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Melanoma incidence in Australian commercial pilots, 2011-2016

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What is already known about this subject?

Commercial pilots have been consistently reported as having increased risks of developing and dying from melanoma; however most studies have been conducted in Northern Hemisphere populations and moreover are not contemporary.

What are the new findings?

Australian-licensed commercial pilots have a modestly raised risk of *in situ* melanoma but no elevation of invasive melanoma compared with the general population.

How might this impact on policy or clinical practice in the foreseeable future?

A re-examination of the risk of melanoma in contemporary commercial pilot cohorts across different latitudes is warranted.

ABSTRACT

Objectives: Occupational exposure to cosmic and ultraviolet radiation may increase airline pilots' risk of cutaneous melanoma. Meta-analyses of available data show a higher than average incidence of melanoma in airline pilots, but the most recent systematic review revealed that few contemporary data are available. Moreover all relevant studies have been conducted in Northern Hemisphere populations. We therefore aimed to examine if Australian commercial pilots have a raised incidence of melanoma compared with the general population.

Methods: We examined all melanoma histologically diagnosed among Australian-licensed commercial pilots in the period 2011-2016 by manually reviewing de-identified data in the medical records system of the Australian Civil Aviation Safety Authority. We estimated age-specific incidence rates and compared these with corresponding population rates using standardised incidence ratios (SIRs) as measures of relative risk. Expected numbers were calculated by multiplying age- and calendar period-specific person-years (PYs) with corresponding rates from the entire Australian population; 95% confidence intervals (CI) were calculated assuming a Poisson distribution of the observed cases.

Results: In this cohort of Australian-licensed commercial pilots observed for 91,370 PYs, 114 developed a melanoma (51 invasive, 63 *in situ*). More than 50% of melanomas occurred on the trunk, and the predominant subtype was superficial spreading melanoma. The SIR for invasive melanoma was 1.20 (95% CI 0.89-1.55) and for melanoma *in situ,* 1.39 (95% CI 1.08-1.78).

Conclusion: Australian-licensed commercial pilots have a modestly raised risk of *in situ* melanoma but no elevation of invasive melanoma compared with the general population.

INTRODUCTION

Although the health of commercial airline pilots is above average, with lower all-cause mortality than the general population,[1] they have been consistently reported as having increased risks of developing and dying from melanoma.[2] Recent meta-analysis of relevant published studies found a significant doubling of incidence of melanoma in airline pilots compared with the general population.[2,3]

Pilots are potentially occupationally exposed to a unique combination of several potentially harmful environmental factors.[4] These factors include high annual exposures to cosmic (ionising) radiation[5] and to ultraviolet (UV)A radiation on the flight deck.[6] Both types of radiation may independently increase the risk of melanoma, though the case for UV is stronger[7] than for ionising radiation.[8,9] The elevated risk of melanoma has been supported by an observed significant increase in other skin cancers in pilots as well, suggesting shared causation by increased UV or ionising radiation or both.[3]

It is also possible that the increased incidence of melanoma and keratinocyte cancer in pilots compared with the general population is partly or wholly explained by higher levels of recreational sun exposure. This is supported by the observation of a similar increase in risk of melanoma[2] and keratinocyte cancer among cabin crew who are not exposed to UV during flights.[3] Also a study of the complexion phototype and recreational sun exposure of aircrews in Iceland in the 1990s found that while the distribution of skin type was not different to the general population, pilots (and cabin crew) had significantly more sunny vacations, and were more likely to have a history of severe sunburns both before and after the age of 19 years.[3] However, the authors considered that the magnitude of the association between aircrews and number of sunny vacations was not sufficient to explain the relatively large difference in melanoma incidence compared with the general population, and postulated the existence of another cause of melanoma in aircrews besides excessive leisure-time sun exposure.[3]

Another potential harm experienced by commercial airline pilots and shared by cabin crew, is circadian rhythm disruption, in particular for those working on long-haul flights; data from the US suggest that a proportion of pilots are affected by sleep disturbance.[10] There is some evidence from animal models that shiftwork that involves circadian disruption is carcinogenic, but there is limited evidence in humans, particularly in relation to melanoma.[11,12]

Given the uncertainty regarding the relation of occupational hazards to risk of melanoma in pilots, and the recent call for further research on the long-standing reports of increased melanoma incidence and mortality in pilots,[13] we addressed the issue in commercial pilots who hold Australian licences and who live and work in the context of high background incidence rates.[14] An investigation of Australian pilots was of additional interest given that the extant literature on melanoma risk in commercial airline pilots is dominated by studies conducted in pilots from the Northern Hemisphere where both ambient UV levels and melanoma incidence rates are lower than for Australia.[3,15] Furthermore, there are few contemporary data; some of the relevant pilot studies date as far back as 1943.[16] Our specific aim therefore was to examine if current Australian-licensed commercial pilots have a raised incidence of melanoma compared with the general population.

METHODS

This was a retrospective study based on the electronic Medical Records System of the Civil Aviation Safety Authority (CASA) and was approved by the Human Research Ethics

Committee of the QIMR Berghofer Medical Research Institute. CASA regulates civil aviation safety in Australia and is responsible for licensing all Australian pilots. The Medical Records System holds data gathered from medical examinations of holders of all commercial certificates, and most private certificates. For the purposes of the present study, we examined the de-identified data of all flight engineers and pilots issued with a valid 'Class 1' medical certificate permitting commercial and air transport operations, in the period 1 Jan 2011 to 31 Dec 2016. These medical certificates are valid for 12 months. For pilots aged 60 years and over seeking air transport licences, medical examinations are required every 6 months. There are several types of licence in the Class 1 category and we prioritized them as follows: Airline Transport Pilot Licence (ATPL); Commercial Pilot Licence (CPL); and 'other/unspecified'. Pilots with an ATPL issued by CASA can be airline pilots, pilots of chartered smaller aircraft, helicopter pilots, transport pilots and flight instructors; pilots with a CPL licence can operate as airline co-pilots. A small group of others with lower level licences (Student Pilot Licence, SPL; Private Pilot Licence, PPL) may also obtain a Class 1 medical certificate.

Commercial pilots in Australia are obliged under the Civil Aviation Act 1988 to disclose a diagnosis of melanoma to their Designated Aviation Medical Examiner upon medical examination. Melanoma diagnoses were identified through a comprehensive search of the Medical Records System followed by manual review of records relating to each diagnosis. Data extracted included date of birth, sex, date of renewal of licence, and state of residence. All study cases were histologically confirmed and details of date of diagnosis, histological subtype, body site, and for invasive melanomas, thickness and ulceration were also extracted.

Age-specific melanoma incidence rates among Class 1 medical certificate holders were compared with corresponding rates in the general population of Australia obtained from the Australian Institute of Health and Welfare (AIHW).[17] For invasive melanoma, national incidence data were available for the years 2011-2015; we thus used age-specific 2015 invasive melanoma incidence rates for the year 2016. Previous analyses have shown that invasive melanoma incidence rates in Australia were stable between the years 2005 and 2011 and were projected to remain stable for the period 2012-2016.[18] For *in situ* melanoma, national incidence rates were available only for the year 2012.[19] We therefore used the age-specific melanoma *in situ* incidence rates from 2012 for the years 2013-2016. We conducted a sensitivity analyses assuming an increased in incidence of melanoma *in situ* over the period 2013-2016 using the rate of increase observed in the state of Queensland (i.e. 4.5% per annum for those aged under 40 years, and 7% per annum for those aged 40 years or more).[20]

We calculated standardized incidence ratios (SIRs) as measures of relative risk using the indirect standardization method. The SIR is the ratio of the observed cases in the pilot population to the expected number of cases (i.e. the number of cases that would be expected in the pilot population if the age-specific rates were the same as for the Australian male population); 95% confidence intervals (CIs) were calculated assuming a Poisson distribution of the observed cases.

The study was approved by the Human Research Ethics Committee of the QIMR Berghofer Medical Research Institute. All data from CASA was de-identified prior to release to the research team.

All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Only few licenced commercial pilots were women (6%) and thus we restricted our analyses to males. Their median age category was 35-39 years and their state of residence was as follows: Queensland 25%; New South Wales 24%; Victoria 18%; Western Australia 11%; South Australia 5%; Tasmania 1%; Northern Territory 2%; Australian Capital Territory; and "unknown/overseas" 7%. The majority of pilots were issued with an ATPL (51%); 34% held a CPL and 15% 'other/unspecified' licence types.

In the study cohort of male commercial pilots, 114 developed a melanoma during 91,370 person-years of follow-up (51 invasive, 63 *in situ*) (Table 1). No pilots were diagnosed with multiple primary melanomas in the study period. The mean age at diagnosis was 49 years (SD 11). The highest number of cases occurred in pilots residing in Queensland (39%), followed by New South Wales (25%), and Victoria (18%) (Table 1). More than 50% of the melanomas occurred on the trunk, and the predominant subtype was superficial spreading melanoma. The average thickness of invasive melanomas was 0.75 mm (median 0.60 mm). Of the invasive cases, 69% held an ATPL, 29% a CPL and 2% an 'other/unspecified' licence type. Of the *in situ* cases 67% held an ATPL, 30% a CPL and 3% an 'other/unspecified' licence type.

The age-standardized incidence rate for invasive melanoma among pilots was 56/100,000, and 65/100,000 for melanoma *in situ*. The observed number of invasive cases among pilots was close to that expected based on the cancer incidence of the general male Australian population, considering age and calendar period. The SIR for invasive melanoma was 1.20 (95% CI 0.89-1.55) (Table 2). In our primary analysis for *in situ* melanoma, the observed number of cases was higher than expected based on incidence in the general population and the SIR was 1.39 (95% CI 1.08-1.78). In our sensitivity analysis which modelled an increase in melanoma *in situ* incidence in the Australian population, the SIR was no longer significant (1.24; 95% CI 0.94-1.54).

Table 1. Baseline characteristics of melanoma cases in Class 1 male pilots.

Parameter	Invasive n=51	*In situ* n=63
Age at diagnosis (years)		
Mean (SD)	47.1 (±10.1)	51.1 (±11.9)
Median (IQR)	48 (43-54)	52 (43-60)
Min	17	24
Max	63	73
Age group, n (%)		
< 20	1 (2)	0 (0)
20–29	2 (4)	5 (8)
30–39	5 (10)	7 (11)
40–49	22 (43)	15 (24)
50–59	16 (31)	19 (30)
60–69	5 (10)	14 (22)
70 +	0 (0)	3 (5)
State of residence, n (%)		
Queensland	19 (37)	26 (41)
New South Wales	12 (24)	16 (25)
Victoria	10 (20)	10 (16)
Western Australia	8 (16)	7 (11)
South Australia	1 (2)	2 (3)
Tasmania	0 (0)	1 (2)
Others (outside Australia)	1 (2)	1 (2)
Body site, n (%)		
Head & Neck	5 (10)	9 (14)
Trunk	27 (53)	30 (48)
Upper limb	10 (20)	8 (13)
Lower limb	8 (16)	14 (22)
Missing	1 (2)	2 (3)
Melanoma type, n (%)		
Superficial spreading	26 (51)	14 (22)
Lentigo maligna		8 (13)
Nodular	4 (8)	
Malignant, NOS	18 (35)	
Other[a]	3 (6)	
In situ, NOS		41 (65)
Invasive thickness (mm)		
Mean (SD)	0.75 (±0.6)	
Median (IQR)	0.60 (0.3-1.02)	
Min	0.2	
Max	3.3	
Ulceration (Invasive), n (%)		
No	51 (100)	
Yes	0 (0)	

IQR – inter-quartile range; SD – standard deviation
[a] Other for invasive melanoma: spindle cell melanoma NOS, desmoplastic malignant melanoma, and epithelioid cell melanoma.

Table 2. Standardised incidence ratios for melanoma for male commercial pilots in Australia.

Case definition	Observed cases	Expected cases	SIR	95% CI
Primary analysis				
Invasive	51	43	1.20	0.89-1.55
In situ	63	45	1.39	1.08-1.78
Sensitivity analysis				
In situ	63	51	1.24	0.96-1.57

DISCUSSION

We have shown that Australian-certified commercial pilots do not have an increased risk of invasive melanoma compared with the general population and their features (site, histology) are the same as for the rest of the population.[21-24] Of the 51 invasive melanomas, 34 (67%) were less than or equal to 1 mm. In the Australian population over the time period 1990-2006, 61% of invasive melanomas diagnosed in men were less than or equal to 1 mm at diagnosis.[23]

The observation of an elevated risk of *in situ* melanoma compared with the general population is consistent with heightened surveillance. It is unlikely to be associated with pilots' occupational exposures because place of residence is an overall determinant of *in situ* melanoma risk in commercial pilots, with the highest proportion of cases occurring among those residing in the northerly state of Queensland as for the general population.[23] Queensland experiences the highest average ambient UV exposure of all Australian states and territories (ASR 72.2/100,000; latitude range 11-29ºS), followed by Western Australia (59.4/100,000; 14-35 ºS), New South Wales (51.2/100,000; 29-37ºS), Tasmania (46.8/100,000; 41-44ºS), South Australia 36.6/100,000; 26-38ºS), and Victoria (40.3/100,000; 34-39ºS).[25] The mean age at diagnosis of melanoma in the pilot cohort was lower than for the general Australian population[26] (47 years vs 63 years, respectively); however this likely reflects the lower age distribution of the occupational cohort. The body site distribution of invasive melanoma cases in the pilot cohort was similar to the distribution in the population of Queensland for the period 2011-2015. Notably, there was no excess in melanoma of the head and neck or upper limbs, which would be expected if occupational UV exposure were causal.

Most of the extant literature relating to melanoma risk in pilots relates to airline pilots. Two recent systematic reviews both reported a significantly elevated risk of melanoma among airline pilots.[2,3] Our findings are not directly comparable with these recent meta-analyses because our cohort included a heterogeneous mix of pilots with a Class 1 commercial licence; approximately half held an ATPL. Of the melanoma cases identified, approximately two-thirds held an ATPL. We were unable to use ATPL status to classify occupational exposures of airline pilots in this cohort due to the diversity of the population of pilots holding this type of licence, and their likely differences in occupational exposures.

Other notable features of most of the studies included in the reviews to date are their restricted locations and time periods of study. Most have been conducted in populations from the northern hemisphere and many include historical pilot cohorts dating back as far as the mid-1900's.[2,3] Several studies included in the systematic review by Sanlorenzo et al.[2] had included military pilots,[27,28] who may have a different suite of occupational exposures compared with airline pilots. Furthermore, one of the included studies lacked consistency in melanoma ascertainment in the pilot cohort and comparison population (i.e. from self-report in the pilot cohort, but histologically confirmed from cancer registry records in the general population).[29] A recently published study conducted in New Zealand which reported a greatly elevated risk (50-fold) of melanoma among New Zealand airline pilots was subject to the same limitation; melanomas were self-reported (not histologically confirmed) in the pilot cohort but histologically confirmed in the general population, and thus the findings are subject to recall and misclassification bias.[30] This recent study was not eligible to be included in the recent systematic review which was restricted to studies that included histologically confirmed cases.[3]

There is no consistent evidence that ionizing radiation causes melanoma, although the evidence base is derived largely from studies in atomic bomb survivors and nuclear workers.[7,9] Air crews are exposed to the highest average annual effective dose of ionizing radiation (ranging from 1.2-5.0 mSv), of all occupationally exposed groups,[8] although current higher altitude, long-haul polar flights may potentially increase total exposure. In the United States an estimated 38% of all occupational exposure occurs in the aviation industry (this compares with 39% for medical workers, and 8% for commercial nuclear power plant workers).[31] The annual effective dose of a few mSv is equivalent to exposure from natural sources (radon, foods and beverages, and from rocks, soil and buildings materials).[31] There are no nationally available data on occupational exposure to ionising radiation among pilots in Australia, but some airlines model the ionising radiation exposure of their aircrews to ensure it is in line with the Australian Radiation Protection and Nuclear Safety Agency's recommended annual reference level of 6 mSv.[32]

Perhaps the most likely explanation for previously observed increased incidence of melanoma and keratinocyte cancer in airline pilots compared with the general population relates to higher levels of recreational sun exposure amongst pilots. It is possible that in the past, airline pilots had greater opportunity for sun exposure during layovers than current work practices allow. Alternatively, our discordant finding of a non-elevated risk in Australian pilots may reflect the varying proportions of occupational vs. recreational UV radiation exposure in comparison with pilots residing in higher latitude locations and with lower ambient UV levels. That is, the contribution of occupational exposure to total UV exposure is likely lower for Australian-certified commercial pilots.

Our study has several strengths. We examined a large nationally representative sample of commercial pilots, with the ability to examine individual level data. We were also able to examine melanoma *in situ* as well as invasive melanoma outcomes. All melanomas were histologically confirmed from pathology records.

We acknowledge some limitations of the analyses. Our estimate of expected cases of melanoma *in situ* in the Australian population may be an underestimate, as data on incidence were available only to 2012, and we assumed that the age-specific rates remained stable over the period 2013-2016. The SIR we have reported for melanoma *in situ* may therefore be an overestimate of the true SIR. We conducted sensitivity analyses modelling an increase in melanoma *in situ* incidence in the Australian population and the SIR was no longer significant.

We also note the possibility of under-reporting of melanoma diagnoses that may occur between compulsory examinations, despite a legal requirement for all commercial pilots to disclose this information. The medical examination includes a consultation, a physical examination and a review of the applicant's medical history. Because we identified our cohort through a licensing body, it is possible that not all licensed pilots were using their qualification, which would result in exposure misclassification; however, we expect that the extent of this premise is small. Pilots may also have entered or left the cohort during the study period. We conducted a sensitivity analysis assuming and applying the observed melanoma incidence rate to the number of pilots who failed to renew their Class 1 licence during the study period (n=285). We assumed, most conservatively, that this group experienced melanoma at five times the rate observed, resulting in one additional melanoma case and no material change to the SIR (1.23; 95% CI 0.93-1.61).

Our analyses were restricted to male pilots and finally, information on personal exposure to both ionising and UV radiation were not available, and we were therefore unable to conduct dose-response analyses. A prospective cohort study with reliable and comprehensive information on occupational and recreational radiation exposures, together with information on phenotype and other environmental risk factors collected in the correct temporal sequence would enable definitive dose-response analyses and causal modelling.

In summary, Australian-certified commercial pilots do not have an elevated risk of invasive melanoma compared with the general population. Our study is the first to report on risk of histologically confirmed melanoma for a southern hemisphere commercial pilot population, and the first to report data on melanoma incidence for a pilot cohort with only recent follow-up (2011-2016). A re-examination of the association in contemporary pilot populations across different latitudes is warranted.

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COMPETING FINANCIAL INTERSTS

None to declare.

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CONTRIBUTORS

CO, KM, and AG designed the study and directed its implementation. JD, MD and PC gathered the data. CO and JD performed the statistical analysis. AG, CO, KM IH, RB, RT, KK, and MN obtained funding for the study. CO and AG drafted the manuscript, and all other authors (KM, JC, IH, RB, MD, PC, JM, RT, KK, and MC) revised the manuscript providing important intellectual content.

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