneity observed.

Another potential confounder we were not able to control for is skin phototype. This may cause bias if fair-skinned individuals were more likely to be hired in flight occupations compared with control occupations. However, most studies included in our meta-analysis were conducted in northern European countries (Table) where the general population, used as the control group for these studies, is characterized by light phototype.

Possible Explanation of the Findings

The elevated risk of melanoma found in pilots and cabin crew could be causally related to occupational exposure to risk factors. The amount of cosmic radiation to which these workers are exposed has been examined in many studies and always found consistently below the allowed dose limit of 20 mSv/y.[14,45,46] On the other hand, UV radiation is a known risk factor for melanoma, and the cumulative exposure of pilots and cabin crew compared with the general population has not been assessed. A Federal Aviation Administration report[49] cites measurements of windshield transmission performed on the following 8 aircrafts: 3 commercial jets (MD 88, Airbus A320, and Boeing 727 and 737); 2 commercial, propeller-driven passenger airplanes (Fokker 27 and ATR 42); 1 small private jet (Raytheon Aircraft Corporation Hawker Horizon); and 2 small general aviation, single-engine, propeller-driven airplanes (Beech Bonanza and Cessna 182). The 2 general aviation aircraft windshields consisted of polycarbonate; the others were multilayer (laminated) composite glass. Transmission of UVB (280-320 nm) through both glass and plastic windshields was less than 1%. On the other hand, UVA (320-380 nm) transmission varied significantly on the basis of the windshield material. While plastic materials blocked almost all UVA radiation, 54% came through glasses. The pathogenic role of UVA in melanoma is established; it is capable of causing DNA damage in cell culture[47] and in animal models.[48] The windshields and cabin windows of airplanes seem to minimally block UVA radiation, and it is known that, for every additional 900 m of altitude above sea level, there is a 15% increase in intensity of UV radiation.[49] At 9000 m, where most commercial aircraft fly, the UV level is approximately twice that of the ground. Moreover, these levels are even higher when flying over thick cloud layers and snow fields, which could reflect up to 85% of UV radiation. Therefore, the cumulative UV exposure for pilots and cabin crew is still of concern, and the higher risk of melanoma evident in our meta-analysis could be due to greater occupation-related exposure to UVA radiation.

It is also possible that the elevated risk of melanoma noted in pilots and cabin crew is not causally associated with occupational exposure and is simply due to biases in observational study design. Specifically, it is possible that other unmeasured confounders may account for higher melanoma risk in pilots. However, a large observational study did not find any substantial difference in the prevalence of risk factors such as history of sunburn, sunbed usage, sunscreen used, or number of sunny vacations when comparing pilots and cabin crew with the general population.[50] Another finding that argues for occupational rather than leisure-activity exposure to explain our findings is the correlation found in several previous studies between increased rates of melanoma in air crew and increased number of flight hours.[17,25,36]

Context of Prior Literature

The 2 most recent meta-analyses found an increased risk of melanoma in male pilots[2] and in female flight attendants.[3] These analyses included only 8 and 7 studies, respectively, and considered incidence of different cancer types rather than focusing on melanoma. Our meta-analysis included substantially more studies, was focused only on melanoma, and confirmed an increased melanoma risk in pilots and cabin crew.

Conclusions

The results of our meta-analysis indicate that pilots and cabin crew have increased incidence of melanoma compared with the general population. This has important implications for occupational health and protection of this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Role of the Sponsor: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: Dr Kainz's role in this study was completed outside of his duties at the US Food and Drug Administration. The views expressed do not represent the views of the agency or the US government. In addition, the content of this report is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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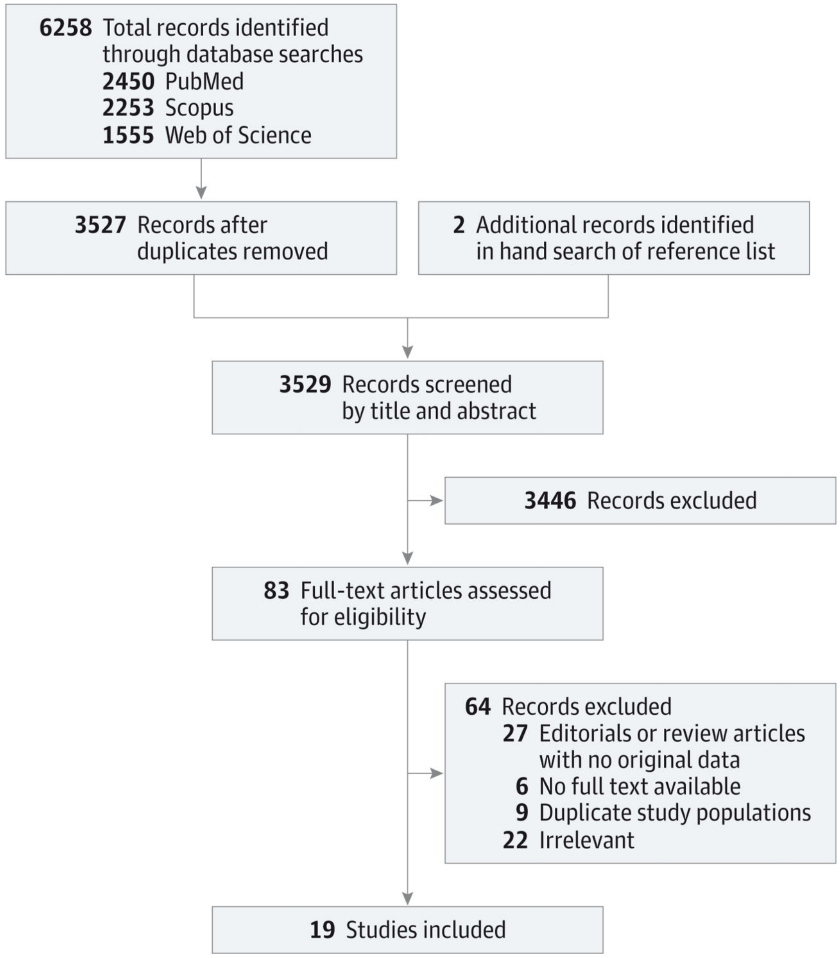

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses Flowchart of Article Search and Study Selection

Nineteen studies met inclusion criteria and were included in the meta-analysis

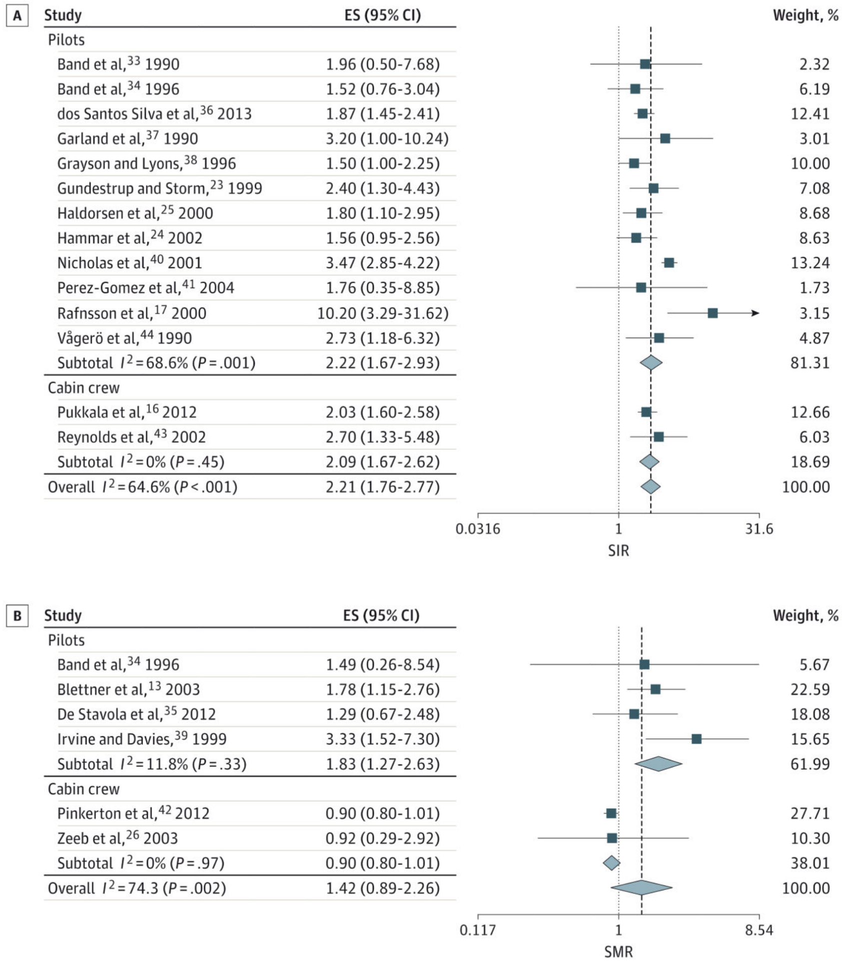

Figure 2. Standardized Incidence Ratio and Standardized Mortality Ratio of Melanoma in the Studies Included in the Meta-analysis

A, The overall summary standardized incidence ratio (SIR) of participants in any flight-based occupations was 2.21 (95% CI, 1.76-2.77; $P < .001$; 14 records). B, The overall summary standardized mortality ratio (SMR) of participants in any flight-based occupation was 1.42 (95% CI, 0.89-2.26; $P = .002$; 6 records). ES indicates effect size. Weight, %, indicates the degree to which the study contributed to the final results

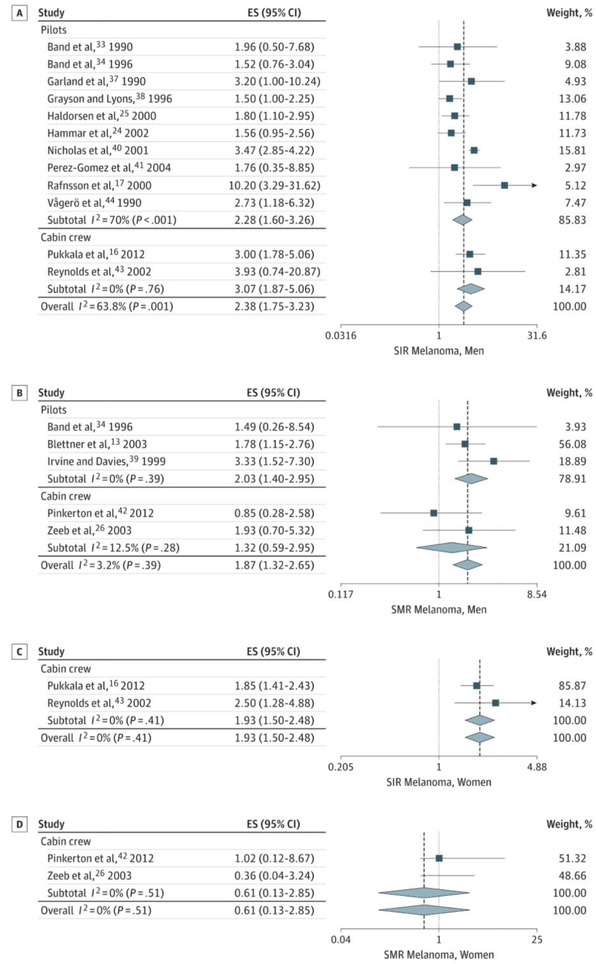

Figure 3. Standardized Incidence Ratio and Standardized Mortality Ratio of Melanoma in the Studies Included in the Meta-analysis Stratified by Sex

For men, the overall summary standardized incidence ratio (SIR) was 2.38 (95% CI, 1.75-3.23; *P* = .001; 12 records) (A), and the overall summary standardized mortality ratio (SMR) was 1.87 (95% CI, 1.32-2.65; *P* = .39; 5 records) (B). For women, the overall summary SIR was 1.93 (95% CI, 1.50-2.48; *P* = .41; 2 records) (C), and the overall summary SMR was 0.61 (95% CI, 0.13-2.85; *P* = .51; 2 records) (D). Weight, %, indicates the degree to which the study contributed to the final results.

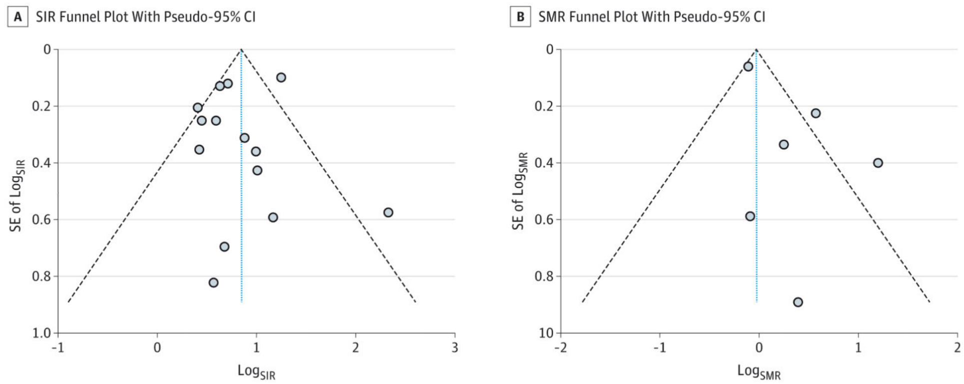

Figure 4. Funnel Plots With Pseudo–95% CIs for the Standardized Incidence Ratio (SIR) and Standardized Mortality Ratio (SMR) of Melanoma

Funnel plots to check the existence of publication bias. SE indicates standard error

Table

Studies Included in the Meta-analysis

Source	Data Collection	Country	Population	Total No. (M/F)	Person-years	Melanoma Risk
Band et al,[33] 1990	1950-1988	Canada	Pilots	891 (891 M)	18 060	SIR (90% CI): 1.96 (0.5-5.1)[a]
Band et al,[34] 1996	1950-1992	Canada	Pilots	2680 (2680 M)	62 449	SIR (90% CI): 1.52 (0.76-2.74)[a]; SMR (90% CI): 1.49 (0.26-4.68)[a]
Blettner et al,[13] 2003	1960-1997	Denmark, Finland, Germany, Greece, Iceland, Italy, Norway, Sweden, and UK	Pilots	27 797 (27 797 M)	547 564	SMR (95% CI): 1.78 (1.15-2.67)[a]
De Stavola et al,[35] 2012	1989-2006	UK	Cockpit crew	16 327 (15 881 M/446 F)	258 650	SMR (95% CI): 1.29 (0.67-2.25)[a]; HR (95% CI): 2.18 (0.28-17.10)[b]
dos Santos Silva et al,[36] 2013	1989-2008	UK	Cockpit crew	16 329 (15 867 M/462 F)	285 259	SIR (95% CI): 1.87 (1.45-2.38)[a]; RR (95% CI): 0.70 (0.41-1.20)[b]
Garland et al,[37] 1990	1974-1984	US	Aviation warfare system operators	Not stated	32 051	SIR (95% CI): 3.20 (1.0-6.7)[a]
Grayson and Lyons,[38] 1996	1975-1989	US	Pilots	59 940 (59 940 M)	532 980.97	SIR (99% CI): 1.50 (1-2.14)[a]
Gundestrup and Storm,[23] 1999	1943-1995	Denmark	Cockpit crew	3790 (3790 M)	61 095	SIR (95% CI): 2.40 (1.3-4.0)[a]
Haldorsen et al,[25] 2000	1953-1996	Norway	Pilots	3701 (3701 M)	>70 560	SIR (95% CI): 1.80 (1.1-2.7)[a]
Hammar et al,[24] 2002	1961-1996	Sweden	Pilots	3658 (3658 M)	105 025	SIR (95% CI): 1.56 (0.95-2.41)[a]
Irvine and Davies,[39] 1999	1950-1992	UK	Pilots and flight engineers	6209 (6209 M)	143 506	SMR (95% CI): 3.33 (1.52-6.32)[a]
Nicholas et al,[40] 2001	1970-1998	US and Canada	Pilots	6533 (6533 M)	117 595	SIR (95% CI): 3.47 (2.85-4.23)[a]
Perez-Gomez et al,[41] 2004	1960-1970	Sweden	Pilots, flight engineers, and navigators	1 890 497 (1 890 497 M)[c]	Not stated	SIR (95% CI): 1.76 (0.35-3.17)[a]
Pinkerton et al,[42] 2012	1960-2007	US	Cabin crew	11 311 (1701 M/ 9610 F)	350 771	SMR (95% CI): 0.90 (0.80-1.26)[a]
Pukkala et al,[16] 2012	1947-2005[d]	Finland, Iceland, Norway, and Sweden	Cabin crew	10 066 (8507 M /1559 F)	237 627	SIR (95% CI) 2.03 (1.60-2.54)[a]
Rafnsson et al,[17] 2000	1955-1997	Iceland	Pilots	458 (458 M)	9215.50	SIR (95% CI): 10.2 (3.29-23.81)[a]
Reynolds et al,[43] 2002	1988-1995	US	Cabin crew	52 741 (8720 M/ 44 021 F)	Not stated	SIR (95% CI): 2.70 (1.33-4.06)[a]
Vågerö et al,[44] 1990	1961-1979	UK and Sweden	Pilots	Not stated	Not stated	SIR (95% CI) 2.73 (1.18-5.38)[a]
Zeeb et al,[26] 2003	1960-1997	Finland, Germany, Greece, Iceland, Italy,	Cabin crew	44 412 (11 079 M/33 063 F)	655 000	SMR (95% CI): 0.92 (0.29-1.55)[a]

Source	Data Collection	Country	Population	Total No. (M/F)	Person-years	Melanoma Risk
		Sweden, Denmark, and Norway				
		Sweden, Denmark, and Norway				

Abbreviations: HR, hazard ratio; RR, relative risk; SIR, standardized incidence ratio; SMR, standardized mortality ratio; UK, United Kingdom; US, United States.

[a]Compared with the general population.

[b]Compared with non–flight officers.

[c]In the overall cohort. Numbers of pilots, flight engineers, and navigators are not separately stated.

[d]Variable per country.