

## FLYING HOURS OF AUSTRALIAN COMMERCIAL PILOTS AND RISK OF CUTANEOUS MELANOMA

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### ABSTRACT

#### *Aim*

To compare occupational flying hours (a surrogate for occupational exposure to radiation) of commercial pilots subsequently diagnosed with melanoma, with those without melanoma.

#### *Methods*

Nested case-control study of de-identified male commercial pilots in Australia 2011-

2016, ascertained through the Civil Aviation Safety Authority (CASA). Cases were pilots diagnosed with melanoma 2011-2016; controls were randomly-selected pilots age-matched 1:2 with invasive cases. Total flying hours and hours flown in the last 6 months in 2011, date of birth and state of residence were also obtained. We estimated the association between total flying hours (in tertile groups), and melanoma by odds ratios adjusted for age and state ( $OR_{adj}$ ; 95% confidence intervals (CIs)).

### Results

During 2011- 2016, 51 pilots developed invasive melanoma and 63, in situ (mean ages 47 and 49 years, respectively). Their median cumulative flying hours in 2011 were 6,108 and 6,900 respectively, compared with 7,500 for 102 control pilots (mean age 48.6). Risk of invasive melanoma did not increase per 1000 total hours flown ( $OR_{adj}=1.00$ ) nor did risk increase in pilots with highest vs lowest total flying hours ( $OR_{adj}=1.18$ , 95% CI 0.44-3.15). Total flying hours were inversely associated with invasive melanoma development in pilots aged < 50 ( $OR_{adj}=0.37$ , not significant), and not associated with melanoma on exposed sites. Recent flying hours were not associated with melanoma. Results were unchanged with inclusion of in situ cases.

### Conclusion

Risk of melanoma in Australian commercial pilots is unrelated to cumulative or recent occupational exposure to radiation as indicated by total and recent flying hours.

### INTRODUCTION

Historically, melanoma has been regarded as a health problem that is overrepresented in airline pilots compared with the general population. Two recent systematic reviews of all published studies on this topic showed that the incidence is raised around 2-fold in pilots compared with the general population<sup>1,2</sup>. Even more concerning were the systematic review findings that melanoma

mortality rates in pilots were also significantly double the rates expected in people in the general population of the same age and sex<sup>1</sup>. The main proposed mechanism underlying these raised melanoma risks among pilots has been high ultraviolet (UV) radiation exposure outside the work environment<sup>1-4</sup>, namely through ambient and recreational sun exposure, but occupational exposures to cosmic (ionizing) radiation and to UVA radiation remain as possible contributors<sup>2</sup>.

Inspection of the published studies that have reported pilots' increased melanoma risk and increased mortality reveals them to be largely out-of-date. Virtually all studies that have been pooled were conducted last century<sup>1</sup>, and some showing high melanoma risk estimates, concerned pilots who were flying aircraft in the 1960s and 1970s<sup>3, 5, 6</sup> and even earlier in the 1940s<sup>7</sup>. Moreover, all studies summarised in the systematic reviews to date were conducted in northern Europe and North America<sup>1</sup>. Consequently, the relevance of the findings of raised melanoma risk from these systematic reviews to modern-day Australian airline pilots is questionable.

In order to address the issues of currency and local relevance, we recently conducted a study of the incidence of cutaneous melanoma in Australian commercial pilots compared with the general population<sup>8</sup>. We used de-identified data from the Australian Civil Aviation Safety Authority (CASA) for commercial pilots who had a histologically diagnosed melanoma in the period 2011-2016, and estimated age-specific incidence rates. When we compared these with corresponding population rates, we found no significant increase in the incidence rate of invasive melanoma, and a modestly raised (by around 40%) incidence rate of in situ melanoma<sup>8</sup>. We interpreted the elevated recorded rates of in situ melanoma as reflecting the more frequent (at least annual) medical surveillance that pilots undergo compared with the general population.

A major weakness of this study of Australian-licensed commercial pilots was the lack of any data regarding level of occupational exposure to radiation, either cosmic or UV. Indeed this has been a weakness of many studies of melanoma risk among airline pilots to date. With regard to ionising radiation, while there are no national occupational exposure data available for pilots in Australia, large airlines perform detailed modelling of the ionising radiation exposure of their aircrews according to their flight paths and flying hours. This suggests that a substantial proportion of Australian pilots are being monitored in this way and are not exceeding annual doses of 6 mSv, the annual reference level recommended by the

Australian Radiation Protection and Nuclear Safety Agency<sup>9</sup> or the 5-year dose limit of 100 mSv. However, while medium-term occupational limits are not exceeded, commercial pilots may be exposed to ionising radiation over lengthy careers of several decades and some pilots (e.g. those flying long haul regularly), may receive high cumulative doses of ionising radiation over their lifetimes. Similarly, concerning UV exposure, it is known that levels of UVB are low to negligible on the flight deck of modern airlines, but UVA levels may be higher<sup>2</sup>.

## AIM

We set out to address these gaps in evidence indirectly, by comparing the number of flying hours, both lifetime total, and subtotal in the previous 6 months, of pilots who subsequently developed cutaneous melanoma, with the flying hours of a group of pilots who did not develop melanoma. We hypothesised firstly that if occupational radiation (cosmic and/or UV) played a causal role, pilots with the highest total flying hours would be at increased risk of developing invasive melanoma compared with those with the lowest number of cumulative hours, and there would be a dose-response association. Given the strong correlation of age and total flying hours, we further hypothesised that any causal positive association would be stronger in younger pilots (<50 years) than in older pilots. Also if occupational UV radiation were causal as opposed to occupational cosmic radiation, we hypothesised that risk of invasive melanoma of exposed sites (head and neck, upper limbs combined) would be increased substantially among those with the highest total flying hours compared with those with the lowest totals. Finally, we speculated that if UV radiation in the last 6 months before the 2011 baseline played a promotional role in melanoma development, we would see an increased risk of invasive melanoma diagnosed in 2011-2012 among those with the highest compared with the lowest flying hours in the last 6 months. Additionally we assessed the corresponding risks of all melanoma (invasive and in situ) in the above scenarios, but this was not the primary outcome because of the likely influence of detection bias on risk of in situ disease.

## METHODS

### *Study Population*

We conducted a case-control study nested within a cohort of male commercial pilots in Australia (there were too few female pilots for meaningful analysis, and so they were excluded *a priori*). The

# ORIGINAL RESEARCH

cohort and data source have been described in detail previously<sup>8</sup>. Briefly, we ascertained the de-identified study population through the electronic Medical Record System (MRS) of CASA. CASA issues a range of licenses for the conduct of aviation in Australia, and it holds data gathered from routine medical examinations of flight crew licensees. Three different classes of medical certificates are issued to applicants who meet relevant medical standards, and commercial pilots, among others, are holders of class 1 medical certificates<sup>8</sup>.

For this study, we analysed the data of all pilots with a valid class 1 licence at any time during the period January 2011 to December 2016. Class 1 medical certificates are valid for one year, except for pilots aged 60 years or older for whom medical examination is required every 6 months. Ethical approval was obtained from the Human Research Ethics Committee of the QIMR Berghofer Medical Research Institute. We ascertained those pilots diagnosed with invasive or in situ melanoma in this period, and matched male pilots with invasive melanoma, in a ratio of 1:2, with male pilots of the same ages, randomly selected from all pilots who held a valid class 1 medical certificate in 2011 and had no melanoma history to the end of 2018. We confirmed details about cases' melanomas including date of diagnosis, anatomical site, and invasiveness by manual review of histopathology reports.

Total cumulative flying hours (including any previous military flying) and hours flown during the last 6 months in relation to pilots' 2011 application were also obtained through the CASA MRS, as well as date of birth and current state of residence.

## Statistical Analyses

We calculated median number of flying hours (inter-quartile range, IQR) at baseline in 2011 for cases and controls, and for dose-response assessment, categorised flying hours by tertile groups based on the distribution of flying hours among control pilots. Using logistic regression analyses, we calculated the crude and adjusted odds ratios (OR) and 95% confidence intervals (CIs) to estimate the association between flying hours and melanoma development, adjusting for age and state of residence as potential confounders. We also modelled flying hours as a linear term and calculated risk of melanoma per 100-hour increments of total flying hours. The primary outcome was invasive melanoma, and we performed sensitivity analyses by repeating the above analyses after the inclusion of cases with in situ melanoma. All statistical analyses were

carried out using SAS 9.4 software (SAS Institute, Cary, NC).

## RESULTS

Between 2011 and 2016, 51 pilots developed invasive melanoma (69% held an Airline Transport Pilot Licence (ATPL); 29% a Commercial Pilot Licence (CPL); 2% an 'other/unspecified' licence type), and 63 developed in situ melanoma (67% ATPL; 30% CPL; 3% 'other/unspecified'). For each invasive case, 2 controls were selected, giving 102 controls (licence types not available) included in the analysis. There was no difference in broad age groups between invasive cases and controls (Table 1) or their mean ages (47 vs. 48.6 years respectively,  $p=0.37$ ) reflecting the matching, though more pilots with in situ than invasive melanoma were aged over 50 years. The majority of pilots with melanoma lived in Queensland (40%), followed by New South Wales (24%), while the majority of pilots in the control group lived in New South Wales (32%) followed by Queensland (28%) (Table 1). Median cumulative flying hours at baseline (2011) were 6,108 for pilots with invasive melanoma; 6,900 for pilots with any melanoma (invasive or in situ); and 7,500 for control pilots, all with similar IQRs (Table 1).

Table 1. Baseline characteristics of male pilots included in the study

Characteristics	Invasive cases only (n=51)	Invasive + in situ cases (n=114)	Controls (n=102)
Age (in years) at diagnosis, mean (SD)	47 (10.1)	49 (11.3)	48.6 (11.3)
Age group, n (%)			
<50	30 (59)	57 (50)	60 (59)
50+	21 (41)	57 (50)	42 (41)
State of residence, n (%)			
QLD	19 (37)	45 (40)	29 (28)
NSW	12 (24)	27 (24)	33 (32)
VIC	10 (20)	20 (18)	15 (15)
Other States	10 (20)	22 (19)	25 (25)
Total flying hours, median (IQR)	6108 (1900-14200)	6900 (2215-15060)	7500 (2725-14150)
Hours flown in last 6 months, median (IQR)	200 (54-350)	200 (70-328)	206 (80-323)

# ORIGINAL RESEARCH

Estimated risk of invasive melanoma per 1000 total flying hours was 0.99 (crude) and 1.00 (95% CI: 0.94-1.04) after adjustment for age and state of residence. Pilots in the highest (median 16,490) vs lowest (median 1,680) tertile group for total flying hours had a slightly decreased crude risk of invasive melanoma (OR<sub>crude</sub>=0.89) which rose slightly after adjustment (OR<sub>adj</sub>=1.18) but non-significantly with very wide 95% CI (0.44- 3.15) (Table 2). Risk of invasive or in situ melanoma (combined) was neither increased on crude nor adjusted analysis (OR<sub>adj</sub>=0.85, 95% CI: 0.40-1.79) when comparing those in the highest and lowest tertile groups of total flying hours (Table 2).

Table 2. Association between flying hours and melanoma risk among class 1 male pilots

Total flying hours	Invasive cases only OR (95% CI) (n=51)	Invasive + in situ cases OR (95% CI) (n=114)
<b>Crude analyses</b>		
Total flying hours (per 1000hrs) <sup>1</sup>	0.99 (0.94-1.04)	1.00 (0.96-1.04)
Total flying hours (Tertile groups [median, range]) <sup>2</sup>		
T1 [1680 (5, 4500)]	Reference	Reference
T2 [7500 (4800, 12378)]	0.94 (0.42-2.13)	0.88 (0.46-1.69)
T3 [16490 (12470, 28000)]	0.89 (0.39-2.03)	0.90 (0.47-1.73)
<b>Adjusted analyses<sup>3</sup></b>		
Total flying hours (per 1000hrs) <sup>1</sup>	1.00 (0.94-1.06)	1.00 (.95-1.04)
Total flying hours (Tertile groups)		
T1	Reference	Reference
T2	1.08 (0.45-2.57)	0.85 (0.43-1.67)
T3	1.18 (0.44-3.15)	0.85 (0.40-1.79)

<sup>1</sup>Total flying hours modelled as linear term per 1000 hours increase

<sup>2</sup>Tertile distribution are presented as [median (min, max)]

<sup>3</sup>Models adjusted for age and state of residence

When we restricted analyses to pilots aged <50 years to minimize residual confounding by age, results were similarly null or negative. After adjustment for state of residence, there was a non-significant 7% decrease in risk of invasive melanoma for every extra 1000 flying hours recorded, and a non-significant inverse association in the pilots aged < 50 years who were in the highest (median 12,985) vs lowest (median 893) groups for total flying hours (OR<sub>adj</sub>=0.37, 95% CI: 0.09-1.36) (Table 3). Including in situ melanoma made no difference to these results.

Table 3. Association between flying hours and melanoma risk among class 1 male pilots ages less than 50 years at time of diagnosis

Total flying hours	Invasive cases only OR (95% CI) (n=30)	Invasive + in situ cases OR (95% CI) (n=57)
Total flying hours (per 1000hrs) <sup>1,2</sup>	0.93 (0.84-1.02)	0.94 (0.86-1.02)
Total flying hours (Tertile groups [median, range]) <sup>2,3</sup>		
T1 [893 (5, 3100)]	Reference	Reference
T2 [5000 (3200, 9800)]	1.04 (0.38-2.89)	1.12 (0.46-2.73)
T3 [12985 (10060, 20561)]	0.37 (0.09-1.36)	0.42 (0.14-1.28)

<sup>1</sup>Total flying hours modelled as linear term per 1000 hours increase

<sup>2</sup>Models adjusted for age and state of residence

<sup>3</sup>Tertile distributions are presented as [median (min, max)]

We next examined risk of melanoma specifically of the head and neck and upper limbs in relation to total flying hours, and again found no increase in invasive melanoma on these exposed sites in pilots with the highest vs lowest flying hours (OR<sub>adj</sub>=0.99, 95% CI: 0.20-4.91) or in risk of invasive and in situ melanoma combined (Table 4).

**Table 4.** Association between flying hours and melanoma risk among class 1 male pilots diagnosed with melanoma on head and neck and upper limbs

Total flying hours	Head & Neck & Upper Limb	
	Invasive cases only OR (95% CI) (n=13)	Invasive + in situ cases OR (95% CI) (n=38)
Total flying hours (per 1000hrs) <sup>1,2</sup>	1.01 (0.91-1.11)	0.99 (0.93-1.05)
Total flying hours (Tertile groups) <sup>2</sup>		
T1	Reference	Reference
T2	0.61 (0.13-2.83)	0.85 (0.33-2.18)
T3	0.99 (0.20-4.91)	0.81 (0.29-2.20)

<sup>1</sup>Total flying hours modelled as linear term per 1000 hours increase

<sup>2</sup>Models adjusted for age and state of residence

Finally, when we assessed associations between number of hours flown in the 6 months before 2011 baseline, and invasive melanoma diagnosed in 2011-2012, we found that they also tended to be inverse after adjusting for age, state and total flying hours. There was a non-significant 15% decrease in invasive melanoma risk for every 50-hour increment in recent flying hours (OR<sub>adj</sub>=0.85, 95% CI: 0.68-1.05) and a non-significant 60% decrease in those with the highest (median 350) vs lowest (median 48) number of hours flown in the previous 6 months (OR<sub>adj</sub>=0.39, 95% CI: 0.09-1.69) (Table 5). There was no substantive difference when pilots with in situ melanoma were included.

**Table 5.** Association between flying hours and melanoma risk among class 1 male pilots diagnosed with melanoma in 2011-2012

Total flying hours	Year of Diagnosis 2011-2012	
	Invasive cases only OR (95% CI) (n=22)	Invasive + in situ cases OR (95% CI) (n=45)
Hours flown in last 6 months (per 50hrs) <sup>1,2</sup>	0.85 (0.68-1.05)	0.98 (0.85-1.13)
Hours flown in last 6 months (Tertile groups [Tertile groups]) <sup>2,3</sup>		
T1 [0.48 (0, 114)]	Reference	Reference
T2 [200 (120, 270)]	0.45 (0.11-1.86)	0.76 (0.26-2.24)
T3 [350 (300-690)]	0.39 (0.09-1.69)	0.66 (0.22-2.05)

<sup>1</sup>Hours flown in last 6 months modelled as linear term per 50 hours increase

<sup>2</sup>Models adjusted for age, state of residence and total flying hours

<sup>3</sup>Tertile distributions are presented as [median (min, max)]

## DISCUSSION

In this study we tested the hypothesis that high exposure to occupational radiation increases the risk of invasive melanoma in Australian commercial pilots, by using total flying hours as a surrogate indicator of accumulated level of exposure. We found no association between total flying hours and development of invasive melanoma overall, and also no increase in risk when we limited the analysis to pilots younger than 50 years to reduce confounding by age. To further test the UV causal hypothesis, we estimated risk of melanoma only on anatomic sites potentially exposed to UV on the flight deck (head, neck and upper limbs combined) in relation to total flying hours, and results again showed no or inverse associations but results were very imprecise due to the small number of eligible cases. Finally, we evaluated the possible promotional role of recent occupational UV radiation in the development of melanoma in pilots, by examining the risk of invasive melanoma in 2011-2012 in those with the highest vs lowest number of hours flown in the previous 6 months. Again, there was a decrease in ORs for invasive melanoma after adjustment for other factors including total flying hours. Corresponding results of the above analyses were unchanged when we expanded the to include in situ melanoma.

These findings are reassuring and are consistent with our previous study that showed no increase in melanoma incidence in commercial pilots compared with the general population<sup>8</sup>. The present results supplement the earlier descriptive evidence by including normative data for flying hours in pilots without melanoma, and then confirming a lack of dose-response relationship between increasing total flying hours among pilots (ranging from the lowest group median of 1,680 to highest group median of 16,490) and melanoma diagnosis. We recognize that total flying hours is an imperfect surrogate for accumulated occupational radiation exposure when this measure takes no account of variation with different cruising altitudes and routes flown, for example, the higher exposure to ionising radiation among pilots who regularly fly polar routes compared with lower latitude routes.

However, we believe that these Australian data can distinguish the melanoma risk of pilots, especially the younger pilots, who have flown many long-haul routes, and thus these data

represent an advance on the amount and quality of evidence regarding dose-response for flying hours and melanoma in contemporary pilots. Some previous studies have also examined flying hours in relation to risk of melanoma, but there were limitations and mixed results. For instance, a study of Icelandic airline pilots was based on only 5 cases of melanoma, and though they reported a strong association between flying hours and melanoma, they were unable to properly evaluate dose-response<sup>10</sup>. A Norwegian study reported a rise in melanoma incidence in pilots with increasing total flying hours, but these were pilots licensed between 1946 and 1994, a time, as the authors acknowledged, when long-range inter-continental flights likely represented increased opportunity for leisure-time sunbathing<sup>7</sup>. A more recent UK study of cancer in pilots found that melanoma rates were increased not only in flight crew with increasing number of flying hours, but also in air traffic controllers with increasing number of radar hours, with no excess rates seen among the pilots compared with the air traffic controllers<sup>4</sup>. Furthermore, melanoma rates in both occupational groups were most strongly predicted by sun-sensitive skin and sunbathing to get a tan<sup>4</sup>. Our previous systematic review found that a few other studies had reported dose-response relationships between estimated exposure to UV or cosmic radiation and cancers of the skin (including melanoma) based on employment duration or flying hours, but the diversity of measures prevented any pooled estimation of dose-response<sup>1</sup>.

Our study of pilots' total cumulative flying hours as a de facto measure of long-term exposure to cosmic radiation adds to evidence that relies mostly on evaluation of annual doses of cosmic radiation<sup>11</sup> or at most 5-year doses. This is because a measure of potential accumulated radiation dose over a pilot's lifetime is likely to be far more pertinent to risk of occupational carcinogenesis in the long term. While the two above-mentioned Nordic studies<sup>7, 10</sup> also modelled cumulative mSv doses in their pilots, small numbers of cases restricted their assessments of a possible association with melanoma.

The relatively small number of pilots with invasive melanoma diagnosed in our study, also limited our own ability to explore detailed hypotheses in subgroups (eg by site or year of diagnosis of melanoma), even though our Australian series was considerably larger than most European series. Also we were unable to adjust for risk factors such as skin phenotype and recreational sun exposure, although confounding by the former is unlikely since flying hours should be unrelated to phenotype. We did adjust for state of residence,

which controlled for ambient UV exposure (assuming stable state of residence for most pilots) and therefore recreational sun exposure to some degree, and as well, this controlled for the large differences in background melanoma incidence in Australia by state<sup>8</sup>. Our cases and controls included a mix of pilots with a class 1 licence, with about two-thirds of the cases holding an ATPL<sup>8</sup> and a presumed half of the controls (since half of all class 1 licence holders at that time held an ATPL<sup>8</sup>). There were 5 control pilots and one case pilot (with in situ melanoma) who reported zero flying hours in the previous 6 months in 2011, and the median recent flying hours in the tertile subgroup of controls with lowest flying hours in the previous 6 months was 48, indicating that most in our study were active commercial pilots.

## CONCLUSION

Notwithstanding the various study limitations, these data add new evidence in favour of the null hypothesis, namely that the risks of invasive melanoma, and of invasive and in situ melanoma combined, do not increase in Australian pilots with increasing accumulated occupational exposure to radiation, cosmic and/ or UV, as measured by total flying hours.

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