The prevalence of occupational health problems in flight crews (pilots and flight attendants): a Systematic Review and Meta-Analysis

Dr Foad Omran

Dissertation in partial fulfilment of the requirements for the degree

MASTER'S OF PUBLIC HEALTH

Faculty of Health Sciences

University of Cape Town

Supervisors:

Professor Mark E. Engel

Associate Professor Shahieda Adams
Ameer Hohlfeld

Department of Public health

University of Cape Town

February 2023

PLAGIARISM DECLARATION

"This thesis/dissertation has been submitted to the Turnitin module (or equivalent similarity and originality checking software) and I confirm that my supervisor has seen my report and any concerns revealed by such have been resolved with my supervisor."

Name: Foad Omran

Student number: OMRFOA001

Signature: Signed by candidate

Date: 10/02/2023

Acknowledgements

First and foremost I am extremely grateful to my supervisors Professor Mark Engel and Associate Professors Shahieda Adams for their invaluable advice, continuous support, and patience during my Master study. I would not have made it without them. I would also like to thank Ameer Hohlfeld and Associate Professor Mahmoud Werfalli for their technical support on my study. I would like to express my gratitude to my parents, my wife and my children. Finally, I would like to thank Doctor Itumelenge Ntatamala for the studentship that allowed me to conduct this thesis.

This work would not have been possible without the University of Cape Town school of Public health accepting me into their programme; I would like to take the opportunity to commend the value the institution keeps adding to the world.

Table of Contents

List of abbreviations

ICAO	The International Civil Aviation Organisation
UN	a United Nations
NCRP	National Council on Radiation Protection
PROSPERO	International Prospective Register of systematic reviews
OR	Odds Ratio
CI	Confidence interval
SMR	Standardized Mortality Ratios
SIR	Standardized Incidence Ratio
PMR	Proportional Mortality Ratio
CMDs	Common Mental Disorders
ACM	Aircrew Members
OHPs	Occupational Health Problems
NIH	The National Institutes of Health
PPR	Pooled Prevalence Rate
FSD	Fatigue/Sleep related disorders
ENT	Ear, Nose and Throat
MSD	Musculoskeletal disorders
PTSD	Post-traumatic stress disorder
IARC	The International Agency for Research on Cancer

PART A: Protocol

ABSTRACT

Introduction: Aircrew members are potentially exposed to many factors that may increase their risk of contracting work-related health problems. Epidemiological studies of aircrews in commercial aviation did not receive much attention until recent decades. To date, there has not been a systematic review of the literature to provide evidence for adverse health consequences related to occupational exposures among aircrew members. We seek to perform a systematic review of observational studies to determine the prevalence of occupational health problems in-flight crews as compared with the general population.

Methods and analysis: We will identify relevant empirical literature through a comprehensive search, using a predefined search strategy, across multiple electronic databases. Electronic databases will include PubMed, Medline, EMBASE, PsycINFO, and the Cochrane Database of Systematic Reviews. Two researchers will independently evaluate the articles retrieved, and from studies meeting pre-specified inclusion criteria, appraise the studies using a peer-reviewed quality assessment tool for observational studies, before extracting relavent data onto a peer-reviewed data extraction form; Any disagreements will be resolved through discussion, consensus and by consulting a third author. We will use RevMan (version 5.2) to analyse the data. This systematic review will be reported according to the PRISMA template.

Ethics and dissemination: Ethics approval is not necessary for the systematic review as it utilises data from published studies; nevertheless, a waiver will be obtained. The findings of this study will be widely disseminated through peer-reviewed publications and conference presentations. Updates of the review will be completed to inform and guide occupational health policy and practice for in-flight crew members.

Prospero Registration Number: CRD42020167631

Introduction

The International Civil Aviation Organisation (ICAO), a United Nations(UN) body, reports that in at least every 15 years, the "global air transport network" doubles in size (1). Since 1931, flight attendants have worked on aircrafts; in 1985 United States airlines employed 40,000 flight attendants (2)and by 2019, the number had increased to almost 120,840 (3).

Given the expectation of aircrew members to be healthier than the general population, potential staff are carefully chosen according to special criteria and undergo regular medical examinations. However, epidemiological studies show that aircrew members are at high risk for several diseases when compared with the general population. These are specific to the industry such as an association between high work demand and musculoskeletal symptoms of the neck (odds ratio (OR)=2.04, (95% confidence interval (CI)1.45-2.88))and lower back (OR=1.42, 95 % CI 1.02-1.96) (4), higher prevalence of cataracts (5, 6), hearing loss (7), infections (8-11) and illnesses related to pesticide exposure (12). Besides, skin conditions including dermatitis (13) and dryness appear to be ~~a~~ frequent contributors to dermatological problems among aircrew members (14, 15). Studies also show that pilots have a higher prevalence of kidney disease compared with the general population (3.3% vs 0.6%) (16). Furthermore, congenital malformations, spontaneous abortion, and premature delivery are higher among aircrew members than the general population (17, 18).

Whereas overall cancer mortality is lower in aircrew members in comparison with the general population (Cockpit crew Standardized Mortality Ratios (SMR) = 0.64, 95% CI 0.51–0.81) and (cabin crew SMR = 0.95, 95% CI 0.72–1.26) for all cancer deaths)(19), studies show that aircrew members were more likely to have skin cancer, probably related to radiation exposure. For example, malignant melanoma in aircrew members has approximately twice the incidence as compared with the general population (8, 20-23).

Crew members are also at an increased risk of reproductive cancers, probably linked to shift work and circadian disruption when compared with the general population (4.9% vs 2.9% respectively)(24, 25). Flight crews have higher rates of female breast cancers than people in the general population (Standardized Incidence Ratio (SIR) = 1.42, 95% CI 1.09–1.83) (21). Other studies have indicated an increased risk of colon cancer (Proportional Mortality Ratio (PMR)= 2.30, 95% CI 1.29-3.80), prostate cancer (PMR=2.68, 95% CI 1.23-5.08) and brain/central nervous system cancer (PMR= 11.40, 95% CI 1.38 - 41.5) in aircrew members (8).

Numerous studies reported higher rates of mental disorders among aircrew members, including Common Mental Disorders (CMDs) that have a prevalence of 29,8% among flight attendants. Flight attendants also had higher rates of psychological distress, depression, fatigue, and sleep disorders ranging from 2 to 5.7 times than those of the general population (24-27). Furthermore, there are also serious emotional and physical

consequences related to sexual harassment resulting, very often, in an inability to perform job functions effectively (28) Sexual harassment was more common among the flight attendants compared to nurses and teachers respectively, 31% vs. 8% and 4% (28). Lastly, there are aircraft accidents have ~~a~~ high mortality and is considered to be a rare cause of death in the general population (SMR = 42.8, 95% CI 27.9-65.6) (29).

Until recently, occupational health within the aircrew members has received very little attention from researchers, despite the unique and wide range of exposure to work-related risk factors (28, 30). During the flight, aircrew members are exposed to several occupational risk factors related to their work environment that affect their health and wellbeing (31) including cosmic ionising radiation, elevated ozone levels, poor cabin air quality, hypoxia, pesticides from cabin disinfection, heavy physical job demands, high levels of occupational noise, and sexual harassment (28, 32, 33). Night shift work and crossing time zones continually lead to circadian rhythm disruption. According to Business Insider's analysis of data collected from the US Department of Labour, flight attendants have one of the unhealthiest jobs in the US (34). The aircrew's poor health is attributable to six major health risks, these include but are not limited to contaminants (such as carbon monoxide (CO), biological agents and various organic chemicals), exposure to radiation, hazardous conditions, risk of cuts, minor burns, bites, stings and time spent sitting (35).

Historically, flight crew members were excluded from the Occupational Safety and Health Administration protections granted to most US employees. In 2014, some limited protections were implemented (36). However, the exposure to ionizing radiation in aircrew members was not monitored, until the National Council on Radiation Protection (NCRP) reported that aircrew members have the largest average annual effective dose of all U.S radiation employees (37, 38). The type of specific occupational hazards aircrew members are potentially exposed to in these work environments are shown in Table 1 below.

Table 1: Occupational hazards aircrew members are exposed to(39-41)

OCCUPATIONAL HAZARD	EXAMPLES
Accident Hazards	Falls, trips, and slips due to multiple dynamic forces of the moving aircraft
Physical and safety	Electromagnetic fields (EMFs), and ionizing radiation of cosmic origin, Oxygen deficiency or hypoxia, noise, changes in pressures and temperatures due to high altitude, abnormal movements, low humidity, physical and sexual harassment.
Biological	Exposure to infectious disease (hepatitis A, malaria), tuberculosis, flue, coronaviruses (Severe Acute Respiratory Syndrome ("SARS"), coronavirus disease 19 (COVID 19), and microorganisms from contaminated food (Escherichia coli, vibrios, Salmonella, and Serratia marcescens).
Chemical	Chemical pollutants and environmental agents at altitude (Ozone, CO, and CO2), flame retardant chemicals, chemicals during aircraft disinfection and aircraft surface cleaners.
Ergonomic	Musculoskeletal injuries relating to the shoulder, neck, and lower back.
Psychosocial	Shift work, sleep deprivation, crossing time zones, tiredness, fatigue, impact of passenger behavior, and sexual harassment.

Previous systematic reviews

There are three systematic reviews published between 2015 and 2019. They include a meta-analysis examining disease-specific morbidity and mortality on a variety of studies on melanoma, other skin cancers, and thyroid cancer in aircrew members (23, 42, 43). All of these studies calculated the standardized incidence ratio and standardized mortality ratio for all airline crew members. However, these studies did not conduct a comprehensive search, failing to include unpublished literature such as conference abstracts. The criteria used to critically appraise systematic reviews and meta-analyses, and summary of findings are in Table 2.

Objectives

Given all that, these previous reviews only focused on a single outcome, viz cancer, the aim of this systematic review is to provide a comprehensive evidence-based synthesis, assessing multiple outcomes, of conditions, beyond cancer, that affect the health and wellbeing of aircrew members.

In addition, this review represents an update for the following reasons: (1) It features a comprehensive search strategy (2) Critical assessment of articles will be included (3) It will include studies beyond the dates of the previous reviews. Ultimately, more specific and comparable outcomes could make systematic reviews more useful to decision-makers.

The specific research question

What is the prevalence of occupational health problems in aircrew members (pilots and flight attendants) as compared with the general population? This is the first systematic review that addresses the occupational health status within aircrew members. It is anticipated that the results of this review will serve to inform occupational health policy and practice of aircrew members.

Table 2 : Critical appraisal of the previous systematic reviews.

	Sanlorenzo M (2014)- The Risk of Melanoma in Airline Pilots and Cabin Crew AMeta-analysis	**Miura (2019)- Do airline pilots and cabin crew have raised risks of melanoma, and other skin cancers? Systematic review and meta-analysis***	**Liu G (2018)- Thyroid cancer risk in airline cockpit and cabin crew: a meta-analysis**
1. Were systematic review questions clear?	Yes	Yes	Yes
2. Did they address questions in our systematic review?	All studies were focused only on a specific outcome, Not directly adds a component of our question by looking at risks of melanoma, other skin cancers and thyroid cancer. Our study looking for multiple outcomes and risk factors that may affect the health and wellbeing of aircrew members.		
3. Was search extensive?	No. They did not search for unpublished data and the Cochrane Library	No. They did not search for unpublished data and the Cochrane Library	No. They did not search for unpublished data and not use MeSH database.
4. Dates of studies included in the reviews	1990 to 2013	1990 to 2017	1996 to 2014
5. Number of studies included.	19	12	8
6. Did they do a quality assessment with peer-reviewed tool?	Quality assessment tool of included studies not mentioned	Newcastle-Ottawa Quality Assessment Scale.	Quality assessment tool of included studies not mentioned
7. Sub-analyses appropriate?	Authors perform subgroup analyses across different subgroups (study design, cockpit vs cabin crew and by sex)	Authors perform subgroup analyses across different subgroups (cockpit vs cabin crew and by study design)	Authors perform subgroup analyses across different subgroups (cockpit vs cabin crew and by study design)
8. Reported according to the preferred Reporting Items in (PRISMA)?	Reported according to Prisma guidelines with some exceptions: Protocol not published nor registered in Prospero, data extraction not explained properly, and reviewers did not conduct risk of bias assessment.	Followed the preferred reporting items (PRISMA) and was registered with Prospero	This study was carried out following the Preferred Reporting Items (PRISMA), but with missing steps: Protocol not published nor registered in Prospero, data extraction not explained properly, reviewers did not conduct risk of bias assessment and inclusion criteria not clear (No mention of the language used)

Method

We will use the Cochrane Handbook (44) as a guide and methodological framework in designing and conducting this systematic review. Thus making the systematic review worthy of critical appraisal and replication. This protocol was published in PROSPERO International Prospective Register of systematic reviews, registration number (CRD42020167631).

Criteria for considering studies for this review

Types of studies

The systematic review will comprise of cross-sectional studies and other observational studies assessing the prevalence of occupational health problems among commercial aircrew members

Studies inclusion criteria

1. Published and unpublished cross-sectional studies reporting the prevalence rate of any occupational health problems among commercial aircrew members and/or its risk factors.
2. Articles in any language will be considered, irrespective of the date of publication.

Studies exclusion criteria

- Air force, Agricultural and Rotary-Wing Aircrew members given the varied nature of this aspect of the industry. These are not good surrogates for commercial aircrew members and are not suitable for our study.
- Studies relating to passengers or health of the general population.
- Studies of the health aspects of pilot or crew members relating to factors not thought to be occupationally related

Types of outcomes: The prevalence of the following outcomes will be of primary interest to us from studies included in this systematic review.

Primary outcomes

Cancers, Musculoskeletal problems, Kidney diseases, Skin diseases, Mental health, sleep disorders, Cataracts, Hearing loss, Mental health issues and physical consequences resulting from sexual harassment, Infections and work-related pesticide illnesses

Secondary outcomes

Deaths due to Aircraft accidents, diabetes, cerebrovascular diseases, cardiovascular diseases, and respiratory diseases.

Search strategy for identification of relevant studies

A comprehensive and sensitive search strategy will be undertaken using several electronic databases to identify prevalence studies irrespective of the date of publication. If need be we will search for a second time within three months before submitting this dissertation.

Electronic databases

1. Electroninc databases will include PubMed/MEDLINE, CINHAL, Google Scholar, EBSCO, and Cochrane Database.
2. Grey literature databases such as Grey Literature Report and in OpenGrey.

Hand searching

1. The reference lists of studies meeting our inclusion criteria will be scanned for further studies.
2. Prominent authors of studies meeting our inclusion criteria will be contacted for further studies, which they may know of.

Bibliographic databases

Database subject headings (MeSH in PubMed/MEDLINE, CINHAL, Google Scholar, EBSCO, and Cochrane Database) will be combined with a range of text words.

The search will performed by cross-referencing the words "aeroplane"," airplane","plane", " aircraft or airline", "commercial aircraft", "aviation", "aviation medicine", "aircrew", “airline pilots” , “aircraft pilots”, " aircrew personnel", "aircrew worker", " aircrew members" ,"flight attendants ", “cabin attendants”, "cabin crew ", " pilots " or " cockpit " with "mental health", "stress", "stress disorders, post-traumatic", "fatigue , psycho- logical", "depression", "anxiety", " sleep ", "sleep disorders" , "circadian rhythm", "jet lag" , "ozone", "physical health", "health status", "health problems ", “infectious diseases”, "sick leave", "mortality", "cancer ", "melanoma ", "cosmic radiations " or "wounds" "injuries", "accidents", "lung diseases", or "respiration disor- ders", "gastrointestinal dis- eases", "cardiovascular diseases", "musculoskeletal diseases", "communicable diseases, "occupational", "occupational disease".

Peer-reviewed journal articles and the grey literature (unpublished studies or unpublished outcomes) will also be searched. Other relevant sources will be identified through reference lists from the potentially included studies and other relevant studies known by the research group.

Selecting studies for inclusion

Retrieved articles from the search will be exported to Rayyan — a web and mobile app for systematic reviews(45). We will develop a screening guide to make sure that the inclusion criteria are followed and consistently applied by all review authors. Two review authors (FEO and ASH), will work independently to screen the titles and abstracts of all studies generated by the search process for eligibility. FEO will obtain the full text of studies considered to be potentially eligible. The two authors (FEO and ASH) independently will assess the full text of each article for eligibility, and compare their results and any point of disagreement will be resolved by discussion, consensus, and consulting a third author (MEE). We will describe the reasons for exclusion for all studies excluded by the assessors. Finally, the review authors will accept the remaining studies as eligible for the systematic review. A flow chart will be used to summarise the study selection process.

Quality appraisal of included studies

Hoy et al developed a a quality assessment tool specifically for use in the systematic review of prevalence data (table 2)(46, 47). Werfalli M, Musekiwa A, Engel ME, et al modified this tool based on a review. This tool will be applied to screen full-text articles to assess the quality of prevalence studies, and further refinement will be considered to improve inter-rater agreement between investigators. For this tool, bias evaluation is determined using quality scoring scale. Studies with scores greater than 8 are considered to be of high quality. Our strategy to evaluate the risk of selection and attrition bias based on the Cochrane approaches as set out in Review Manager V.5.2 (http://review-manager.software.informer.com/5.2/). This will help us to select and appraise the studies for a pooled analysis. Any disagreements should be discussed and resolved by consensus in consultation with the third author to resolve debate discrepancies.

Table 3: Quality assessment criteria for prevalence studies(46)

Items	Quality score
External validity 1. Was the study's target population a close representation of the national population in relation to relevant variables?	(1 point)
2. Was the sampling frame a true or close representation of the target population?	(1 point)
3. Was some form of random selection used to select the sample, OR was a census undertaken?	(1 point)
4. Was the likelihood of non-response bias minimal?	(1 point) Total (4 points)
Internal validity 1. Were data collected directly from the participants (as opposed to a proxy)?	(1 point)
2. Was an acceptable case definition used in the study?	(1 point)
3. Was the study instrument that measured the parameter of interest shown to have validity and reliability?	(1 point)
4. Was the same mode of data collection used for all participants?	(1 point)
5. Was the length of the shortest prevalence period for the parameter of interest appropriate?	(1 point)
6. Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	(1 point) Total (6 points)

Data extraction and management

After assessing methodological quality, two review authors (FEO and ASH) will extract data onto a pre-designed data extraction sheet and will independently encapsulate essential results for the eligible studies. These summaries will be compared, followed by resolution of any discrepancies by discussion and consensus with a third reviewer (MEE). Study characteristics will include authors, year of publication, the country where the study was conducted, study design, statistical method, journal, the language of publication, key explanatory variable and criteria for sample selection and sample size, outcomes variables and their diagnostic criteria, outcome(s) measured results and notes/comments will be presented in tables. The final data will be entered into the Cochrane Collaboration Review Manager V.5.2 statistical software (http://review-manager.software.informer.com/5.2/) by one author (FEO) the second author (ASH) will cross-check the data for data entry errors. We are anticipating that some eligible studies will not have prevalence data but will allow us to calculate the prevalence from existing data. We will contact the corresponding authors for missing information if their studies are deemed relevant for this review. References will be managed using Endnotes 20.3 (48).

Data synthesis including assessment of heterogeneity

We will calculate the summary prevalence of health conditions for all airline crew members using the Cochrane Collaboration Review Manager V.5.2 statistical software (http://review-manager.software.informer.com/5.2/). Prevalence estimates and their respective 95% Cl and p values will be calculated. Heterogeneity will be assessed by visually inspecting forest plots initially, then through, Cochran's Chi^2 test where the heterogeneity is considered statistically significant if the p-value <0.10. This will be followed by the I^2 statistic tests, where the guide for interpretation is: 0%-40% might not be important, 30%-60%, moderate heterogeneity, 50%-90%, substantial heterogeneity and 75%-100% considerable heterogeneity (49). We will use a fixed-effects model only if studies are judged to be homogeneous, otherwise the random-effects model will be employed (50). We plan to conduct subgroup analyses based upon the location on the plane, cockpit crew (e.g. pilots), cabin crew (e.g. flight attendants), and use the following variable; age, sex.

Furthermore, we plan to do sensitivity analyses to determine the potential sources of heterogeneity and we will determine the impact of including only high-quality studies on the result. The findings will be presented as a narrative form if the heterogeneity remains significant including tables and figures to highlight the main existing evidence. The narrative summary will be written by the first author and then checked independently by the other reviewers; all reviewers will discuss any disagreements.

Assessment of reporting biases

Funnel plots will be generated, and using Begg's and Egger's tests**,** where possible, to assess for potential publication or selective reporting bias (51, 52).

Reporting of this review

This systematic review and meta-analysis will be reported according to the preferred Reporting Items in (PRISMA), flow diagrams will be used to summarise the study selection process(53). We will include a PRISMA checklist. Where necessary, we will adapt the reporting to ensure that all items relevant to this review are included**.**

Ethics and dissemination

Ethics approval is not required for the systematic review as it based on previously published data. A supervisor with expertise in methodology (systematic review) will review the study protocol, and then it will be submitted to the University of Cape Town Departmental Research Committee for approval. The findings of this study will be widely disseminated through peer-reviewed publications and conference presentations. Updates of the review will be completed to inform and guide occupational health practice.

Authors' contributions

FEO, ASH, and MEE conceived the review. FEO, ASH, SA, and MEE undertook the drafting of the protocol manuscript. FEO, ASH, SA and MEE will analyse the data and interpret the results. All authors who developed and designed the protocol will be involved with data acquisition and have given their approval for the final version for publication**.**

Acknowledgements

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Morris H. How many planes are there in the world right now? The Telegraph. 2017.

2. Council NR. The airliner cabin environment: air quality and safety: National Academies Press; 1986.

3. Statistics UBoL. May 2016 national occupational employment and wage estimates United States. 2019.

4. Runeson-Broberg R, Lindgren T, Norbäck D. Musculoskeletal symptoms and psychosocial work environment, among Swedish commercial pilots. International archives of occupational and environmental health. 2014;87(7):685-93.

5. Nicholas JS, Butler GC, Lackland DT, Tessier GS, Mohr JL, Hoel DG. Health among commercial airline pilots. Aviation, space, and environmental medicine. 2001;72(9):821-6.

6. Rafnsson V, Olafsdottir E, Hrafnkelsson J, Sasaki H, Arnarsson A, Jonasson F. Cosmic radiation increases the risk of nuclear cataract in airline pilots: a population-based case-control study. Archives of ophthalmology. 2005;123(8):1102-5.

7. Hong O, Kim M. Factors associated with hearing loss among workers of the airline industry in Korea. ORL-head and neck nursing: official journal of the society of otorhinolaryngology and head-neck nurses. 2001;19(1):7-13.

8. Irvine D, Davies DM. British Airways flightdeck mortality study, 1950-1992. Aviation, space, and environmental medicine. 1999;70(6):548-55.

9. Wilder-Smith A, Paton NI, Goh KT. Low risk of transmission of severe acute respiratory syndrome on airplanes: the Singapore experience. Tropical Medicine & International Health. 2003;8(11):1035-7.

10. Leder K, Newman D. Respiratory infections during air travel. Internal medicine journal. 2005;35(1):50-5.

11. Byrne NJ, Behrens RH. Airline crews' risk for malaria on layovers in urban sub-Saharan Africa: Risk assessment and appropriate prevention policy. Journal of travel medicine. 2004;11(6):359-63.

12. Sutton PM, Vergara X, Beckman J, Nicas M, Das R. Pesticide illness among flight attendants due to aircraft disinsection. American journal of industrial medicine. 2007;50(5):345-56.

13. Lindgren T, Norbäck D. Heath and perception ofcabin air quality among Swedish commercial airlinecrew. Indoor Air. 2005;15 65–72:65-72.

14. Nagda NL, Hodgson M. Low relative humidity and aircraft cabin air quality. Indoor air. 2001;11(3):200-14.

15. Méndez AM. Urolithiasis among flight personnel (author's transl). Medicina clinica. 1979;72(2):65-70.

16. Sykes AJ, Larsen PD, Griffiths RF, Aldington S. A study of airline pilot morbidity. Aviation, space, and environmental medicine. 2012;83(10):1001-6.

17. dos Santos Silva I, Pizzi C, Evans A, Evans S, De Stavola B. Reproductive history and adverse pregnancy outcomes in commercial flight crew and air traffic control officers in the United Kingdom. Journal of occupational and environmental medicine. 2009;51(11):1298-305.

18. Hinst J, Bruchac D. The influence of civil aviation upon the reproductive system of the woman (author's transl). Ceskoslovenska gynekologie. 1981;46(6):456-9.

19. Zeeb H, Hammer GP, Langner I, Schafft T, Bennack S, Blettner M. Cancer mortality among German aircrew: second follow-up. Radiation and environmental biophysics. 2010;49(2):187-94.

20. Council NR. Health Effects Associated with Exposure to Airliner Cabin Air. The Airliner Cabin Environment: Air Quality and Safety: National Academies Press (US); 1986.

21. Reynolds P, Cone J, Layefsky M, Goldberg DE, Hurley S. Cancer incidence in California flight attendants (United States). Cancer Causes & Control. 2002;13(4):317-24.

22. Blettner M, Zeeb H, Auvinen A, Ballard TJ, Caldora M, Eliasch H, et al. Mortality from cancer and other causes among male airline cockpit crew in Europe. International journal of cancer. 2003;106(6):946-52.

23. Miura K, Olsen CM, Rea S, Marsden J, Green AC. Do airline pilots and cabin crew have raised risks of melanoma and other skin cancers? Systematic review and meta-analysis. British Journal of Dermatology. 2018.

24. McNeely E, Gale S, Tager I, Kincl L, Bradley J, Coull B, et al. The self-reported health of US flight attendants compared to the general population. Environmental Health. 2014;13(1):13.

25. McNeely E, Mordukhovich I, Tideman S, Gale S, Coull B. Estimating the health consequences of flight attendant work: comparing flight attendant health to the general population in a cross-sectional study. BMC public health. 2018;18(1):346.

26. Feijo D, Luiz RR, Camara VM. Common mental disorders among civil aviation flight attendants. Aviation, space, and environmental medicine. 2014;85(4):433-9.

27. Grajewski B, Whelan E, Nguyen M, Kwan L, Cole R. Sleep disturbance among female flight attendants and teachers in a reproductive biomonitoring study. American Journal of Epidemiology. 2000;151(11).

28. Ballard T, Romito P, Lauria L, Vigiliano V, Caldora M, Mazzanti C, et al. Self perceived health and mental health among women flight attendants. Occupational and environmental medicine. 2006;63(1):33-8.

29. De Stavola BL, Pizzi C, Clemens F, Evans SA, Evans AD, dos Santos Silva I. Cause-specific mortality in professional flight crew and air traffic control officers: findings from two UK population-based cohorts of over 20,000 subjects. International archives of occupational and environmental health. 2012;85(3):283-93.

30. Lee H, Wilbur J, Kim MJ, Miller AM. Psychosocial risk factors for work-related musculoskeletal disorders of the lower-back among long-haul international female flight attendants. Journal of Advanced Nursing. 2008;61(5):492-502.

31. Nagda NL, Koontz MD. Review of studies on flight attendant health and comfort in airliner cabins. Aviation, space, and environmental medicine. 2003;74(2):101-9.

32. Rayman RB. Cabin air quality: an overview. Aviation, space, and environmental medicine. 2002;73(3):211-5.

33. Griffiths RF, Powell D. The occupational health and safety of flight attendants. Aviation, space, and environmental medicine. 2012;83(5):514-21.

34. Kiersz A, Gillett R, Hoff M. The 47 jobs that are most damaging to your health 2020 [Available from: https://www.businessinsider.com/most-unhealthy-jobs-in-america-2017-4?IR=T.

35. https://www.businessinsider.com/most-unhealthy-jobs-in-america-2017-4?IR=T.

36. United States Department of Labour. Occupational Safety and Health Administration. Applicability of Certain OSHA Standards to Cabin Crew Members on Aircraft in Operation 2014 [Available from: https://www.osha.gov/dep/letters/04012014_AircraftCabinCrewmembers.html.

37. Linton OW, Mettler Jr FA, editors. National council on radiation protection and measurements. National conference on dose reduction in CT, with an emphasis on pediatric patients AJR Am J Roentgenol; 2003.

38. Centers for Disease Control and Prevention. The National Institute for Occupational Safety and Health (NIOSH). Aircrew Safety and Health 2019 [Available from: https://www.cdc.gov/niosh/topics/aircrew/default.html.

39. Kim JN, Lee BM. Risk factors, health risks, and risk management for aircraft personnel and frequent flyers. Journal of Toxicology and Environmental Health, Part B. 2007;10(3):223-34.

40. International hazard datasheets on occupation (occupation physician). http://www.onetonline.org/link/summary/53-2031.00

41. Lim M, Koh D. SARS and occupational health in the air. BMJ Publishing Group Ltd; 2003.

42. Sanlorenzo M, Wehner MR, Linos E, Kornak J, Kainz W, Posch C, et al. The risk of melanoma in airline pilots and cabin crew: a meta-analysis. JAMA dermatology. 2015;151(1):51-8.

43. Liu GS, Cook A, Richardson M, Vail D, Holsinger FC, Oakley-Girvan I. Thyroid cancer risk in airline cockpit and cabin crew: a meta-analysis. Cancers of the head & neck. 2018;3(1):7.

44. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systematic reviews. 2016;5(1):210.

45. Werfalli M, Musekiwa A, Engel ME, Ross I, Kengne AP, Levitt NS. The prevalence of type 2 diabetes mellitus among older people in Africa: a systematic review study protocol. BMJ open. 2014;4(6):e004747.

46. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. Journal of clinical epidemiology. 2012;65(9):934-9.

47. Reuters T. ISI Research-Soft Endnote 90. 2019 [Available from: http://www.endnote.com.

48. Rohwer A, Garner P, Young T. Reading systematic reviews to answer clinical questions. Clinical Epidemiology and Global Health. 2014;2(1):39-46.

49. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Research synthesis methods. 2010;1(2):97-111.

50. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Bmj. 1997;315(7109):629-34.

51. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994:1088-101.

52. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009;151(4):264-9.

Appendix

Detailed evaluation of existing systematic reviews

In the First study, (Sanlorenzo (42)) published in 2014, various electronic databases were searched using the following (PubMed, Web of Science, and Scopus). However, they did not search for the Cochrane Library, which is a very important database. The search strategy used for each is detailed in the appendix in the Supplement. This review included 19 studies published between 1990 and 2013 , which is an old search. The review authors did not mention the method or the tools for assessing the risk of bias in each individual of included studies, only publication bias was assessed. The Reviewers authors neither published a protocol for this review nor registered in PRESPERO. The appropriate analysis was conducted, and Heterogeneity of results was analyzed with Chi-square tests. Appropriate statistical tests were used depending on the outcome of this test - random effects model was used. Meta-analyses within subgroups were done appropriately (study design, cockpit vs cabin crew, and by sex). Funnel plots were constructed to examine for possible publication bias. Review authors follow the Prisma guidelines except for some points. Author did not conduct an assessment of the risk of bias, the authors did not describe the method of data extraction properly (No mention of piloting forms or independent data extraction) and review protocol does not exist and author did not register~~ed~~ in Prospero.

In the Second study (Miura (23)) published in 2018, various electronic databases were searched using the following (MEDLINE, ISI Science Citation Index, Embase, SCOPUS, and CINAHL). However, they did not search for the Cochrane Library, which is a very important database. The search strategy used, and relevant keywords were referenced and searched for other additional studies, this review included 12 studies published between 1990 and 2017. The review authors used a satisfactory technique for assessing the risk of bias in individual studies that were included in the review (Newcastle–Ottawa Quality Assessment Scale) and they ~~were~~ used the Preferred Reporting Items for Systematic reviews and Meta-Analysis statement to guide reporting. The review protocol was registered with PROSPERO. The appropriate analysis was conducted, and Heterogeneity of results was analyzed with Chi-square tests. Appropriate statistical tests were used depending on the outcome of this, test - random effects model was used. Meta-analyses and subgroup analysis were performed by study design and work location; however, they did not do analysis by sex, which is an important factor for heterogeneity between the studies. Funnel plots were constructed to examine for possible publication bias.

In the third study (Lui (43)) published in 2018, Just two electronic databases were searched (PubMed and Cochrane Database without using the MeSH database to identify the concepts and choose all appropriate terms) and searched the reference lists / bibliographies of included studies. The search strategy was included in the review. This review included 8 studies published between 1996 and 2014, The review authors did not mention the method or the tools for assessing the risk of bias in each individual of included studies. The Reviewers authors neither published a

protocol for this review nor registered in PRESPERO. The appropriate analysis was conducted, and Heterogeneity of results was analyzed with Chi-square tests. Appropriate statistical tests were used depending on the outcome of this, test - random effects model was used. Meta-analyses and subgroup analysis were performed by study design and work location; however, they did not do analysis by sex, which is an important factor for heterogeneity between the studies. Funnel plots were constructed to examine for possible publication bias. Review authors follow the Prisma guidelines except for some steps. The author did not conduct an assessment of the risk of bias, the authors did not describe the method of data extraction properly (No mention of piloting forms or independent data extraction), review protocol does not exist, and author did not register in Prospero. In addition, Specific study characteristics not as clear as language used.

PART B: Journal Manuscript (Journal of Occupational and Environmental Medicine)

The prevalence of occupational health problems in-flight crews (pilots and flight attendants: a Systematic Review and Meta-Analysis

ABSTRACT

Background: The International Civil Aviation Organisation (ICAO), a United Nations (UN) body, reports that the "global air transport network" doubles in size, at least, every 15 years. Researchers have become increasingly aware that aircrew members (ACMs) are at high risk for several diseases when compared to the general population. We conducted a systematic review and meta-analysis to estimate the prevalence of occupational health problems in aircrew members (pilots and flight attendants) as compared with the general population.

Methods: We identified relevant literature by searching several electronic databases including PubMed, EBSCOhost: CINAHL, PsycINFO, Web of Science, Scopus and Google Scholar and included all observational studies reporting occupational health problems among ACMs. We included published and unpublished cross-sectional studies reporting the prevalence rate of any OHPs among commercial ACMs and/or its risk factors. Articles in any language, irrespective of the date of publication, were taken into consideration. The main outcome was the prevalence of OHPs and its related factors among ACM. Meta-analysis (random-effects model) was employed to derive the summary estimate; subgroup analysis was conducted, given the high heterogeneity. Study quality was assessed using the modified Hoy et al Scale for cross-sectional studies and the National Institutes of Health (NIH) Quality Assessment Tool for Observational Cohort studies. The study protocol was registered in PROSPERO (CRD42020167631).

Results: Our search of the literature addressing occupational health among commercial ACMs returned 846 studies, of which 51 articles were included in our systematic review and meta-analysis. The studies were published between (1996 - 2021) and most were cross-sectional in design (n=47) while 4 studies estimated the incidence of occupational health diseases or mortality from different sources. ACMs had various OHPs and workplace accidents and injuries were relatively common. The Pooled Prevalence Rate (PPR) by subgroup analysis showed the second most common OHPs to be Fatigue/Sleep related disorders(FSDs) (diseases or symptoms), which was higher in cockpit crew [PPR=66.64%, 95% confidence interval (CI): 52.65%–79.29%] compared to cabin crew [PPR=44.45%, 95% CI: 31.78%–57.49%]. Cabin crew had higher prevalence rates of respiratory conditions [PPR=24.08%, 95% CI: 14.18%– 36.64%] compared to cockpit crew [PPR=14.61%, 95%l CI: 4.47%–29.20%]. Musculoskeletal disorders (MSDs) were also commonly reported in cockpit crew [PPR=25.78%, 95% CI 10.31–45.27]), cabin crew [PPR=36.90, 95% CI 25.51–49.08] and increased in ACMs [PPR=72.08%, 95% CI: 67.82%–75.97%]. The PPR of neurological conditions was found to be 13.42%, 95% CI:2.30%–31.55% in cockpit and 22.33% ,95% CI:9.69%–38.34% in cabin crew. The PPR for ENT conditions was 28.28% ,95% CI:25.96%–30.67% in cockpit and 26.8% ,95% CI:19.88%–34.36% in cabin crew. The PPR for gastrointestinal was 40.14% ,95% CI:24.05%–57.40% in cockpit and 17.29% ,95% CI:16.31%–18.33% in cabin crew. Metabolic disorder prevalence was 19.76% ,95% CI:9.43%–32.72% in cockpit and 37.13% ,95% CI :21.70%–54.04% in cabin crew. The PPR for other conditions were relatively lower and fewer studies reported on these; cardiovascular disease prevalence was 2.42% ,95% CI: 1.99%–2.94 %in cabin crew; ophthalmological disorders 18.93%,95% CI: 18.03%–19.84% in cabin and 2.80%,95% CI: 2.32%–3.38% in cockpit crew; Cancer 0.37% ,95% CI:0.20%–0.69% in cockpit and 17.11% (95% CI:16.12%–18.14%) in cabin crew. PPR for occupational injuries was low at 0.83% ,95% CI:0.69%–0.97% in cockpit and high at 48.14%,95% CI:42.73%–53.48% in cabin crew whilst for sexual harassment it was 24.01% ,95% CI:12.64%–37.65% in cabin crew.

Conclusion: There is a high prevalence of work-related illness and injuries among aircrew members supporting the hypothesis that they are at increased risk. This is the first systematic review that addresses the occupational health status of aviation personnel and it found the most prevalent problems in cockpit crew to be FSDs, gastrointestinal disorders, MSDs, ENT disorders and respiratory disorders. For cabin crew the most prevalent

conditions were FSDs, occupational injuries, metabolic disorders, MSDs and sexual harassment. Governments, businesses and policy makers should support efforts to improve occupational health and safety measures among this occupational group.

Keywords: Occupational; health; medicine; hazard; exposure; disease; illness; injuries; aircrew; flight crew; cabin; cockpit; flight attendants; pilot; observational; cross sectional

INTRODUCTION

The International Civil Aviation Organisation (ICAO), a United Nations(UN) body, reports that, the "global air transport network" doubles in size approximately every 15 years(54). Flight attendants have worked on aircrafts since 1931 ; in 1985 the United States airlines employed 40,000 flight attendants(55) and by 2019, the number had increased to almost 120,840 (3).

Research concerning health of aircrew (namely pilots and flight attendants) is relatively scant and of varying quality (33). Results have been varied, but clearly demonstrated the association between high work demand and MSDS (4), higher prevalence of cataracts(6, 56), hearing loss(7), infections(8-11),skin conditions including dermatitis(57) and dryness appear to be a frequent contributor to dermatological problems among ACM(14, 58). On the other hand ,studies also show that pilots have a higher prevalence of kidney disease compared with the general population(16) . Furthermore, adverse reproductive outcome such as congenital malformations, spontaneous abortion, and premature delivery are higher among ACM than the general population(18, 59). Whereas overall cancer mortality is lower in aircrew members in comparison with the general population(19), studies show increased rates of skin cancers (8, 21, 60)and breast cancers (21), adverse reproductive and perinatal outcomes(61, 62) as well as an increased risk of colon cancer, prostate cancer and brain/central nervous system cancer in aircrew members(8).

A number of studies reported higher rates of mental disorders among aircrew members, including Common Mental Disorders (CMDs) among flight attendants. Flight attendants also had higher rates of psychological distress, depression, fatigue, and sleep disorders ranging from 2 to 5.7 times those of the general population (26, 61-63). Furthermore, there are also serious emotional and physical consequences related to sexual harassment (a psychosocial hazard) resulting, very often, in an inability to perform job functions effectively(28). Lastly, aircraft accidents whilst infrequent, have a high mortality and is considered to be a rare cause of death in the general population(29).

ACMs are exposed to a unique and wide range of exposure to work-related risk factors(28, 30). During the flight, ACMs are exposed to several occupational risk factors related to their work environment that affect their health and wellbeing(31) including cosmic ionising radiation, elevated ozone levels, poor cabin air quality, hypoxia, pesticides from cabin disinfection, heavy physical job demands, high levels of occupational noise, and sexual harassment(28, 32, 33). Night shift work and crossing time zones continually leads to circadian rhythm disruption. According to Business Insider's analysis of data collected from the US Department of Labor, flight attendants have one of the unhealthiest jobs in the US(64). The aircrew's poor health is attributable to six major health risks, these include but are not limited to contaminants (such as carbon monoxide (CO), biological agents and various organic chemicals), exposure to radiation, hazardous conditions, risk of cuts, minor burns, bites, stings and time spent sitting. The types of specific occupational hazards ACMs is potentially exposed to in these work environments are shown in Table 4 below(39, 65).

There are a few systematic reviews published between 2015 and 2022(42, 66-68) with meta-analyses examining disease-specific morbidity and mortality on a variety of studies on melanoma, other skin cancers, breast cancer and thyroid cancer in aircrew members. All of these studies calculated the standardized incidence ratio and standardized mortality ratio for all airline crew members. A critical appraisal of these published reviews revealed gaps in the evidence, warranting conducting the current review. (The criteria used to critically appraise systematic reviews and meta-analyses, and summary of findings are in Table 5).

Purpose

Aim: Given all that, these previous reviews only focused on a single outcome, viz cancer, the aim of this systematic review is to provide a comprehensive evidence-based synthesis, assessing multiple outcomes, of conditions, beyond cancer, that affect the health and wellbeing of aircrew members.

Objectives: Specifically, this systematic review and meta-analysis sought to estimate the prevalence of occupational health problems in aircrew members (pilots and flight attendants) as compared with the general population by employing a more rigorous and comprehensive search strategy to gather evidence aimed at: (1) comparing reported OHPs prevalence in ACMs as compared with the general population (2) calculating an updated PPR of OHPs among ACMs; (3) providing the first synthesis of the existing evidence for negative health consequences within ACMs as result of harmful work conditions and individual differences.

METHODS

The present systematic review complies with Cochrane Handbook (44) as a guide and methodological framework in designing and conducting this systematic review. This protocol has been published in PROSPERO International Prospective Register of Systematic Reviews, with the registration number (CRD42020167631).

Study eligibility

We identified relevant studies based on the following criteria: (1) Published observational studies reporting the prevalence rate of any OHPs among commercial ACMs and/or its risk factors; (2) Articles in any language were considered, irrespective of the date of publication ; (3) Among the studies addressing the air force, agricultural and rotary-wing aircrew , studies relating to passengers or health of the general population and studies of the health aspects of pilot or crew members relating to factors not thought to be occupationally related were not included . The exposure of interest was any work condition that causes harm to the ACMs. The outcome of interest included cancers, MSDs, kidney diseases, skin diseases, cataracts, hearing loss, mental health, FSDs and physical consequences resulting from sexual harassment, infections, diabetes, cerebrovascular diseases, cardiovascular diseases, respiratory diseases and deaths due to Aircraft accidents.

Search strategy

A comprehensive and sensitive search strategy was undertaken from inception to August 2022 (search date: 16 August 2022) among several electronic databases to identify studies that meet the inclusion criteria, assess study quality, and extract data from these studies.

Electronic databases☹1) Electronic databases searched were: PubMed, EBSCOhost: CINAHL, PsycINFO, Web of Science: Core collection and Google Scholar ;(2) Grey literature databases such as Grey Literature Report and in OpenGrey.

Hand searching: (1) The reference lists of studies meeting our inclusion criteria were scanned for further studies; (2) Prominent authors of studies meeting our inclusion were contacted for further studies.

We employed the services of staff in the libraries of University of Cape Town in requesting articles.
Database subject headings (MeSH in PubMed, EBSCOHOST: CINAHL, PsycINFO, Web of Science: Core collection and Google Scholar) were combined with a range of text words. (Appendix)

The search was performed by cross-referencing the words and the full search strategy was documented in the complimentary content Table (6). Peer-reviewed journal articles and the grey literature were searched. Other relevant sources were identified through reference lists from the potentially included studies and other relevant studies known by the research group.

Selecting studies for inclusion

Retrieved articles from the search were exported to endnote (version 20.3) and two review authors (FEO and MW), worked independently to screen the titles and abstracts of all studies generated by the search process for eligibility. FEO obtained the full text of studies considered to be potentially eligible. The two authors (FEO and MW) independently assessed the full text of each article for eligibility, and compared their results. Points of disagreement were resolved by discussion, consensus, and consulting a third author (MEE). Reasons for exclusion for all studies excluded by the assessors were recorded inTable 7. Finally, the review authors accepted the remaining studies as eligible for inclusion in the systematic review. A flow chart was used to summarise the study selection process (69)(Figure 1).

Quality assessment and data extraction

The quality of each eligible study was assessed by (FEO and MW) using The National Institutes of Health (NIH) Quality Assessment Tool for cohort studies Table 8 (70) and the modified Hoy et al a quality assessment tool for cross sectional studies (Table 9)(46, 47). Both tools were applied to screen full-text articles to assess the quality of prevalence studies, and further refinement was considered to improve inter-rater agreement between investigators. For the NIH assessment tool each study was assigned a poor, good, overall rating to each of the 14 criteria and, bias evaluation was determined using quality scoring scale by modified Hoy et al. Studies with scores greater than 8 were considered to be of high quality. This informed the selection and appraisal of studies for a pooled analysis. Any disagreements were discussed and resolved by consensus in consultation with the third reviewer and discrepancies resolved.

After assessing the methodological quality, all data were extracted by two review authors (FEO and ASH) onto a pre-designed data extraction Excel spread sheet and independently encapsulate essential results for the eligible studies. These summaries were compared, followed by resolution of any discrepancies by discussion and consensus with a third reviewer (MEE). Study characteristics include first author, year of publication, country of origin, hazard category, study design, study population, data source and sample size. The final data was entered into Stata software (version 15.1) according to the Cochrane Collaboration(44) by first author (FEO) and the second author (ASH) cross-checked the data for data entry errors. The prevalence rate for some eligible studies,

which do not have prevalence data, was calculated by using the formula ;(Prevalence = (Incidence Rate) x (Average Duration of Disease)(71). References were managed using Endnote (Version 20.3).

Data synthesis including assessment of heterogeneity

We used Stata software (version 15.1) to calculate the combined prevalence estimate, along with 95% confidence intervals, of health conditions among all airline crew members. We applied the random-effects meta-analysis model. To account for between-study variability, we incorporated the Freeman-Tukey transformation which minimises the influence from studies with extremely small prevalence or extremely large prevalence estimates (72). Heterogeneity was assessed by the Cochrane's Chi^2 test where the heterogeneity is considered statistically significant if the p-value <0.001 and the I^2 statistic tests, where the guide for interpretation is: 0%-40% might not be important, 30%-60%, moderate heterogeneity, 50%-90%, substantial heterogeneity and 75%-100% considerable heterogeneity(49). We conducted subgroup analyses to explore the source of heterogeneity giving the priority to staff category, cockpit crew (e.g. pilots), cabin crew (e.g. flight attendants).

RESULTS

Characteristics of studies

A narrative synthesis of the findings, documenting all the key outcome measures from the studies included in this review, is provided. The search identified 846 articles the various sources of data on different OHPs among ACM of various occupations (including cockpit crew, cabin crew members). There were 234 articles retrieved from PubMed, 40 from Scopus, 9 from EBSCOhost (Psycinfo), 12 from EBSCOhost (CINHAL), 23 from Web of Science (core collection), 508 from Google scholar while 20 studies were retrieved from citation search (Fig.1). Following removal of duplicate studies, 367 publications remained for screening and analysis. From these, 89 articles were assessed for full text reviewing. About half (n=38) were excluded after reading the full text for the following reasons: primary outcome not reported (n=21), inappropriate study design (n=11), analysed a different/incorrect population (n=5), or not related to occupational factors (n=1) (Fig1 and Table 7). Finally, 51 studies were included in this systematic review.

The studies were published between (1996 – 2021) and the main studies characteristics are shown in Table 10. Most of the studies were cross-sectional in design (n=47)(16, 26, 28, 30, 61, 62, 73-112) conducted in the U.S.A (n=14), China (n=7), Sweden (n=4), Saudi Arabia (n=4) Brazil (n=4), UK (n=2) and Italy (n=1), Denmark (n=1), Norway (n=1), New Zealand (n=1), Japan (n=1), Spain (n=1), Sri Lanka (n=1), India (n=1), Thailand (n=1), Portugal (n=1), Poland (n=1), Netherland (n=1). The four cohort studies (103, 113-117) were conducted in USA, Canada, Netherland and Sweden and ascertained the incidence of occupational health diseases or mortality from different sources. Where reported, the mean age of ACMs distribution was 30 -50 years in 34 studies, above 50 years old in 11 studies, and below 30 years old in 2 studies.

As a proxy for occupational exposures, some studies used the length of employment, which varied among the ACMs. The average employment period was more than 10 years stated in 21 studies, less than 10 years stated in 4 studies and unknown stated in the rest of the studies. Moreover, most studies (n=43) did not include Body Mass Index. The majority of the studies considered sex and type of ACMs according to position in the aircraft, including all personnel who operate the aircraft), cockpit (pilot and copilot) and cabin crew (flight attendants) Table 10. Some studies did not take into account specific occupational hazards; thus, we deduced the likely type of hazard Table 10 from the data.

Prevalence of occupational health problems (by diseases category)

Most of the studies showed high prevalence rate of occupational health problems among ACMs and details of each subgroup analysis based upon the location on the plane, ACMs (e.g. all staff), cockpit crew (e.g. pilots) and cabin crew (e.g. flight attendants) are provided in supplementary Tables 11 and (Figure 2__22).

Respiratory and Cardiovascular diseases

Ten studies (n=16,460 participants)(16, 61, 62, 76, 77, 98, 106, 111, 116, 117) were included in the PPR of respiratory symptoms among ACMs including bronchitis, cough, asthma or wheezing . In 3/10 studies (n=2,265)(16, 111, 116) the estimated PPR for respiratory disorders in cockpit crew was 14.61% ,95% CI: 4.47%–29.20%, and in 7/10 studies(n=1419)(61, 62, 76, 77, 98, 106, 117) estimated PPR for respiratory disorders among cabin crew was 24.08 % ,95% CI: 14.18%–35.64% . Heterogeneity was observed across studies (I^2 =99.51%) (Fig.2). One study (n=4,001)(61) investigated the prevalence of cardiovascular disorders among cabin crew and reported a PPR of 2.42%, 95% CI: 1.99%–2.94 % (Fig3). We conclude that the prevalence of respiratory and cardiovascular problems among the ACMs is consistently high compared with the general population and that cabin crew are more likely to have respiratory symptoms compared to cockpit crew.

Gastrointestinal diseases

Five studies (n=7,582)(62, 81, 92, 104, 111) summarized the prevalence of gastrointestinal symptoms/disorders among ACMs. It was found that cockpit crew had a PPR of 40.14%,95% CI: 24.05%–57.40% , while cabin crew had a PPR of 17.29%, 95% CI: 16.31–18.33% based on data from 4/5 studies(n=2,216) (81, 92, 104, 111) and 1/5 study (n=5,366)(62) (Fig 4). Heterogeneity was observed across studies (I^2 =98.24%). We concluded that gastrointestinal symptoms are relatively high especially among the cockpit groups compared to cabin crew.

Psychological/Neurological diseases

As shown in Figure5, 8 studies (n=16571)(16, 26, 28, 61, 62, 73, 75, 102) reported psychological and neurological disorders (depression, common mental disorders, anxiety and PTSD) among ACMs. PPR was 13.42%,95% CI: 2.30%–31.55% in the cockpit crew based on 3/8 studies (n=2,749)(16, 73, 75) and PPR was 22.33%,95% CI: 9.69%–38.34% in the cabin crew based on 5/8 studies (n=13,822)(26, 28, 61, 62, 102). Heterogeneity was observed across studies (I^2 =99.7%). In summary, cabin crew had higher prevalence of psychological and neurological disorders than the cockpit crew.

Fatigue/Sleep related disorders (FSDs)

FSDs were the second most common problems among the ACMs. Pooled data from 12 studies(n=14141)(61, 62, 75, 81, 89, 94, 95, 97, 101, 103, 104, 111) revealed that the prevalence of FSDs was 66.64%,95% CI: 52.65%–79.29% in cockpit crew from 8/12 studies (n=3491)(75, 81, 94, 95, 97, 103, 104, 111) and was 44.45%, 95% CI: 31.78%–57.49% in cabin crew from 4/12 studies (n=10650)(61, 62, 101, 104). There is high between-study heterogeneity across all pooled estimate (I^2 =98.49% and 99.33% respectively) (Fig 6). In conclusion, 12 studies have reported that ACMs have greater FSDs than the general population.

Dermatological diseases

For dermatological symptoms, we extracted data from the 2 studies (n=2559)(89, 117); we found higher prevalence estimates in cabin crew from 1/2 study (n=1,046)(117) 17.97%, 95% CI: 15.76%–20.42 %, whilst the other study with lower sample size reported a lower prevalence (n=1,513)(89) 12,03%, 95% CI: 10.49%–13.77%(Fig 7).

ENT and Ophthalmological diseases

Of the 11 studies (n=14,979)(62, 76, 77, 89, 90, 98, 106-109, 117) reporting ENT symptoms (Fig8), the PPR from 3/11 studies (n=3,387)(89, 90, 107) in ACMs was 19.62%,95% CI: 9.66%–32.02%. For the 2/11 studies(n=1,408)(108, 109) in cockpit crew the PPR was 28.28%, 95% CI: 25.96%–30.67 %. In 6/11 studies(n=10,184)(62, 76, 77, 98, 106, 117) , the PPR in cabin crew was 26.815%, 95% CI: 19.88%–34.36%. Heterogeneity across studies is observed (I^2 =98.22 %). Moreover, the PPR for the ophthalmological symptoms from 4 studies (n=12483)(62, 79, 89, 98) (Fig 9) was 10.97%, 95% CI: 9.49%–12.65% in ACMs from ¼ study (n=1513)(89) , was 2.80%, 95% CI: 2.32%–3.38% from ¼ study (n=3780)(79) in cockpit crew and was 18.93%, 95% CI: 18.03%–19.84% from 2/4 studies (n=7190)(62, 98) in cabin crew . In conclusion air crew members suffer from ENT and ophthalmological problems, and it is an open question whether ENT symptoms are higher than in the general population.

Musculoskeletal diseases

Figure 10 presents the PPR for MSDs based on the data from 12 included studies(n=111,289)(16, 30, 62, 82, 84, 88, 93, 96, 99, 104, 111, 112) from different countries, 1/12 study (n=462)(88) estimated prevalence among MSDs in ACMs was 72.08%,95% CI: 67.82%–75.97%, 4/12 studies(n=2929)(16, 93, 104, 111) , estimated prevalence for MSDs among cockpit crew was 25.78 %,95% CI: 10.31%–45.27% and 8/12 studies(n=7737)(30, 62, 82, 84, 96, 99, 104, 112) and estimated prevalence for MSDs among cabin crew was 36.90%,95% CI: 25.51%–49.08%. Heterogeneity across studies is observed (I^2 among cockpit studies =99.2 % and among cabin crew studies =89.4). In conclusion, the studies provide some evidence of increased MSDs and significantly impact ACMs health.

Renal and Reproductive/Endocrine diseases

Only one study(n=595)(16) reported on renal conditions and found the PPR for renal problems among the cockpit crews to be 3.19%, 95% CI: 2.05%–4.93% (Fig 11). Pooling three studies(n=811)(74, 85, 100) that assessed reproductive /endocrine disorders prevalence in cabin crews indicated an increased occurrence compared with the general population 9.45%,95% CI: 0.00%–41.04%) (Fig 12).

Metabolic diseases

Eight studies (n=14,395)(16, 61, 62, 83, 86, 87, 101, 112) reported the PPR of metabolic disorders in ACMs including diabetes , obesity and metabolic syndrome. We found significantly higher PPR in cabin crews 37,13%, 95% CI: 21.70%–54.04% extracted from 4/8 studies (n=10,408)(61, 62, 101, 112) than PPR in cockpit crews 19.76%, 95% CI: 9.43%–32.72% extracted from 4/8 studies (n=3,987)(16, 83, 86, 87). Heterogeneity across studies is observed (I^2=99.6%and 89.9% respectively) (Fig 13).

Allergies diseases

A meta-analysis of three studies (n=10,380)(61, 62, 76) on allergies symptoms (linked to pollen, dust, mold exposures) . Showed elevation among the cabin crews (PPR=34.56%, 95% CI: 26.61%–42.96%(Fig 14). Most of the symptoms were asthma, allergic rhinitis , sinusitis and eczema .Some studies provide evidence of impact of aeroallergens factors on occurrence and intensity of eczema and atopic dermatitis(118).

Cancers

Table 11 shows, PPR separately for each cancer site. Two studies(n=8,046)(78, 113) assessed all site cancer prevalence, one study in cockpit crew (n=2,680)(113) and a study in cabin crew(n=5,366)(78) found that the PPR was 0.37%,95% CI: 0.20%–0.69% and 17.11% ,95% CI: 16.12%–18.14%, respectively. One study (n=5,366)(78) looking at for breast cancer occurrence in female cabin crew showed a raised PPR 3.63% ,95% CI: 3.17%–4.17% compared to the general population. The PPR for thyroid cancer was 0.61%,95% CI: 0.44%–0.86% based on data from a large study(n=5366)(78) in cabin crew, while the PPR for reproductive cancer in cabin crew was 3.86%,95% CI: 3.31%–4.51% based on one study(n=4011)(61).
The estimated PPR for melanoma in cockpit crew was 1.85%,95% CI: 1.04%–3.28% based on one study (n=595)(16) , whereas in cabin crew it was 2.48 %,95% CI: 2.10%–2.93% based on another study (n=5366)(78) . A study (n=5366) (78) assessing the non-melanoma prevalence in cabin crew found that PPR was 9.00%,95% CI: 8.26%–9.80% (Fig15-20). In conclusion, PPR was lower for all cancer sites among cockpit crew and thyroid cancer among the cabin crew, while other studies show increased prevalence rates of breast cancers, reproductive cancer, melanoma, and non-melanoma cancers among the cabin crew.

Occupational Injuries/Accident

Three studies (105, 111, 115) reported on occupational injuries or accidents in ACMs (N= 17,701) One study (n=322)(115) revealed that the PPR for occupational injury among cabin crew was 48.14 %,95% CI: 42.73%–53.58%, whilst among cockpit crew it was 0.83%,95% CI: 0.69%–0.97% based on three studies (n=17,379)(105, 111)(Fig21).

Sexual harassment conditions

Based on data from three included studies (n=12,542)(28, 110) , that reported on sexual harassment prevalence among the cabin crew ,we found a high PPR for sexual harassment in cabin crew 24.01% ,95% CI: 124%–37.65%(Fig 22). In conclusion, these workers are consistently exposed to sexual harassment, which represents a significant health risk, potentially leading to adverse health outcomes.

Findings from assessment of risk bias in included studies

Table 9 shows the results for the risk of bias assessment according to the modified Hoy et al (46, 47). Eighteen contributions were deemed to be of moderate methodological quality while the remaining 31 contributions included were deemed to be of high methodological quality (low risk of bias).

The results from the National Institutes of Health Quality assessment tool are shown in Tables 8. All the studies were of a good quality. In contrast, there is some weaknesses in the studies such as the nature of the intervention, the study participants and providers were not blinded to the group assignment, and the outcome assessors were not blinded to the participant group assignment (Li, G 2016). Furthermore, there was no documentation of blinding of the outcome assessors and no justification and power calculation for the sample size used in the studies (Van Drongelen 2013(114) and McNeely 2017(117)

Discussion

To our knowledge, this systematic review is the first attempt at meta-analysis of the prevalence of an extensive range of OHPs outcomes among ACMs. This review shows a high prevalence of MSDs, FSDs, gastrointestinal, respiratory, ENT , Metabolic disorders, dermatological disorders and sexual harassment. However, PPR for cardiovascular, renal, reproductive, cancers and ophthalmological disorders were comparatively lower, with fewer studies reporting these outcomes. Additionally, the estimate for occupational injuries was lower in the cockpit crew compared to the cabin crew. Finally, ACMs were not found to have high prevalence rate of thyroid cancer relative to general population in cabin crew.

This review indicates that ACMs suffer from multiple MSDs (72.08%), the most commonly indicated sites being shoulders, knees, back, and neck. Of note, there is a much higher prevalence of these conditions amongst cabin crew 36.90% compared to cockpit crew 25.78%. Our study reported a high prevalence of MSDs similar to the result reported in Iranian workers and other sanitation workers from different countries(119, 120). This is mainly a reflection of an increase in the ergonomic demands of their occupation. The ergonomic demands may include but are not limited to awkward posture (bending and twisting), repetitive movement of arms , standing for a prolonged time, assisting old or heavy passengers and carrying loads especially lifting luggage into overhead .These differences must be taken into account by occupational health providers and policy makers in conducting ergonomic training, policy development and improvement of injury prevention program in the aviation industry.

This review also shows elevated prevalence rates of FSDs (fatigue, insomnia, sleep problems, risk of obstructive sleep apnoea, unintentional sleep). We found that approximately 44.45% of cabin crew and 66.64% of the cockpit crew were suffering from FSDs. Based on our study, FSDs are the second most prevalent disorders, a study (121) conducted by the European Cockpit Association on pilots in eight European countries found that 4 out of 5 cockpit crew have to cope with fatigue that can influence health and interfere with in-flight performance; another fatigue study(33) reported that 83% of cabin crew had experienced fatigue and sleep problems in their duties. We found a lower prevalence of fatigue in our study. Aircrew member work shifts including full nights, long working hours twice per week and with desynchronisation of circadian rhythm may increase sleep deprivation. The sleep deprivation is known to be associated with fatigue and sleep disturbances in this group of workers.(122, 123). Therefore, careful screening of and appropriate intervention in these FSDs and training of the ACMs are required and should be supported by researchers, clinicians and educators in a timely and consistent manner

This review found a high prevalence (14.61% in cockpit and 24.08 % in cabin crew, respectively) of respiratory symptoms, which included, asthma, bronchitis, pneumonia, cough and wheezing. Moreover, one study revealed that the prevalence of cardiovascular disease among cabin crew was 2.42%, which is lower than reported in other study investigated cardiac health among cockpit crew (124). The increased prevalence rate of respiratory symptoms among ACMs may be explained by increased suboptimal air quality impacted by humidity, pressure ,

presence of a lot of people in little space and some contaminants including degradation products of the combustion of engine oils or hydraulic fluids and ozone(98). Thus, it would be beneficial for future epidemiological research to report the prevalence of respiratory and cardiovascular disease, in order to better inform researchers on the impact of these conditions across the ACMs. Furthermore, the findings do have implications for occupational health medical surveillance programmers aimed at early detection and management of cardiorespiratory problems at pre, periodic and exit physical examinations

In this review the prevalence of mental health disorders in cabin crew and cockpit crew was increased at 22.33% and 13.42% and respectively. Our findings are similar to results reported in ambulance personnel in Norway(125). The authors believe that mental health problems (depression, common mental disorders, anxiety, PTSD)"may represent a critical occupational health issue for the commercial civil aviation industry today. There is a significant difference based on the job location in a plane according to subgroup analysis, the cabin crew were shown to be at greater risk (may be due to excessive emotion work ,anxiety about passenger safety and confusion to communicate with cockpit crew and sexual harassment by passenger and other airline staff) which could inform occupational health decisions granting them clearance to fly. Depression was the most common disorder followed by anxiety in ACM. Both factors can have a negative impact on performance, leading to a decreased response/reaction rate during emergencies and an increased risk of suicidal thoughts and actions, as exemplified by the Germanwings plane crash on March 25, 2015 where a depressed pilot intentionally downed the aircraft(126). This highlights the importance of (1) regular screening for mental health illnesses, (2) promoting stronger collaboration among mental health service providers, and (3) ensuring easy access to mental health services.

There was also largely consistent evidence of elevated prevalence of gastrointestinal conditions based on five studies. Our study, shows that pooled prevalence of gastrointestinal conditions was higher in cockpit crew (40.14%) compared to cabin crew (17.29%). The most common gastrointestinal symptoms reported were bloating and functional gastrointestinal disorders which may be linked to irregular sleep , meals and intestinal gas expansion due to the low atmospheric pressure at high altitude according to Boyle's law (81, 127). The implications of these findings are unclear at present.

In the meta-analyses conducted, 19.62% of ACMs had ENT problems with the most prevalent symptoms being sinus and optic barotrauma and 10.97% of ACMs had reported ophthalmological symptoms including cataract, dry eyes and other eye symptoms .The studies were homogenous and the finding shows that cockpit crew had similar ENT symptom prevalence (28.28%) as cabin crew (26.81%). However, cockpit crew had lower prevalence of ophthalmological symptoms (2.80%) than cabin crew (18.93%). Working as an ACMs exposes one to frequent pressure changes and very dry air , which explains the higher prevalence rate of sinus and ear barotrauma(128). The difference of ophthalmological symptoms reported among cockpit and the cabin crew may be explained by differences in the cabin air quality or may be related to reporting bias as cockpit crew may not report health problems due to perception that it may impact their job security adversely. These findings point to the need to focus more intensively on the issue of ENT symptoms among ACMs, since it can affect flight safety. ENT symptoms especially tinnitus and barotrauma among airline crew interfere with the communication between cockpit crew and cabin crew and air traffic control , which increases the potential for error and missing the warning sounds .

Dermatological symptoms were also common among the ACMs (pooled prevalence = 12.03%) with the most prevalent symptoms being hives, rashes, dry and flushed skin. Among cabin crew, the pooled prevalence of dermatological symptoms was 17.97%. We found that the pooled prevalence for renal disorder among the cockpit crew is 3.19%. Because the data were based on only one study, we conclude the result as tentative. The pooled prevalence of reproductive/endocrine symptoms was high among cabin crew (9.45%, P=0.15). However, these findings were not statistically significant and should be interpreted with caution. High prevalence rates were also reported for metabolic problems, with most frequently occurring conditions being diabetes, overweight and obesity. We found that the cabin crew had more prevalent metabolic problems (37.13%) compared to the cockpit

crew (19. 76%). The study further found that about 34.56% of cabin crew had an allergy (pollen, dust, and mold). The implications of these study findings is that, aircrew members need more attention including careful screening of and proper intervention in dermatological disorders , reproductive /endocrine disorders , metabolic disorders and allergies symptoms and give the clinician, occupational health practice more information to support occupational health and safety.

Cancers in aircrew members are an occupational hazard for those who fly regularly. The International Agency for Research on Cancer (IARC) has classified cabin air as "possibly carcinogenic (category 2A)(129, 130)," based on limited evidence from epidemiological studies of flight attendants with heavy exposure to jet fuel fumes and other combustion products ((57, 62, 89, 131, 132). In this systematic review, we did a meta-analysis of this cancer prevalence's to find out which ones are more common than others. The systematic reviews and meta-analysis by Buja et al(2006)(133) , Weinmann e t al(68), found that the incidence of melanoma and breast carcinoma in cabin crew was higher than expected. Another systematic review by Terriballard et al(2000)(134) investigated the incidence and risk factors of cancer in ACMs and showed increased mortality incidence among ACMs for melanoma , brain ,prostate and breast cancers. A systematic review and meta-analysis by Miura et al (2019)(66) to assess the incidence of melanoma and other skin cancers among ACMs found that ACMs has twice the risk of melanoma and keratinocyte cancer compared to the general population. Whilst , a recent systematic review by Liue et al(2018) (67)(2018) found that ACMs did not have a significantly elevated risk of thyroid cancer incidence compared to the general population. Our findings on cancer risk are in keeping with those reported on the previous systematic reviews. We found that the pooled prevalence cancer in all sites are 0.37% in cockpit crew and 17.11% in cabin crew. In cabin crew we also found that the prevalence rate for breast cancer to be 3.63%, for reproductive cancer 3.86%, for melanoma 2.48%, for non-melanoma 9.00% and thyroid cancer 0.61%.The estimated prevalence for melanoma in cockpit crew is 1.85% . The higher prevalence rates of breast cancers, melanoma and non-melanoma skin cancers found in cabin crew was postulated to be related to occupational exposure to risk factors such as ionizing radiation and circadian rhythm disruption. Exposure to cosmic ionizing radiation is the most likely cause of increased risk for skin cancers among the cabin crew followed by air quality of the cabin which may include some hazardous chemical exposures (62, 135) . Moreover, second-hand tobacco smoke is a known cause of increased cancer risk before it was prohibited by civil aviation authority (132, 136).However , the studies among the cabin crew in relation to breast cancer found no association with circadian rhythm disruption or cosmic ionizing radiation (68) . Bias and confounding in observational study design may also account in part for the estimates of cancers among the ACMs. These are important findings as they indicate the necessity and urgency of providing periodic screening of and appropriate intervention in these cancers among aircrew members, more contemporary research on mechanisms and provide sufficient occupational protection is needed.

According to our study, about half (48.14%) of cabin crew had a reported a workplace injury or accident which is very high compared with cockpit crew 0.83%. Work related injury and accident is a common occupational hazard for cabin crew, which need more targeted preventive strategies to mitigate risk. A high percentage (24.01%) of cabin crew had experienced sexual harassment in our study. It is difficult to demonstrate the causative factors linked to sexual harassment (passengers or colleagues or crew dealing with the public). However, the high estimates reported warrant further investigation and additional focus of airline companies is needed to reduce onboard accidents, the resulting injuries, sexual harassment and sickness absence especially among cabin crew.

This study highlights the need for aircrews to be aware of the occupational hazards encountered in their work environment. An understanding of occupational exposures, potential health impacts and their own health status and susceptibility could lead to a greater understanding of the risk to their health and occupational fitness. This should inform, preventive strategies, training, occupational health service provision and risk management in this occupational group.

Strengths and limitations of the study

The key strength of this study is that it is one of the first to provide a comprehensive overview of the current knowledge on occupational health problems among ACMs. Furthermore, this study provides the first pooled updated prevalence estimates for occupational health outcomes among the ACMs globally. Unlike previous reviews on occupational health problems in ACMs, we conducted a quality assessment of the included studies and we identified their limitations. The results of our study will be highly relevant to the civil aviation medical associations, human resource managers and occupational health service providers to the aviation industry. It provides an important overview and profile of several occupational health risks and common health conditions prevalent among ACMs.

The systematic review and meta-analysis has some limitations, many of which are common in systematic reviews of observational studies, and show that there is a need for more research in this area. The limitations of this study mainly arise from the nature of observational studies. Some studies that were included may be biased and selective reporting especially since most of them used self-reporting surveys and scales influences some. Further limitations include the inclusion of overlapping populations, which is often unavoidable in a systematic review and should be taken into account. Further, the healthy worker effect may be an important limitation given that those with disease may have left the industry and not be included in the populations included in this review, thus leading to a falsely low estimate. Lastly, there is heterogeneity among the studies in terms of case definitions and outcome assessments that limit the potential for synthesizing studies using meta-analysis or Meta regression.

Since the studies included in this review are mainly descriptive. We did not assess publication bias expecting the impact to be negligible**.**

Implications of our findings

The finding that ACMs have a high prevalence of OHPs, including accidents and injury, call for vigilance as regards cabin and cockpit crew's health status becoming a priority for occupational health providers in the sector. Based on our study, MSDs are the most prevalent problem followed by FSDs, which can pose significant risk to the safety of the individual, crew and passengers if undetected. It is important to focus on early identification and help seeking to improve aircrew member's well-being. Until now, the health of ACMs has not received much attention in research and policy. Although the airline industry should support these working groups by providing careful screening, programme to improve mitigate OHPs and well-designed longitudinal studies are necessary to further observe health outcomes, consequences and associated risk factors. Government, policy makers, clinicians and occupational health authorities must work and focus to develop and adapt occupational health measures and safety policies to prevent adverse outcomes and protect the health of aircrew members.

CONCLUSION

This review shows a high prevalence of MSDs, FSDs, gastrointestinal, respiratory, ENT, Metabolic disorders, dermatological disorders and sexual harassment. However, PPR for cardiovascular, renal, reproductive, cancers and ophthalmological disorders were comparatively lower, with fewer studies reporting these outcomes. Additionally, the estimate for occupational injuries was lower in the cockpit crew compared to the cabin crew. Finally, ACMs were not found to have high prevalence rate of thyroid cancer in cabin crew, relative to the general population**.**

This view highlights the need to provide appropriate resources and training to the aviation industry and insurers. The occupational health risks and health status of crew members have the potential to adversely affect the safety of themselves, their passengers and the public and is of public health importance, warranting further consideration.

In terms of research, the findings indicate the need for further research on the issues reported to compare the health problems experienced by ACMs with those experienced by other similar occupations and the general population. We suggest the use of validated and appropriate scales and instruments to assess health in studies on ACMs, which allows for comparison with other studies. Further observational studies are required, to understand how longitudinal exposures may influence health status of ACMs over time when compared to baseline health status. These have the potential to inform preventative strategies to enhance the occupational and general health status of ACMs.

REFERENCES

1. Morris H. How many planes are there in the world right now? The Telegraph. 2017.
2. Council NR. The airliner cabin environment: air quality and safety: National Academies Press; 1986.
3. Statistics UBoL. May 2016 national occupational employment and wage estimates United States. 2019.
4. Runeson-Broberg R, Lindgren T, Norbäck D. Musculoskeletal symptoms and psychosocial work environment, among Swedish commercial pilots. International archives of occupational and environmental health. 2014;87(7):685-93.
5. Nicholas JS, Butler GC, Lackland DT, Tessier GS, Mohr JL, Hoel DG. Health among commercial airline pilots. Aviation, space, and environmental medicine. 2001;72(9):821-6.
6. Rafnsson V, Olafsdottir E, Hrafnkelsson J, Sasaki H, Arnarsson A, Jonasson F. Cosmic radiation increases the risk of nuclear cataract in airline pilots: a population-based case-control study. Archives of ophthalmology. 2005;123(8):1102-5.
7. Hong O, Kim M. Factors associated with hearing loss among workers of the airline industry in Korea. ORL-head and neck nursing: official journal of the society of otorhinolaryngology and head-neck nurses. 2001;19(1):7-13.
8. Irvine D, Davies DM. British Airways flightdeck mortality study, 1950-1992. Aviation, space, and environmental medicine. 1999;70(6):548-55.
9. Wilder-Smith A, Paton NI, Goh KT. Low risk of transmission of severe acute respiratory syndrome on airplanes: the Singapore experience. Tropical medicine & international health. 2003;8(11):1035-7.
10. Leder K, Newman D. Respiratory infections during air travel. Internal medicine journal. 2005;35(1):50-5.
11. Byrne NJ, Behrens RH. Airline crews' risk for malaria on layovers in urban sub-Saharan Africa: Risk assessment and appropriate prevention policy. Journal of travel medicine. 2004;11(6):359-63.
12. Sutton PM, Vergara X, Beckman J, Nicas M, Das R. Pesticide illness among flight attendants due to aircraft disinsection. American journal of industrial medicine. 2007;50(5):345-56.
13. Lindgren T, Norbäck D. Heath and perception ofcabin air quality among Swedish commercial airlinecrew. Indoor Air. 2005;15 65–72:65-72.
14. Nagda NL, Hodgson M. Low relative humidity and aircraft cabin air quality. Indoor air. 2001;11(3):200-14.
15. Méndez AM. Urolithiasis among flight personnel (author's transl). Medicina clinica. 1979;72(2):65-70.
16. Sykes AJ, Larsen PD, Griffiths RF, Aldington S. A study of airline pilot morbidity. Aviation, space, and environmental medicine. 2012;83(10):1001-6.
17. dos Santos Silva I, Pizzi C, Evans A, Evans S, De Stavola B. Reproductive history and adverse pregnancy outcomes in commercial flight crew and air traffic control officers in the United Kingdom. Journal of occupational and environmental medicine. 2009;51(11):1298-305.
18. Hinst J, Bruchac D. The influence of civil aviation upon the reproductive system of the woman (author's transl). Ceskoslovenska gynekologie. 1981;46(6):456-9.
19. Zeeb H, Hammer GP, Langner I, Schafft T, Bennack S, Blettner M. Cancer mortality among German aircrew: second follow-up. Radiation and environmental biophysics. 2010;49(2):187-94.
20. Council NR. Health Effects Associated with Exposure to Airliner Cabin Air. The Airliner Cabin Environment: Air Quality and Safety: National Academies Press (US); 1986.
21. Reynolds P, Cone J, Layefsky M, Goldberg DE, Hurley S. Cancer incidence in California flight attendants (United States). Cancer Causes & Control. 2002;13(4):317-24.

22. Blettner M, Zeeb H, Auvinen A, Ballard TJ, Caldora M, Eliasch H, et al. Mortality from cancer and other causes among male airline cockpit crew in Europe. International journal of cancer. 2003;106(6):946-52.
23. Miura K, Olsen CM, Rea S, Marsden J, Green AC. Do airline pilots and cabin crew have raised risks of melanoma and other skin cancers? Systematic review and meta-analysis. British Journal of Dermatology. 2018.
24. McNeely E, Gale S, Tager I, Kincl L, Bradley J, Coull B, et al. The self-reported health of US flight attendants compared to the general population. Environmental Health. 2014;13(1):13.
25. McNeely E, Mordukhovich I, Tideman S, Gale S, Coull B. Estimating the health consequences of flight attendant work: comparing flight attendant health to the general population in a cross-sectional study. BMC public health. 2018;18(1):346.
26. Feijo D, Luiz RR, Camara VM. Common mental disorders among civil aviation flight attendants. Aviation, space, and environmental medicine. 2014;85(4):433-9.
27. Grajewski B, Whelan E, Nguyen M, Kwan L, Cole R. Sleep disturbance among female flight attendants and teachers in a reproductive biomonitoring study. American Journal of Epidemiology. 2000;151(11).
28. Ballard T, Romito P, Lauria L, Vigiliano V, Caldora M, Mazzanti C, et al. Self perceived health and mental health among women flight attendants. Occupational and environmental medicine. 2006;63(1):33-8.
29. De Stavola BL, Pizzi C, Clemens F, Evans SA, Evans AD, dos Santos Silva I. Cause-specific mortality in professional flight crew and air traffic control officers: findings from two UK population-based cohorts of over 20,000 subjects. International archives of occupational and environmental health. 2012;85(3):283-93.
30. Lee H, Wilbur J, Kim MJ, Miller AM. Psychosocial risk factors for work-related musculoskeletal disorders of the lower-back among long-haul international female flight attendants. Journal of Advanced Nursing. 2008;61(5):492-502.
31. Nagda NL, Koontz MD. Review of studies on flight attendant health and comfort in airliner cabins. Aviation, space, and environmental medicine. 2003;74(2):101-9.
32. Rayman RB. Cabin air quality: an overview. Aviation, space, and environmental medicine. 2002;73(3):211-5.
33. Griffiths RF, Powell D. The occupational health and safety of flight attendants. Aviation, space, and environmental medicine. 2012;83(5):514-21.
34. Kiersz A, Gillett R, Hoff M. The 47 jobs that are most damaging to your health 2020 [Available from: https://www.businessinsider.com/most-unhealthy-jobs-in-america-2017-4?IR=T.
35. https://www.businessinsider.com/most-unhealthy-jobs-in-america-2017-4?IR=T.
36. United States Department of Labour. Occupational Safety and Health Administration. Applicability of Certain OSHA Standards to Cabin Crew Members on Aircraft in Operation 2014 [Available from: https://www.osha.gov/dep/letters/04012014_AircraftCabinCrewmembers.html.
37. Linton OW, Mettler Jr FA, editors. National council on radiation protection and measurements. National conference on dose reduction in CT, with an emphasis on pediatric patients AJR Am J Roentgenol; 2003.
38. Centers for Disease Control and Prevention. The National Institute for Occupational Safety and Health (NIOSH). Aircrew Safety and Health 2019 [Available from: https://www.cdc.gov/niosh/topics/aircrew/default.html.
39. Kim JN, Lee BM. Risk factors, health risks, and risk management for aircraft personnel and frequent flyers. Journal of Toxicology and Environmental Health, Part B. 2007;10(3):223-34.
40. International hazard datasheets on occupation (occupation physician). http://www.onetonline.org/link/summary/53-2031.00
41. Lim M, Koh D. SARS and occupational health in the air. BMJ Publishing Group Ltd; 2003.
42. Sanlorenzo M, Wehner MR, Linos E, Kornak J, Kainz W, Posch C, et al. The risk of melanoma in airline pilots and cabin crew: a meta-analysis. JAMA dermatology. 2015;151(1):51-8.

43. Liu GS, Cook A, Richardson M, Vail D, Holsinger FC, Oakley-Girvan I. Thyroid cancer risk in airline cockpit and cabin crew: a meta-analysis. Cancers of the head & neck. 2018;3(1):7.
44. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. Cochrane handbook for systematic reviews of interventions: John Wiley & Sons; 2019.
45. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systematic reviews. 2016;5(1):210.
46. Werfalli M, Musekiwa A, Engel ME, Ross I, Kengne AP, Levitt NS. The prevalence of type 2 diabetes mellitus among older people in Africa: a systematic review study protocol. BMJ open. 2014;4(6):e004747.
47. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. Journal of clinical epidemiology. 2012;65(9):934-9.
48. Reuters T. ISI Research-Soft Endnote 90. 2019 [Available from: http://www.endnote.com.
49. Rohwer A, Garner P, Young T. Reading systematic reviews to answer clinical questions. Clinical Epidemiology and Global Health. 2014;2(1):39-46.
50. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Research synthesis methods. 2010;1(2):97-111.
51. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Bmj. 1997;315(7109):629-34.
52. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994:1088-101.
53. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009;151(4):264-9.
54. Morris H. How many planes are there in the world right now. The Telegraph. 2017.
55. Council NR. The airliner cabin environment: air quality and safety. 1986.
56. Nicholas JS, Butler GC, Lackland DT, Tessier GS, Mohr Jr L, Hoel DG. Health among commercial airline pilots. Aviation, space, and environmental medicine. 2001;72(9):821-6.
57. Lindgren T, Norbäck D. Health and perception of cabin air quality among Swedish commercial airline crew. Indoor Air. 2005;15:65-72.
58. Martín AM. Urolithiasis among flight personnel (author's transl). Medicina clinica. 1979;72(2):65-70.
59. dos Santos Silva I, Pizzi C, Evans A, Evans S, De Stavola B. Reproductive history and adverse pregnancy outcomes in commercial flight crew and air traffic control officers in the United Kingdom. Journal of occupational and environmental medicine. 2009:1298-305.
60. Council NR. Health Effects Associated with Exposure to Airliner Cabin Air. The Airliner Cabin Environment: Air Quality and Safety. 1986.
61. McNeely E, Gale S, Tager I, Kincl L, Bradley J, Coull B, et al. The self-reported health of US flight attendants compared to the general population. Environmental Health. 2014;13(1):1-11.
62. McNeely E, Mordukhovich I, Tideman S, Gale S, Coull B. Estimating the health consequences of flight attendant work: comparing flight attendant health to the general population in a cross-sectional study. BMC Public Health. 2018;18(1):1-11.
63. Grajewski B, Whelan E, Nguyen M, Kwan L, Cole R, editors. Sleep disturbance among female flight attendants and teachers in a reproductive biomonitoring study. AMERICAN JOURNAL OF EPIDEMIOLOGY; 2000: OXFORD UNIV PRESS INC JOURNALS DEPT, 2001 EVANS RD, CARY, NC 27513 USA.
64. Kiersz A, Gillett R, Hoff M. The 27 jobs that are most damaging to your health. Business Insider. 2015.
65. Che Huei L, Ya-Wen L, Chiu Ming Y, Li Chen H, Jong Yi W, Ming Hung L. Occupational health and safety hazards faced by healthcare professionals in Taiwan: A systematic review of risk factors and control strategies. SAGE open medicine. 2020;8:2050312120918999.

66. Miura K, Olsen CM, Rea S, Marsden J, Green AC. Do airline pilots and cabin crew have raised risks of melanoma and other skin cancers? Systematic review and meta-analysis. British Journal of Dermatology. 2019;181(1):55-64.
67. Liu GS, Cook A, Richardson M, Vail D, Holsinger FC, Oakley-Girvan I. Thyroid cancer risk in airline cockpit and cabin crew: a meta-analysis. Cancers of the Head & Neck. 2018;3(1):1-8.
68. Weinmann S, Tanaka LF, Schauberger G, Osmani V, Klug SJ. Breast cancer among female flight attendants and the role of the occupational exposures: A systematic review and meta-analysis. Journal of Occupational and Environmental Medicine. 2022.
69. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Systematic reviews. 2021;10(1):1-11.
70. Etherington C, Deng M, Boet S, Johnston A, Mansour F, Said H, et al. Impact of physician's sex/gender on processes of care, and clinical outcomes in cardiac operative care: a systematic review. BMJ open. 2020;10(9):e037139.
71. King C, Aylin P, Holmes A. Converting incidence and prevalence data: an update to the rule. Infection Control & Hospital Epidemiology. 2014;35(11):1432-3.
72. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Archives of Public Health. 2014;72:1-10.
73. Wu AC, Donnelly-McLay D, Weisskopf MG, McNeely E, Betancourt TS, Allen JG. Airplane pilot mental health and suicidal thoughts: a cross-sectional descriptive study via anonymous web-based survey. Environmental health. 2016;15(1):1-12.
74. Yang Y, Zhang W, Chan A, Li C, He X, Cui L, et al. An epidemiological study of reproductive health in female civil aviation employees. Aviation, Space, and Environmental Medicine. 2013;84(6):625-9.
75. Aljurf TM, Olaish AH, BaHammam AS. Assessment of sleepiness, fatigue, and depression among Gulf Cooperation Council commercial airline pilots. Sleep and Breathing. 2018;22(2):411-9.
76. Ebbert JO, Croghan IT, Schroeder DR, Murawski J, Hurt RD. Association between respiratory tract diseases and secondhand smoke exposure among never smoking flight attendants: a cross-sectional survey. Environmental Health. 2007;6(1):1-8.
77. Beatty AL, Haight TJ, Redberg RF. Associations between respiratory illnesses and secondhand smoke exposure in flight attendants: A cross-sectional analysis of the Flight Attendant Medical Research Institute Survey. Environmental Health. 2011;10(1):1-8.
78. McNeely E, Mordukhovich I, Staffa S, Tideman S, Gale S, Coull B. Cancer prevalence among flight attendants compared to the general population. Environmental Health. 2018;17(1):1-9.
79. Kagami S, Bradshaw SE, Fukumoto M, Tsukui I. Cataracts in airline pilots: prevalence and aeromedical considerations in Japan. Aviation, space, and environmental medicine. 2009;80(9):811-4.
80. Chen X, Liu Y, Yu Q, Zheng L, Hong X, Yan F, et al. Dental caries status and oral health behavior among civilian pilots. Aviation, Space, and Environmental Medicine. 2014;85(10):999-1004.
81. Lindgren T, Runeson R, Wahlstedt K, Wieslander G, Dammström B-G, Norbäck D. Digestive functional symptoms among commercial pilots in relation to diet, insomnia, and lifestyle factors. Aviation, space, and environmental medicine. 2012;83(9):872-8.
82. Jia N, Zhang H, Ling R, Liu Y, Li G, Ren Z, et al. Epidemiological Data of Work-Related Musculoskeletal Disorders—China, 2018–2020. China CDC Weekly. 2021;3(18):383.
83. de Souza Palmeira ML, Marqueze EC. Excess weight in regular aviation pilots associated with work and sleep characteristics. Sleep science. 2016;9(4):266-71.
84. Rau P-LP, Tsao L, Dong L, Liu X, Ma L, Wang J. General and passenger-relevant factors of work-related musculoskeletal disorders (WMSDs) among Chinese female flight attendants. Work. 2020;66(4):861-9.
85. Heidecker B, Spencer RM, Hayes V, Hall S, Parikh N, Stock EO, et al. High prevalence and clinical/sociodemographic correlates of miscarriages among flight attendants. The American Journal of Medicine. 2017;130(12):1397-401.

86. Alonso-Rodríguez C, Medina-Font J. High sensitivity C-reactive protein in airline pilots with metabolic syndrome. Aviation, space, and environmental medicine. 2012;83(5):504-8.
87. Bhat KG, Verma N, Pant P, Singh Marwaha MP. Hypertension and obesity among civil aviation pilots. Aerospace Medicine and Human Performance. 2019;90(8):703-8.
88. Cobb S, Russo T, Kutash M, Kellems R. Medical flight crew perceived work-related musculoskeletal symptoms and related characteristics. Air Medical Journal. 2012;31(1):36-41.
89. Lindgren T, Andersson K, Dammström B-G, Norbäck D. Ocular, nasal, dermal and general symptoms among commercial airline crews. International archives of occupational and environmental health. 2002;75(7):475-83.
90. Pinto JA, Nunes HdSS, Soeli dos Santos R, Cavallini A, Freitas G, Knoll D, et al. Otitis Media with Effusion in Aircrew Members. Aerospace Medicine and Human Performance. 2019;90(5):462-5.
91. Yu Q, Liu Y, Chen X, Chen D, Xie L, Hong X, et al. Prevalence and associated factors for temporomandibular disorders in Chinese civilian pilots. International archives of occupational and environmental health. 2015;88(7):905-11.
92. Li C, Xu J, Yin D, Zhang Y, Shan D, Jiang X, et al. Prevalence and trigger factors of functional gastrointestinal disorders among male civil pilots in China. Scientific Reports. 2021;11(1):1-13.
93. Prombumroong J, Janwantanakul P, Pensri P. Prevalence of and biopsychosocial factors associated with low back pain in commercial airline pilots. Aviation, space, and environmental medicine. 2011;82(9):879-84.
94. Jackson CA, Earl L. Prevalence of fatigue among commercial pilots. Occupational medicine. 2006;56(4):263-8.
95. Reis C, Mestre C, Canhão H. Prevalence of fatigue in a group of airline pilots. Aviation, space, and environmental medicine. 2013;84(8):828-33.
96. Chen P-H, Liu X, Dong L, Rau P-LP. Prevalence of musculoskeletal discomfort among female cabin crew in Taiwan. Journal of Occupational Health. 2021;63(1):e12286.
97. Alhejaili F, Hafez A, Wali S, Alshumrani R, Alzehairi AM, Balkhyour M, et al. Prevalence of obstructive sleep apnea among Saudi pilots. Nature and Science of Sleep. 2021;13:537.
98. Whelan E, Lawson C, Grajewski B, Petersen M, Pinkerton L, Ward E, et al. Prevalence of respiratory symptoms among female flight attendants and teachers. Occupational and environmental medicine. 2003;60(12):929-34.
99. Ezzat HM, Al-Sultan A, Al-Shammari A, Alyousef D, Al-Hamidi H, Al-Dossary N, et al. Prevalence of neck pain among cabin crew of Saudi Airlines. Journal of back and musculoskeletal rehabilitation. 2015;28(3):425-31.
100. Radowicka M, Pietrzak B, Wielgoś M. Prolactin secretion pattern among female flight attendants. International Journal of Occupational Medicine and Environmental Health. 2021;34(3):351-61.
101. Wahlstedt K, Lindgren T, Norbäck D, Wieslander G, Runeson R. Psychosocial work environment and medical symptoms among Swedish commercial airline cabin crew. American journal of industrial medicine. 2010;53(7):716-23.
102. Lating JM, Sherman MF, Everly Jr GS, Lowry JL, Peragine TF. PTSD reactions and functioning of American Airlines flight attendants in the wake of September 11. The Journal of nervous and mental disease. 2004;192(6):435-41.
103. van Drongelen A, Boot CR, Hlobil H, Smid T, van der Beek AJ. Risk factors for fatigue among airline pilots. International archives of occupational and environmental health. 2017;90(1):39-47.
104. Omholt ML, Tveito TH, Ihlebæk C. Subjective health complaints, work-related stress and self-efficacy in Norwegian aircrew. Occupational Medicine. 2017;67(2):135-42.
105. Evans S, Radcliffe S-A. The annual incapacitation rate of commercial pilots. Aviation, space, and environmental medicine. 2012;83(1):42-9.
106. Shargorodsky J, Zheng L, Stillman F, Soong A, Navas-Acien A, Reh D, editors. The association between airline flight and sinonasal symptoms. International Forum of Allergy & Rhinology; 2016: Wiley Online Library.
107. Sultani I, Khayat S, Garout I, Alahmad L, Alzahrany A. The prevalence and risk factors of otic barotraumas among aircrew members. Int J Life Sci Pharma Res. 2019;9(2):24-30.

108. Lindgren T, Wieslander G, Dammström B-G, Norbäck D. Tinnitus among airline pilots: prevalence and effects of age, flight experience, and other noise. Aviation, space, and environmental medicine. 2009;80(2):112-6.
109. Rosenkvist L, Klokker M, Katholm M. Upper respiratory infections and barotraumas in commercial pilots: a retrospective survey. Aviation, space, and environmental medicine. 2008;79(10):960-3.
110. Węziak-Białowolska D, Białowolski P, Mordukhovich I, McNeely E. Work, gender, and sexual harassment on the frontlines of commercial travel: A cross-sectional study of flight crew well-being. The International Journal of Aerospace Psychology. 2020;30(3-4):171-89.
111. Marqueze EC, Nicola ACB, Diniz DH, Fischer FM. Working hours associated with unintentional sleep at work among airline pilots. Revista de saude publica. 2017;51.
112. Lee H, Wilbur J, Conrad KM, Mokadam D. Work-related musculoskeletal symptoms reported by female flight attendants on long-haul flights. Aviation, space, and environmental medicine. 2006;77(12):1283-7.
113. Band PR, Le ND, Fang R, Deschamps M, Coldman AJ, Gallagher RP, et al. Cohort study of Air Canada pilots: mortality, cancer incidence, and leukemia risk. American Journal of Epidemiology. 1996;143(2):137-43.
114. Van Drongelen A, Boot CR, Pas WL, Penders JG, Hlobil H, van der Beek AJ, et al. Flight schedules and occupational accidents among cabin crew: a longitudinal study. Aviation, space, and environmental medicine. 2013;84(12):1281-5.
115. Agampodi SB, Dharmaratne SD, Agampodi TC. Incidence and predictors of onboard injuries among Sri Lankan flight attendants. BMC Public Health. 2009;9(1):1-5.
116. Fu X, Lindgren T, Wieslander G, Janson C, Norbäck D. Respiratory illness and allergy related to work and home environment among commercial pilots. PloS one. 2016;11(10):e0164954.
117. McNeely E, Staffa SJ, Mordukhovich I, Coull B. Symptoms related to new flight attendant uniforms. BMC public health. 2017;17(1):1-8.
118. Reid CE, Gamble JL. Aeroallergens, allergic disease, and climate change: impacts and adaptation. EcoHealth. 2009;6:458-70.
119. Parno A, Sayehmiri K, Parno M, Khandan M, Poursadeghiyan M, Maghsoudipour M, et al. The prevalence of occupational musculoskeletal disorders in Iran: A meta-analysis study. Work. 2017;58(2):203-14.
120. Oza HH, Lee MG, Boisson S, Pega F, Medlicott K, Clasen T. Occupational health outcomes among sanitation workers: A systematic review and meta-analysis. International Journal of Hygiene and Environmental Health. 2022;240:113907.
121. Titelbach A. Barometer on pilot fatigue. Brussels (Belgium): European Cockpit Association. 2012.
122. Pasha T, Stokes PR. Reflecting on the Germanwings disaster: a systematic review of depression and suicide in commercial airline pilots. Frontiers in psychiatry. 2018;9:86.
123. Borbély AA. A two process model of sleep regulation. Hum neurobiol. 1982;1(3):195-204.
124. Wilson D, Driller M, Johnston B, Gill N. The prevalence of cardiometabolic health risk factors among airline pilots: a systematic review. International Journal of Environmental Research and Public Health. 2022;19(8):4848.
125. Sterud T, Ekeberg Ø, Hem E. Health status in the ambulance services: a systematic review. BMC health services research. 2006;6:1-10.
126. Soubrier J-P. Self-crash murder–suicide: Psychological autopsy essay and questions about the Germanwings crash. 2016.
127. DeHart RL. Health issues of air travel. Annual review of public health. 2003;24:133.
128. Frank P. Aviation physiology. Zeitschrift fur arztliche Fortbildung und Qualitatssicherung. 1999;93(7):476-9.
129. Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, et al. Carcinogenicity of shift-work, painting, and fire-fighting. Elsevier; 2007.

130. Lyon F. IARC monographs on the evaluation of carcinogenic risks to humans. Some industrial chemicals. 1994;60:389-433.
131. Winder C, Balouet J-C. The toxicity of commercial jet oils. Environmental research. 2002;89(2):146-64.
132. Lee PN, Hamling JS. Environmental tobacco smoke exposure and risk of breast cancer in nonsmoking women. An updated review and meta-analysis. Inhalation toxicology. 2016;28(10):431-54.
133. Buja A, Mastrangelo G, Perissinotto E, Grigoletto F, Frigo AC, Rausa G, et al. Cancer incidence among female flight attendants: a meta-analysis of published data. Journal of women's health. 2006;15(1):98-105.
134. TERRIBALLARD D, SUSANNALAGORIO M. Cancer incidence and mortality among flight personnel: a meta-analysis. Aviation, space, and environmental medicine. 2000;71(3):216-24.
135. Fink CA, Bates MN. Melanoma and ionizing radiation: is there a causal relationship? Radiation Research. 2005;164(5):701-10.
136. Leonardi-Bee J, Ellison T, Bath-Hextall F. Lifestyle factors of smoking, BMI and alcohol on the risk of Non-Melanoma Skin Cancer in adults: A systematic review. JBI Evidence Synthesis. 2012;10(6):352-98.

Appendix

Figure 1: PRISMA flow diagram summarizing study selection

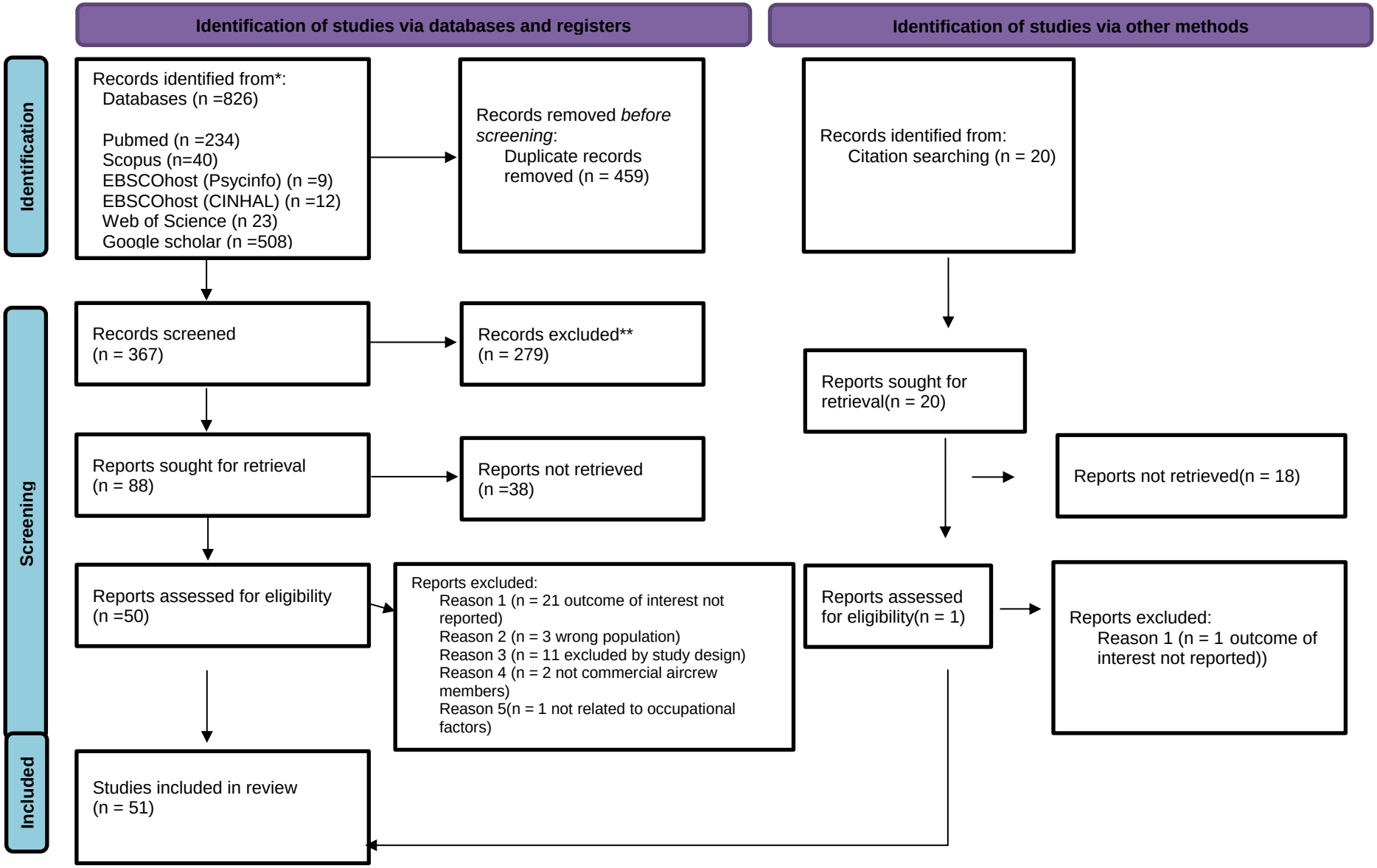

Table 4: Occupational hazards and exposures of aircrew members

OCCUPATIONAL HAZARD	EXAMPLES
Accident Hazards	Falls, trips, and slips due to multiple dynamic forces of the moving aircraft
Physical and safety	Electromagnetic fields (EMFs), and ionizing radiation of cosmic origin, Oxygen deficiency or hypoxia, noise, changes in pressures and temperatures due to high altitude, abnormal movements, low humidity, physical and sexual harassment.
Biological	Exposure to infectious disease (hepatitis A, malaria), tuberculosis, flue, coronaviruses (Severe Acute Respiratory Syndrome ("SARS"), coronavirus disease 19 (COVID 19), and microorganisms from contaminated food (Escherichia coli, vibrios, Salmonella, and Serratia marcescens).
Chemical	Chemical pollutants and environmental agents at altitude (Ozone, CO, and CO2), flame retardant chemicals, chemicals during aircraft disinfection and aircraft surface cleaners.
Ergonomic	Musculoskeletal injuries relating to the shoulder, neck, and lower back.
Psychosocial	Shift work, sleep deprivation, crossing time zones, tiredness, fatigue, impact of passenger behavior, and sexual harassment.

Table 5: Critical appraisal of the previous systematic reviews

	Sanlorenzo M (2014)	Miura (2019)	Liu G (2018)	Weinmann, (2022)
1. Were systematic review questions clear?	Yes	Yes	Yes	Yes
2. Did they address questions in our systematic review?	Partially	Partially	Partially	Partially
3. Was search extensive?	No. They did not search for unpublished data and the Cochrane Library	No. They did not search for unpublished data and the Cochrane Library	No. They did not search for unpublished data and did not use MeSH database.	No. They did not search for unpublished data and the Cochrane Library
4. Dates of studies included in the reviews	1990 to 2013	1990 to 2017	1996 to 2014	from inception to January 2022 (search date: 24 January 2022)
5. Number of studies included.	19	12	8	9
6. Did they do a quality assessment with peer-reviewed tool?	Quality assessment tool of included studies not mentioned	Newcastle-Ottawa Quality Assessment Scale.	Quality assessment tool of included studies not mentioned	Newcastle-Ottawa Quality Assessment Scale.
7. Sub-analyses appropriate?	Authors perform subgroup analyses across different subgroups (study design, cockpit vs cabin crew and by sex)	Authors perform subgroup analyses across different subgroups (cockpit vs cabin crew and by study design)	Authors perform subgroup analyses across different subgroups (cockpit vs cabin crew and by study design)	No

8. Reported according to the preferred Reporting Items in (PRISMA)?	Reported according to Prisma guidelines with some exceptions: Protocol not published nor registered in Prospero, data extraction not explained properly, and reviewers did not conduct risk of bias assessment.	Followed the preferred reporting items (PRISMA) and was registered with Prospero	This study was carried out following the Preferred Reporting Items (PRISMA), but with missing steps: Protocol not published nor registered in Prospero, data extraction not explained properly, reviewers did not conduct risk of bias assessment and inclusion criteria not clear (No mention of the language used)	Yes

Table 6: Search strategies

(Pubmed)

Search conducted 16 August 2022

Search	Query	Records retrieved
#1	"Occupational Health"[Mesh] Sort by: Most Recent	36,081
#2	"Occupational Medicine"[Mesh] Sort by: Most Recent	23,448
#3	"Occupational Injuries"[Mesh] Sort by: Most Recent	3,357
#4	"Occupational Exposure"[Mesh] Sort by: Most Recent	68,370
#5	"Occupational Diseases"[Mesh] Sort by: Most Recent	140,394
#6	"Aerospace Medicine"[Mesh] Sort by: Most Recent	15,102
#7	Occupational health OR industrial Hygiene OR employee health OR Occupational safety OR Occupational hazard OR occupational hazards OR Occupational medicine OR occupational disease OR occupational diseases OR Occupational Illness OR Occupational Illnesses OR occupational exposure OR occupational exposures OR Occupational injury OR Occupational Injuries OR aviation medicine OR aerospace medicine	465,221
#8	"Pilots"[Mesh] Sort by: Most Recent	675
#9	airline pilot OR airline pilots or flight crew or flight crews or cabin crew or cabin crews OR flight attendant or flight attendants OR cabin attendant OR cabin attendants OR aircrew personnel OR flight personnel OR aircrew worker OR aircrew workers OR airline crew OR airline crews	7628
#10	"Cross-Sectional Studies"[Mesh] Sort by: Most Recent	435984
#11	Cross Sectional Study OR Cross Sectional Studies OR Cross-Sectional Study OR Cross-Sectional Studies OR Cross Sectional Analysis OR Cross Sectional Analyses OR Cross-Sectional Analysis OR Cross-Sectional Analyses Disease Frequency Surveys OR Cross-Sectional Survey OR Cross Sectional Survey OR Cross-Sectional Surveys OR Disease Frequency Survey OR Disease Frequency Surveys OR Prevalence Studies OR Prevalence Study	1080608
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6	251,003
#13	#7 OR #12	465,197
#14	#8 OR #9	7893
#15	#10 OR #11	1080608
#16	*#7 OR #12 AND #8 OR #9 AND #10 OR #11	234

*https://www.ncbi.nlm.nih.gov/sites/myncbi/1LwlVrv_cv_5m/collections/62084723/public/

Web of Science: Core collection

Search conducted 16 August 2022

Search	Query	Records retrieved
#1	“Occupational health” OR “Industrial Hygiene” OR “employee health” OR “Occupational safety” OR “Occupational hazard*” OR “Occupational medicine” OR “occupational disease*” OR “Occupational Illness*” OR “occupational exposure*” OR “Occupational injury” OR “Occupational injuries” OR “aviation medicine” OR “aerospace medicine” (All Fields)	98,589
#2	“airline pilot*” OR “flight crew*” OR “cabin crew*” OR “flight attendant*” OR “cabin attendant*” OR “aircrew personnel” OR “flight personnel” OR “aircrew worker*” OR “airline crew*” (All Fields)	4,985
#3	“Cross Sectional Study” OR “Cross Sectional Studies” OR “Cross-Sectional Study” OR “Cross-Sectional Studies” OR “Cross Sectional Analysis” OR “Cross Sectional Analyses” OR “Cross-Sectional Analysis” OR “Cross-Sectional Analyses” OR “Disease Frequency Survey*” OR “Cross-Sectional Survey*” OR “Cross Sectional Survey*” OR “Prevalence Study” OR “Prevalence Studies” (All Fields)	300,763
#4	#1 AND #2 AND #3	23

(Scopus)

Search conducted 16 August 2022

Search	Query	Records retrieved
#1	TITLE-ABS-KEY ("Occupational health" OR "Industrial Hygiene" OR "employee health" OR "Occupational safety" OR "Occupational hazard*" OR "Occupational medicine" OR "occupational disease*" OR "Occupational Illness*" OR "occupational exposure*" OR "Occupational injury" OR "Occupational injuries" OR "aviation medicine" OR "aerospace medicine")	320,700
#2	TITLE-ABS-KEY ("airline pilot*" OR "flight crew*" OR "cabin crew*" OR "flight attendant*" OR "cabin attendant*" OR "aircrew personnel" OR "flight personnel" OR "aircrew worker*" OR "airline crew*")	4,933
#3	TITLE-ABS-KEY ("Cross Sectional Study" OR "Cross Sectional Studies" OR "Cross-Sectional Study" OR "Cross-Sectional Studies" OR "Cross Sectional Analysis" OR "Cross Sectional Analyses" OR "Cross-Sectional Analysis" OR "Cross-Sectional Analyses" OR "Disease Frequency Survey*" OR "Cross-Sectional	621,121

	Survey*" OR "Cross Sectional Survey*" OR "Prevalence Study" OR "Prevalence Studies")	
#4	#1 AND #2 AND #3	40

PsycInfo (EBSCOhost)

Search conducted 16 August 2022

Search	Query	Records retrieved
S1	"Occupational health" OR "Industrial Hygiene" OR "employee health" OR "Occupational safety" OR "Occupational hazard*" OR "Occupational medicine" OR "occupational disease*" OR "Occupational Illness*" OR "occupational exposure*" OR "Occupational injury" OR "Occupational injuries" OR "aviation medicine" OR "aerospace medicine"	30,792
S2	"airline pilot*" OR "flight crew*" OR "cabin crew*" OR "flight attendant*" OR "cabin attendant*" OR "aircrew personnel" OR "flight personnel" OR "aircrew worker*" OR "airline crew*"	1,516
S3	"Cross Sectional Study" OR "Cross Sectional Studies" OR "Cross-Sectional Study" OR "Cross-Sectional Studies" OR "Cross Sectional Analysis" OR "Cross Sectional Analyses" OR "Cross-Sectional Analysis" OR "Cross-Sectional Analyses" OR "Disease Frequency Survey*" OR "Cross-Sectional Survey*" OR "Cross Sectional Survey*" OR "Prevalence Study" OR "Prevalence Studies"	96,591
S4	S1 AND S2 AND S3	9

CINHAL Complete (EBSCOhost)

Search conducted 16 August 2022

Search	Query	Records retrieved
S1	"Occupational health" OR "Industrial Hygiene" OR "employee health" OR "Occupational safety" OR "Occupational hazard*" OR "Occupational medicine" OR "occupational disease*" OR "Occupational Illness*" OR "occupational exposure*" OR "Occupational injury" OR "Occupational injuries" OR "aviation medicine" OR "aerospace medicine"	94,099
S2	"airline pilot*" OR "flight crew*" OR "cabin crew*" OR "flight attendant*" OR "cabin attendant*" OR "aircrew personnel" OR "flight personnel" OR "aircrew worker*" OR "airline crew*"	385
S3	"Cross Sectional Study" OR "Cross Sectional Studies" OR "Cross-Sectional Study" OR "Cross-Sectional Studies" OR "Cross Sectional Analysis" OR "Cross Sectional Analyses" OR "Cross-Sectional Analysis" OR "Cross-Sectional	259,222

	Analyses" OR "Disease Frequency Survey*" OR "Cross-Sectional Survey*" OR "Cross Sectional Survey*" OR "Prevalence Study" OR "Prevalence Studies"	
S4	S1 AND S2 AND S3	12

(Google scholar) Thesis, Dissertation & Conference proceedings

Search conducted 16 August 2022

#1	Flight crew OR Aircrew member "OCCUPATIONAL HEALTH " source:Conference	392
#2	Flight crew OR Aircrew member "OCCUPATIONAL HEALTH " source:THESIS	31
#3	Flight crew OR Aircrew member "OCCUPATIONAL HEALTH " source:Dissertation	9
#4	Flight crew OR Aircrew member "OCCUPATIONAL MEDICINE" source:Dissertation	2
#5	Flight crew OR Aircrew member "OCCUPATIONAL MEDICINE" source:THESIS	8
#6	Flight crew OR Aircrew member "OCCUPATIONAL MEDICINE" source:Conference	66

Table 7: List of excluded studies

Number	Reference	Summary comment for exclusion
1.	Omar MM, Al-Mulla KF, Al-Seleem TA, Murad B, Radovanovic Z. Middle East aircrew use of alcohol, tobacco, coffee, and medicaments. Aviation, space, and environmental medicine. 2005 Apr 1;76(4):395-8	a. The primary outcome not reported
2.	Salamanca MA, Fajardo HA. Estimating the morbidity profile amongst Colombian civil aviation personnel. Revista de salud publica. 2009 Jun;11(3):425-31.	a. Target population is not specific to aircrew member (mixed with air traffic controllers) b. Rotary-Wing Aircrew members given the varied nature of this aspect of the industry
3.	Cox L, Michaelis S. A survey of health symptoms in BAe 146 aircrew. Journal of Occupational Health and Safety Australia and New Zealand. 2002;18(4):305-12.	a. The primary outcome not reported
4.	Lee MY, Kim MS, Park BR. Adaptation of the horizontal vestibuloocular reflex in pilots. The laryngoscope. 2004 May;114(5):897-902	a. The primary outcome not reported
5.	Li G, Baker SP, Qiang Y, Rebok GW, McCarthy ML. Alcohol violations and aviation accidents: findings from the US mandatory alcohol-testing program. Aviation, space, and environmental medicine. 2007 May 1;78(5):510-3.	**a.** Excluded by study design
6.	Buila NB, Bantu JM, Kabanda GK, Bayauli PM, Nkodila AN, Lepira FB, Ditu SM, M'Buyamba-Kabangu JR. Atherosclerotic cardiovascular disease short-term risk estimate among civilian licensed aircrew. World Journal of Cardiovascular Diseases. 2019 Jan 30;9(2):92-108.	a. The primary outcome not reported
7.	Co M, Kwong A. Breast Cancer Rate and Mortality in Female Flight Attendants: A Systematic Review and Pooled Analysis. Clinical Breast Cancer. 2020 Oct 1;20(5):371-6.	**a.** Excluded by study design
8.	Ady Wirawan I, Wu R, Abernethy M, Aldington S, Larsen PD. Calcium scores in the risk assessment of an asymptomatic population: Implications for airline pilots. Aviation, Space, and Environmental Medicine. 2014 Aug 1;85(8):812-7.	a. The primary outcome not reported

9.	Whelan EA. Cancer incidence in airline cabin crew. Occupational and environmental medicine. 2003 Nov 1;60(11):805-6.	a. The primary outcome not reported
10.	Ady Wirawan I, Aldington S, Griffiths RF, Ellis CJ, Larsen PD. Cardiovascular investigations of airline pilots with excessive cardiovascular risk. Aviation, Space, and Environmental Medicine. 2013 Jun 1;84(6):608-12.	a. The primary outcome not reported
11.	Zeeb H, Langner I, Blettner M. Cardiovascular mortality of cockpit crew in Germany: cohort study. Zeitschrift für Kardiologie. 2003 Jun;92(6):483-9.	a. The primary outcome not reported
12.	Junttila IS, Vuorio A, Budowle B, Laukkala T, Sajantila A. Challenges in investigation of diabetes-related aviation fatalities—an analysis of 1491 subsequent aviation fatalities in USA during 2011–2016. International journal of legal medicine. 2018 Nov;132(6):1713-8.	a. Excluded by study design
13.	Fajardo Rodriguez HA, Ortiz Mayorga VA. Characterization of low back pain in pilots and maintenance technicians on a commercial airline. Aerospace medicine and human performance. 2016 Sep 1;87(9):795-9.	a. Air force, Agricultural and Rotary-Wing Aircrew members given the varied nature of this aspect of the industry
14.	Chorley AC, Evans BJ, Benwell MJ. Civilian pilot exposure to ultraviolet and blue light and pilot use of sunglasses. Aviation, Space, and Environmental Medicine. 2011 Sep 1;82(9):895-900.	a. Excluded by study design
15.	Reneman L, Schagen SB, Mulder M, Mutsaerts HJ, Hageman G, de Ruiter MB. Cognitive impairment and associated loss in brain white microstructure in aircrew members exposed to engine oil fumes. Brain imaging and behavior. 2016 Jun;10(2):437-44.	a. Excluded by study design
16.	Dumser T, Borsch M, Wonhas C. Coronary artery disease in aircrew fatalities: morphology, risk factors, and possible predictors. Aviation, space, and environmental medicine. 2013 Feb 1;84(2):142-7.	a. Air force Aircrew members given the varied nature of this aspect of the industry. These are not good surrogates for commercial

		aircrew members and are not suitable for our study
17.	Sexton JB, Thomas EJ, Helmreich RL. Error, stress, and teamwork in medicine and aviation: cross sectional surveys. Bmj. 2000 Mar 18;320(7237):745-9.	a. The primary outcome not reported
18.	McCooey S, Ison D. Female Cabin Crew Radiation Exposure and Cancer Development: A Cross-Study Inquiry. International Journal of Aviation Research. 2017 Feb 5;9(1).	a. Excluded by study design
19.	Pukkala E, Auvinen A, Wahlberg G. Incidence of cancer among Finnish airline cabin attendants, 1967-92. Bmj. 1995 Sep 9;311(7006):649-52.	a. The primary outcome not reported
20.	Pukkala E, Aspholm R, Auvinen A, Eliasch H, Gundestrup M, Haldorsen T, Hammar N, Hrafnkelsson J, Kyyrönen P, Linnersjö A, Rafnsson V. Incidence of cancer among Nordic airline pilots over five decades: occupational cohort study. Bmj. 2002 Sep 14;325(7364):567.	a. The primary outcome not reported
21.	Hu C-J, Hong R-M, Yeh G-L, Hsieh I-C. Insomnia, work-related burnout, and eating habits affecting the work ability of flight attendants. Aerosp Med Hum Perform. 2019; 90(7):601-605.	a. The primary outcome not reported
22.	MacDonald LA, Deddens JA, Grajewski BA, Whelan EA, Hurrell JJ. Job stress among female flight attendants. Journal of occupational and environmental medicine. 2003 Jul 1:703-14.	a. The primary outcome not reported
23.	McNeely E, Mordukhovich I, Staffa S, Tideman S, Coull B. Legacy health effects among never smokers exposed to occupational secondhand smoke. PloS one. 2019 Apr 18;14(4): e0215445.	a. The primary outcome not reported
24.	Byrne N. Low prevalence of TB on long-haul aircraft. Travel Medicine and Infectious Disease. 2007 Jan 1;5(1):18-23.	a. The primary outcome not reported b. The target population mixed
25.	Liu R, Dix-Cooper L, Hammond SK. Modeling flight attendants' exposure to secondhand smoke in commercial aircraft: historical trends from 1955 to 1989. Journal of Occupational and Environmental Hygiene. 2015 Mar 4;12(3):145-55.	a. The primary outcome not reported

26.	Müller R, Schneider J. Noise exposure and auditory thresholds of German airline pilots: a cross-sectional study. BMJ Open 2017;7: e012913. doi:10.1136/bmjopen-2016-012913	a. The primary outcome not reported
27.	Irgens Å, Irgens LM, Reitan JB, Haldorsen T, Tveten U. Pregnancy outcome among offspring of airline pilots and cabin attendants. Scand J Work Environ Health 2003;29(2):94–99.	a. The primary outcome not reported b. The target population not determined
28.	Winter M, Blettner M, Zeeb H. Prevalence of risk factors for breast cancer in German airline cabin crew: a cross-sectional study. Journal of occupational medicine and toxicology. 2014 Dec;9(1):1-5.	a. Excluded by study design
29.	Lewis B. Risk factors for coronary heart disease—assessment in airline pilots. European Heart Journal. 1984 Jan 1;5(suppl_A):17-24.	a. The primary outcome not reported
30.	Düz OA, Yilmaz NH, Olmuscelik O. Restless legs syndrome in aircrew. Aerosp Med Hum Perform. 2019; 90(11):934–937.	a. Excluded by study design
31.	Lewis B. Risk factors for coronary heart disease—assessment in airline pilots. European Heart Journal. 1984 Jan 1;5(suppl_A):17-24. medicine. 2003 Nov 1;60(11):815-20.	a. Excluded by study design
32.	Rafnsson V, Hrafnkelsson J, Tulinius H, Sigurgeirsson B, Olafsson JH. Risk factors for cutaneous malignant melanoma among aircrews and a random sample of the population. Occupational and environmental	a. Excluded by study design
33.	Kojo K, Helminen M, Pukkala E, Auvinen A. Risk factors for skin cancer among Finnish airline cabin crew. Annals of occupational hygiene. 2013 Jul 1;57(6):695-704.calcification. JACC: Cardiovascular Imaging. 2013 Jun;6(6):651-7. 1;63(1):33-8.	a. Excluded by study design
34.	Yankelevitz DF, Henschke CI, Yip R, Boffetta P, Shemesh J, Cham MD, Narula J, Hecht HS, Famri-Ielcap Investigators. Second-hand tobacco smoke in never smokers is a significant risk factor for coronary artery calcification. JACC: Cardiovascular Imaging. 2013 Jun;6(6):651-7. 1;63(1):33-8.	a. Cannot find the target population. The author does not tell in their writing is that aircrew members or not
35.	Sveinsdottir H, Gunnarsdóttir H, Friðriksdóttir H. Self-assessed occupational health and working environment of female nurses, cabin crew and	a. The primary outcome not reported

	teachers. Scandinavian journal of caring sciences. 2007 Jun;21(2):262-73.	
36.	van Drongelen A, van der Beek AJ, Penders GB, Hlobil H, Smid T, Boot CR. Sickness absence and flight type exposure in flight crew members. Occupational Medicine. 2015 Jan 1;65(1):61-6.	a. The primary outcome not reported
37.	Chorley AC, Evans BJW, Benwell MJ. Solar eye protection practices of civilian aircrew. Aerosp Med Hum Perform. 2015; 86(11):9 53– 9 61.	a. The primary outcome not reported b. Studies of the health aspects of pilot or crew members relating to factors not thought to be occupationally related
38.	Li G, Baker SP, Grabowski JG, Rebok GW. Factors associated with pilot error in aviation crashes. Aviation, space, and environmental medicine. 2001 Jan 1;72(1):52-8. 1;77(12):1283-7.	a. The primary outcome not reported

Table 8: The National Institutes of Health (NIH) Quality Assessment Tool for cohort studies

Questions	(Li, G 2007)	(Van Drongelen 2013)	(Fu, X 2016)	McNeely 2017
1. Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes
2. Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes
3. Was the participation rate of eligible persons at least 50%?	Yes	Yes	Yes	Yes
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?	Yes	Yes	Yes	Yes
5. Was a sample size justification, power description, or variance and effect estimates provided?	No	Yes	Yes	Yes
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Yes	Yes	Yes	Yes
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes- 2 years	Yes- 3 years	Yes- 3 years	Yes- 3 years
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	N/A	Yes	Yes-	Yes-

9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes-enrolment was dependent one exposure	Yes- enrolment was dependent one exposure	Yes- 3 years	Yes- 3 years
10. Was the exposure(s) assessed more than once over time?	N/A	NO the exposure was assessed once only	Yes- exposure(s) assessed more than once over time	Yes- exposure(s) assessed more than once over time
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes
12. Were the outcome assessors blinded to the exposure status of participants?	No	NO	NO	Yes
13. Was loss to follow-up after baseline 20% or less?	Yes	Yes	Yes	Yes
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	NO	Yes	Yes	No

Table 9:Results of the risk of bias analysis according to modified hoy et al scale

Studies	1. Was the target population representative of the population in relation to relevant studies?	2. Was the sampling frame a true or close representation of the target population	3. Was some form of random selection used to select the sample,	4. Was the likelihood of non-response bias minimal in the study?	5. Were data collected directly from the subjects (as opposed to a proxy)?	6. Was an acceptable case definition used in the study?	7. Was the study instrument that measured the parameter of interest shown to have validity and reliability?	8. Was the same mode of data collection used for all subjects?	9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	10. Were the numerator(s) for the parameter of interest appropriate?	11. Summary score on the overall risk of study bias	Risk of bias
LEE H et.al,2008	√	√	√	**NS**	√	√	**NS**	√	√	√	**8**	**Moderate**
Dorota et.al, 2022	√	**NS**	**NS**	√	√	√	**NS**	√	√	√	**7**	**Moderate**
LINDGREN T et.al, 2009	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Sultani, I et.al ,2019	√	**NS**	**NS**	√	√	√	**NS**	√	√	√	**7**	**Moderate**
Shargorodsky et.al,2016	√	√	√	**NS**	√	√	√	√	√	√	**9**	**low**
McNeely et.al,2018	√	√	**NS**	√	√	√	√	√	√	√	**9**	**Low**
Lee H et.al 2006	√	√	√	√	√	√	√	√	√	√	**10**	**Low**
Marqueze et.al,2017	√	√	√	√	√	√	√	√	√	√	**10**	**Low**
Evans S, et.al, 2012	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Rosenkvist et.al,2012	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Omholt ML, et.al, 2017	√	√	**NS**	**NS**	√	√	√	√	√	√	**7**	**Moderate**

Studies	1. Was the target population representative of the population in relation to relevant studies?	2. Was the sampling frame a true or close representation of the target population	3. Was some form of random selection used to select the sample,	4. Was the likelihood of non-response bias minimal in the study?	5. Were data collected directly from the subjects (as opposed to a proxy)?	6. Was an acceptable case definition used in the study?	7. Was the study instrument that measured the parameter of interest shown to have validity and reliability?	8. Was the same mode of data collection used for all subjects?	9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	10. Were the numerator(s) for the parameter of interest appropriate?	11. Summary score on the overall risk of study bias	Risk of bias
Ballard TJet.al 2006	√	**NS**	**NS**	√	√	√	√	√	√	√	**8**	**Moderate**
van Drongelen et.al 2017	√	√	√	√	√	√	√	√	√	√	**8**	**Moderate**
Lating JM et.al, 2004	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Wahlstedtet.al 2010	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Radowicka et.al, 2021	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Whelan EA et.al,2003	√	**NS**	**NS**	**NS**	√	√	√	√	√	√	**7**	**Moderate**
Ezzat et.al,2015	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Alhejaili Fet.al,2021	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Chen PHet.al,2021	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Reis C et.al 2013	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Jackson et.al 2006	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Li C, Xu et.al ,2021	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Yu Q, Liu et.al,2015	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Pinto JA et.al,2019	√	√	√	√	√	√	√	√	√	√	**10**	**low**

Studies	1. Was the target population representative of the population in relation to relevant studies?	2. Was the sampling frame a true or close representation of the target population	3. Was some form of random selection used to select the sample,	4. Was the likelihood of non-response bias minimal in the study?	5. Were data collected directly from the subjects (as opposed to a proxy)?	6. Was an acceptable case definition used in the study?	7. Was the study instrument that measured the parameter of interest shown to have validity and reliability?	8. Was the same mode of data collection used for all subjects?	9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	10. Were the numerator(s) for the parameter of interest appropriate?	11. Summary score on the overall risk of study bias	Risk of bias
Prombumroong et.al,2011	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Lindgren T et.al,2002	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Cobb S et.al,2012	√	√	√	**NS**	√	√	√	√	√	√	**9**	**low**
Agampodiet.al,2009	√	√	**NS**	√	√	√	√	√	√	√	**9**	**low**
Alonso-Rodríguez, et.al,2012	√	√	√	√	√	√	√	√	√	√	**10**	**Low**
Heidecker et.al,2017	√	√	√	**NS**	√	√	√	√	√	√	**9**	**low**
McNeely. et.al, 2014	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Rau PL. et.al, 2020	√	√	√	√	√	√	√	√	√	√	**10**	**low**
de Souza et.al, 2019	√	√	√	√	√	√	√	√	√	√	**10**	**Low**
Jia N et.al, 2021	√	√	√	√	√	√	√	√	√	√	**10**	**Low**
McNeely et.al,2018	√	√	√	√	√	√	√	√	√	√	**10**	**Low**
Chen X, et.al,2014	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Feijo D,, et.al,2014	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Kagami S, et.al,2009	√	√	√	**NS**	√	√	√	√	√	√	**9**	**low**
Beay AL et.al,2002	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**

Studies	1. Was the target population representative of the population in relation to relevant studies?	2. Was the sampling frame a true or close representation of the target population	3. Was some form of random selection used to select the sample,	4. Was the likelihood of non-response bias minimal in the study?	5. Were data collected directly from the subjects (as opposed to a proxy)?	6. Was an acceptable case definition used in the study?	7. Was the study instrument that measured the parameter of interest shown to have validity and reliability?	8. Was the same mode of data collection used for all subjects?	9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	10. Were the numerator(s) for the parameter of interest appropriate?	11. Summary score on the overall risk of study bias	Risk of bias
Aljurf et.al,2018	√	√	√	√	√	√	√	√	√	√	**10**	**Low**
Ebbert JO, et.al,2007	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**Moderate**
Wu AC,. et.al, 2016	√	√	√	√	√	√	√	√	√	√	**10**	**low**
Sykes AJ.et .al, 2012	√	√	**NS**	**NS**	√	√	**NS**	√	√	√	**7**	**low**
Yang Y et .al, 2013	√	√	√	**NS**	√	√	√	√	√	√	**9**	**low**
Beatty AL et.al,2011	√	√	**NS**	**NS**	√	√	**NS**	√	√	√	**7**	**Moderate**
Bhat KG et.al,2019	√	√	**NS**	**NS**	√	√	√	√	√	√	**8**	**low**
Risk of bias	**Low if >8**	**Moderate if 6-8**	**High if ≤5**									
Yes	√											
NS	**Not Stated**											

Table 10: Characteristics of included studies

Author, year	**Country**	**Study Design**	**Hazard Category A, Accident P, physical C, chemical B, biological E, ergonomic Ps, psychosocial U, undefined**	**Population Aircrew Cockpit Cabin**	**Total No. (M/F)**	**Age mean (years)**	**BMI**	**Employment period**
Sykes et al 2012	New Zealand	Cross-sectional	P	Cockpit	595 (574M/21F)	49.5	27.1	Not stated
Wu AC et al 2016	USA	Cross-sectional	Ps	Cockpit	1826 (1576M/250F)	50.5	Not stated	16
Yang Y et al 2013	China	Cross-sectional	P+Ps	Cabin	563 (563F)	30	19.5	9
Aljurf TM et al 2018	Saudi Arabia	Cross-sectional	P+Ps	Cockpit	328 (324M/4F)	41.4	27.6	12.1
Ebbert JO et al 2017	USA	Cross-sectional	C	Cabin	1003 (893M/110F)	54	Not stated	Not stated

Beatty AL et al 2011	USA	Cross-sectional	C	Cabin	362 Not stated	58.2	Not stated	Not stated
McNeely E et al 2018	USA	Cross-sectional	P+Ps	Cabin	5366 (1073M/4293F)	52	Not stated	20
Kagami S et al 2009	Japan	Cross-sectional	P	Cockpit	3780 (3780M)	51	Not stated	Not stated
Band PR et al 1996	Canada	Cohort	P	Cockpit	2680 (2680M)	50.5	Not stated	20.8
Feijo D et al 2014	Brazile	Cross-sectional	Ps	Cabin	440 (157M/283F)	33.6	Not stated	Not stated
Chen X et al 2014	China	Cross-sectional	P	Cockpit	556 (556M)	31.48	Not stated	Not stated
Lindgren T et al 2012	Sweden	Cross-sectional	P+Ps	Cockpit	354 (322M/32F)	51	25.2	Not stated
Jia N et al 2021	China	Cross-sectional	E	Cabin	1365 Not stated	32.3	Not stated	32.3
McNeely E et al 2018	USA	Cross-sectional	U	Cabin	5366 (510M/4856)	51.5	Not stated	20.4

de Souza et al 2016	Brazile	Cross-sectional	P+Ps	Cockpit	1198 (1198M)	39.2	Not stated	15.3
Van Drongelen A et al 2013	Netherland	Cohort	A+Ps	Cabin	6311 (1181M/5130F)	Not stated	Not stated	Not stated
Rau PL et al 2020	China	Cross-sectional	E+Ps	Cabin	46 (46F)	25.7	53.1	4.2
McNeely E et al 2014	UAS	Cross-sectional	U	Cabin	4011 (802M/3209F)	46.7	Not stated	20
Heidecker et al B 2017	USA	Cross-sectional	P+Ps	Cabin	145 (145F)	61	24	Not stated
Alonso-Rodríguez C et al 2012	Spain	Cross-sectional	P+Ps	Cockpit	1009 (1009M)	41	Not stated	Not stated
Bhat KG et al 2019	India	Cross-sectional	U	Cockpit	1185 (1071M/114F)	34.8	Not stated	Not stated
Agampodi SB et al 2009	Sri lanka		E	Cabin	322 (98M/224F)	31	Not stated	10
Cobb S et al 2012	USA	Cross-sectional	P+E	Aircrew	462 Not stated	43	Not stated	7.82

Lindgren T et al 2002	Sweden	Cross-sectional	P+Ps	Aircrew	1513 (703M/810F)	43	Not stated	Not stated
Pinto JA et al 2019	Brazil	Cross-sectional	P	Aircrew	1607 (829M/778F)	Not stated	Not stated	Not stated
Yu Q et al 2015	China	Cross-sectional	Ps	Cockpit	616 (616M)	31.4	Not stated	Not stated
Li C, Xu et al 2021	China	Cross-sectional	Ps	Cockpit	212 (212M)	33.83	Not stated	Not stated
Prombumroong J et al 2001	Thailand	Cross-sectional	Ps+E	Cockpit	684 Not stated	40.3	Not stated	Not stated
Jackson CA et al 2006	UK	Cross-sectional	P+Ps	Cockpit	162 (152M/10F)	38.3	Not stated	Not stated
Reis C et al 2013	Portugal	Cross-sectional	P+Ps	Cockpit	456 (442M/14F)	39.31	Not stated	Not stated
Chen PH et al 2021	China	Cross-sectional	E	Cabin	88 (88F)	26	53.2	>4
Alhejaili F et al 2021	Saudi Arabia	Cross-sectional	Ps	Cockpit	39 Not stated	43.26	Not stated	Not stated

Whelan EA et al 2003	USA	Cross-sectional	P+Ps+C	Cabin	1824 (1824F)	38.2	Not stated	13
Ezzat HM et al 2015	Saudi Arabia	Cross-sectional	E	Cabin	105 Not stated	Not stated	Not stated	Not stated
Radowicka M et al 2021	Poland	Cross-sectional	Ps	Cabin	103 (103F)	35	22.4	Not stated
LEE H et al 2007	USA	Cross-sectional	Ps+E	Cabin	164 (164F)	54.24	23.3	31.21
Wahlstedt K et al 2010	Sweden	Cross-sectional	Ps	Cabin	846 (164M/682F)	45.5	Not stated	19
Lating JM et al 2004	USA	Cross-sectional	A+Ps	Cabin	2050 (382M/1648F)	42.86	Not stated	Not stated
Fu X et al 2016	Sweden	Cohort	Ps	Cockpit	436 (413M/23F)	45	Not stated	12
van Drongelen A et al 2017	Netherland	Cross-sectional	Ps	Cockpit	502 (468M/34F)	40.5	24.1	Not stated
Ballard TJ et al 2005	Italy	Cross-sectional	Ps	Cabin	1955 Not stated	37.1	Not stated	Not stated

Omholt ML et al 2016	Norway	Cross-sectional	P+PS	Cockpit	416 (398M/18F)	Not stated	Not stated	10
Omholt ML et al 2016	Norway	Cross-sectional	P+PS	Cabin	427 (107M/320F)	Not stated	Not stated	10
McNeely E et al 2017	USA	Cohort	C	Cabin	1046 (172M/874F)	46	Not stated	Not stated
Evans S et al 2012	UK	Cross-sectional	Ps	Cockpit	16145 (15528M/617F)	45	Not stated	Not stated
Shargorodsky J et al 2016	USA	Cross-sectional	PS+C	Cabin	583 (181M/402F)	41.5	Not stated	15
Sultani I et al 2019	Saudi Arabia	Cross-sectional	PS	Aircrew	267 (173M/94F)	Not stated	Not stated	Not stated
L INDGREN T et al 2009	Sweden	Cross-sectional	P	Cockpit	460 (418M/42F)	47.5	Not stated	Not stated
Rosenkvist L et al 2008	Denmark	Cross-sectional	P	Cockpit	948 (920M/28F)	43.8	Not stated	20.8
Dorota Węziak-Białowolska et al 2020	USA	Cross-sectional	Ps	Cabin	8700 (1723M/6977F)	49.8	Not stated	18.5

Dorota Węziak-Białowolska et al 2020	USA	Cross-sectional	Ps	Cabin	1887 (642M/1245F)	45.5	Not stated	19.7
Marqueze EC et al 2017	Brazil	Cross-sectional	Ps	Cockpit	1234 (1198M/36F)	39.1	Not stated	15.2
Lee H et al 2006	USA	Cross-sectional	E	Cabin	185 (185F)	54	Not stated	30

Table 11: Stratified analyses of pooled prevalence rate for included studies

	Crude		Aircrew Stratified analysis				Cockpit Stratified analysis				Cabin Stratified analysis			
	No. of studies	No. of cases	No. of studies	No. of cases	Pooled PR (95%CI)	Heterogeneity (p-value	No. of studies	No. of cases	Pooled PR (95%CI)	Heterogeneity (p-value	No. of studies	No. of cases	Pooled PR (95%CI)	Heterogeneity (p-value
Respiratory	10	16460					3	2265	14.61% (4.47, 29.20)	<.001	7	14195	24.08% (14.18, 35.64)	<.001
Cardiovascular	1	4011									1	4011	2.42% (1.99, 2.94)	<.001
gastrointestinal	5	7582					4	2216	40.14 % (24.05, 57.40)	<.001	1	5366	17.29% (16.31, 18.33)	<.001
Psych/Neuro	8	16571					3	2749	13.42% (2.30, 31.55)	<.001	5	13822	22.33% (9.69, 38.34)	<.001
Sleep related	12	14141					8	3491	66.64% (52.65, 79.29)	<.001	4	10650	44.45% (31.78, 57.49)	<.001
Dermatological	2	2559	1	1513	12.03% (10.49, 13.77)						1	1046	17.97% (15.76, 20.42)	<.001
ENT	11	14979	3	3387	19.62% (9.66, 32.02)		2	1408	28.28% (25.96, 30.67)	<.001	6	10184	26.81% (19.88, 34.36)	<.001
Ophthalmological	4	12483	1	1513	10.97% (9.49, 12.65)		2	3780	2.80% (2.32 , 3.38)	<.001	1	7190	18.93% (18.03, 19.84)	<.001
Musculoskeletal	13	11128	1	462	72.08% (67.82, 75.97)		4	2929	25.78% (10.31, 45.27)	<.001	8	7737	36.90% (25.51, 49.08)	<.001
Renal	1	595					1	595	3.19% (2.05 , 4.93)	<.001				<.001
Reproductive/ Endocrine	3	811									3	811	9.45% (0.00, 41.07)	0.15
Metabolic	8	14395					4	3987	19.76% (9.43, 32.72)	<.001	4	10408	37.13% (21.70, 54.04)	<.001

Allergies	3	10380									3	10380	34.56% (26.61, 42.96)	<.001
Cancer	2	8046					1	2680	0.37% (0.20, 0.69)	<.001	1	5366	17.11% (16.12 , 18.14)	<.001
Breast Cancer	1	5366								<.001	1	5366	3.63% (3.17, 4.17)	<.001
Thyroid Cancer	1	5366								<.001	1	5366	0.61% (0.44, 0.86)	<.001
Reproductive Cancer	1	4011								<.001	1	4011	3.86% (3.31, 4.51)	<.001
Melanoma	2	5961					1	595	1.85% (1.04, 3.28)	<.001	1	5366	2.48% (2.10, 2.93)	<.001
Non-Melanoma	1										1	5366	9.00% (8.26, 9.80)	<.001
Occupational injuries	3	17701					2	17379	0.83% (0.69, 0.97)	<.001	1	322	48.14% (42.73 , 53.58)	<.001
Sexual harassment	3	12542								<.001	3	12542	24.01% (12.64 , 37.65)	<.001
Dental	2	1172					2	1172	35.48% (32.76, 38.24)	<.001				

Figure 2-22: Forest plot of prevalence of having occupational health diseases among ACMs

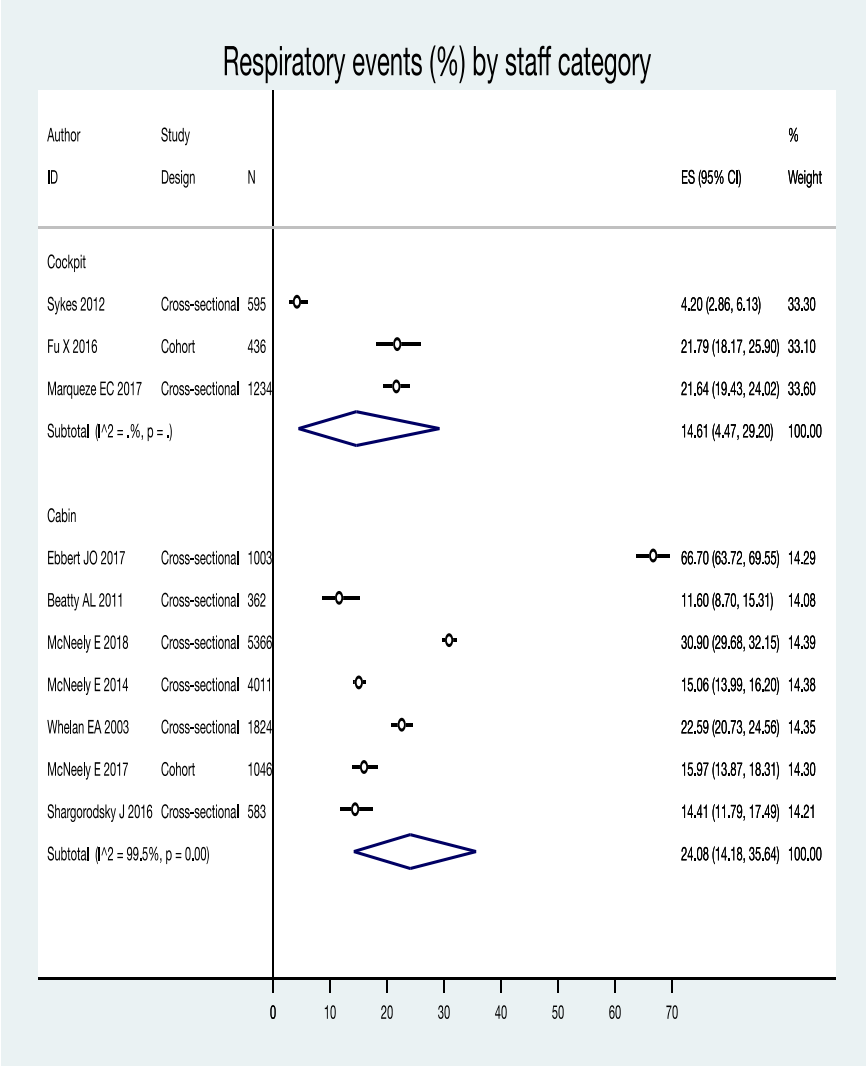

Figure 2: Forest plot of prevalence of having a respiratory diseases among ACMs

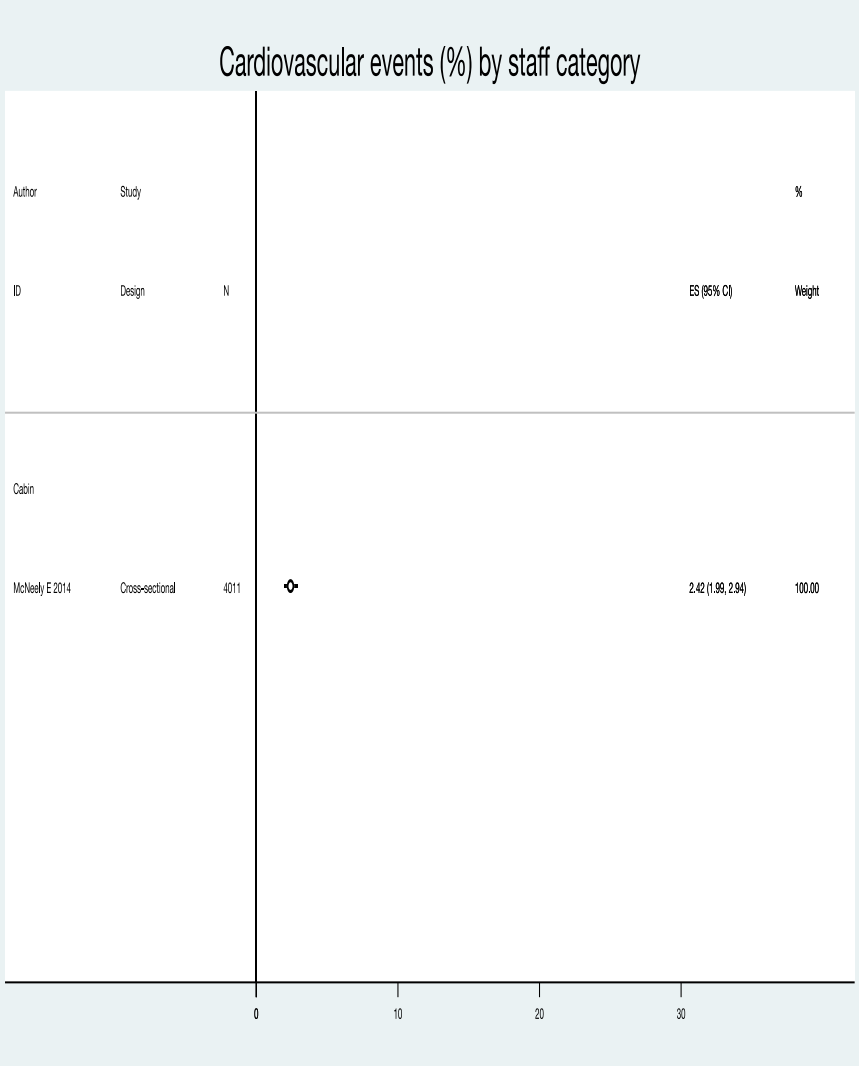

Figure 3: Forest plot of prevalence of having a cardiovascular diseases among ACMs

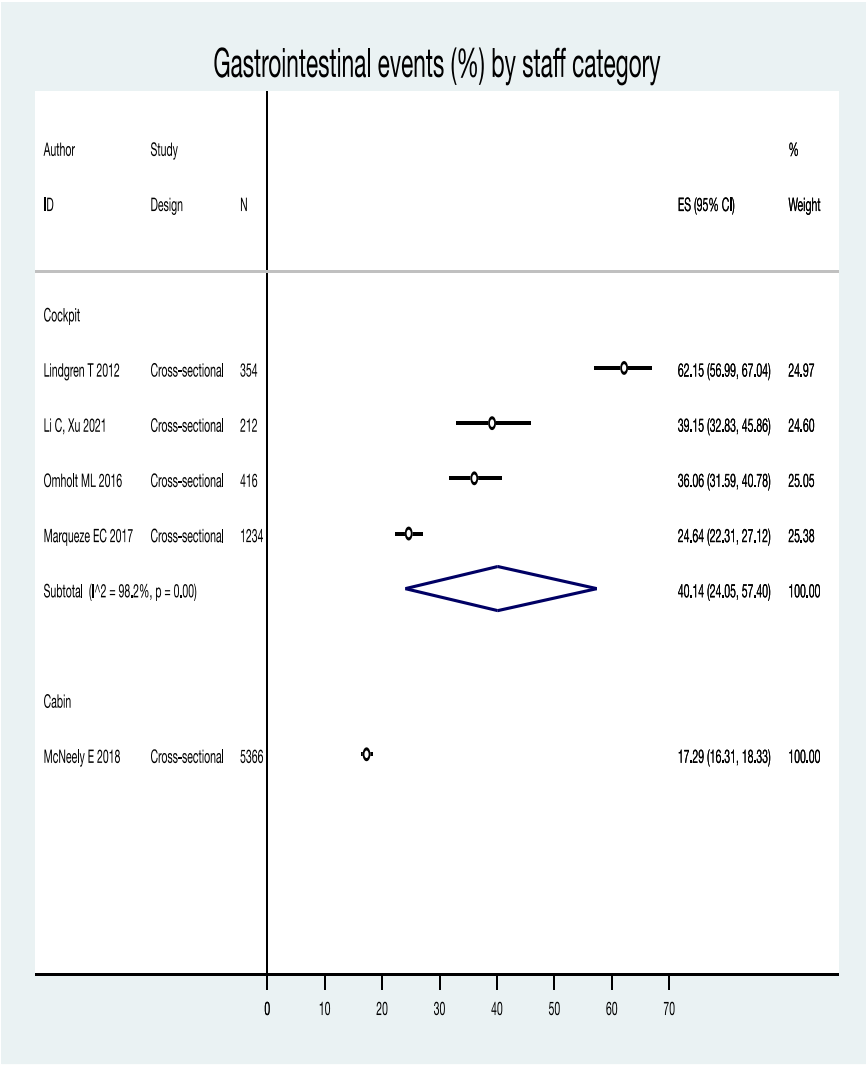

Figure 4: Forest plot of prevalence of having a Gastrointestinal diseases among ACMs

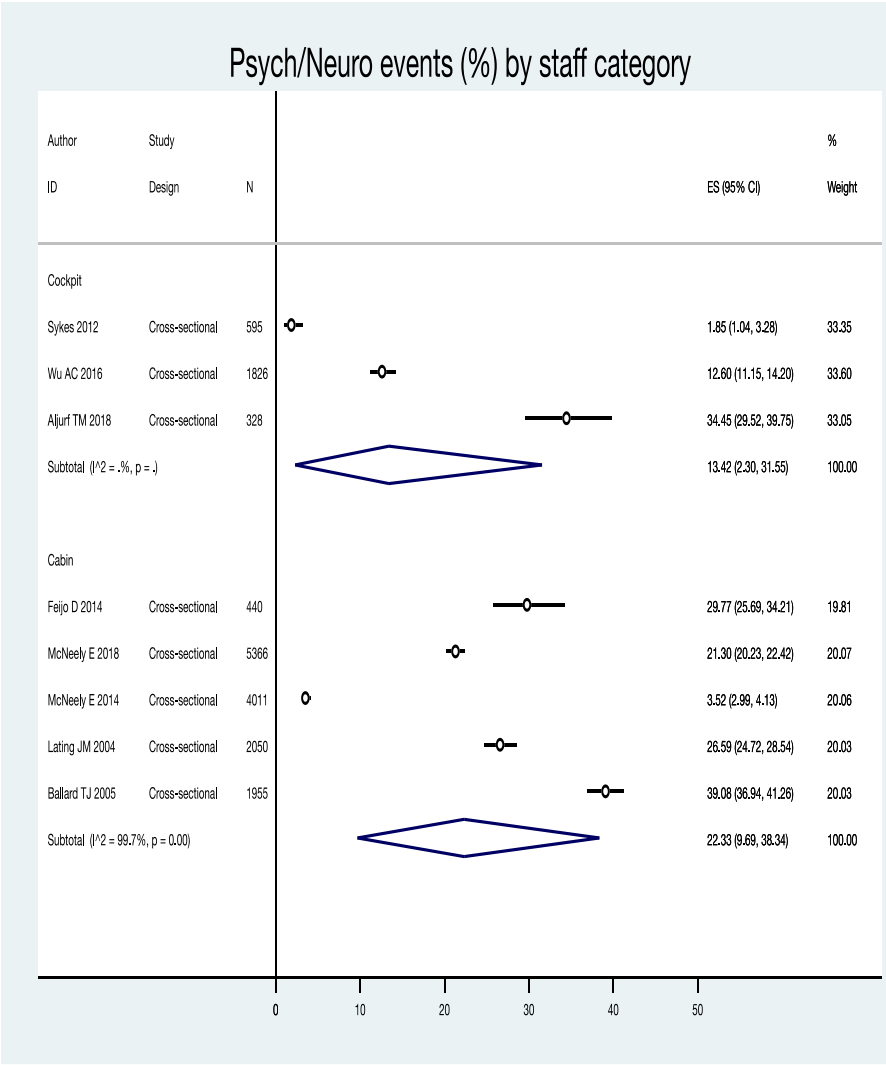

Figure 5: Forest plot of prevalence of having a psychological/neurological diseases among ACMs

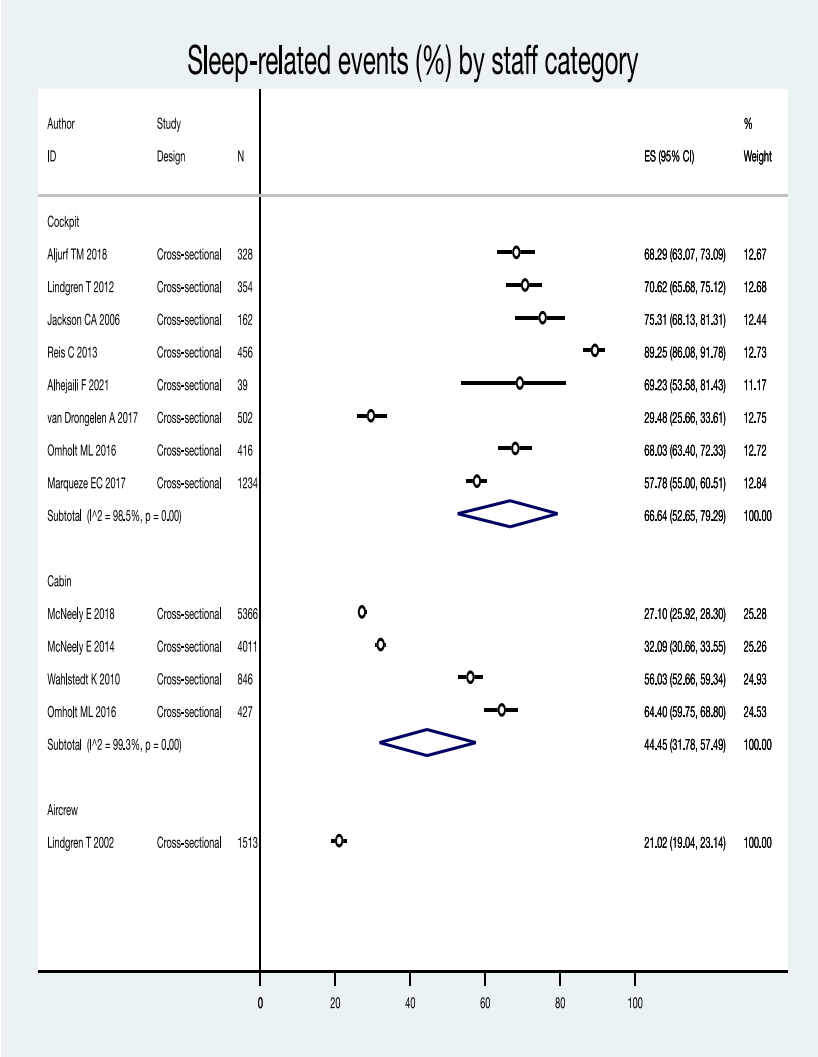

Figure 6: Forest plot of prevalence of having a fatigue/sleep related diseases among ACMs

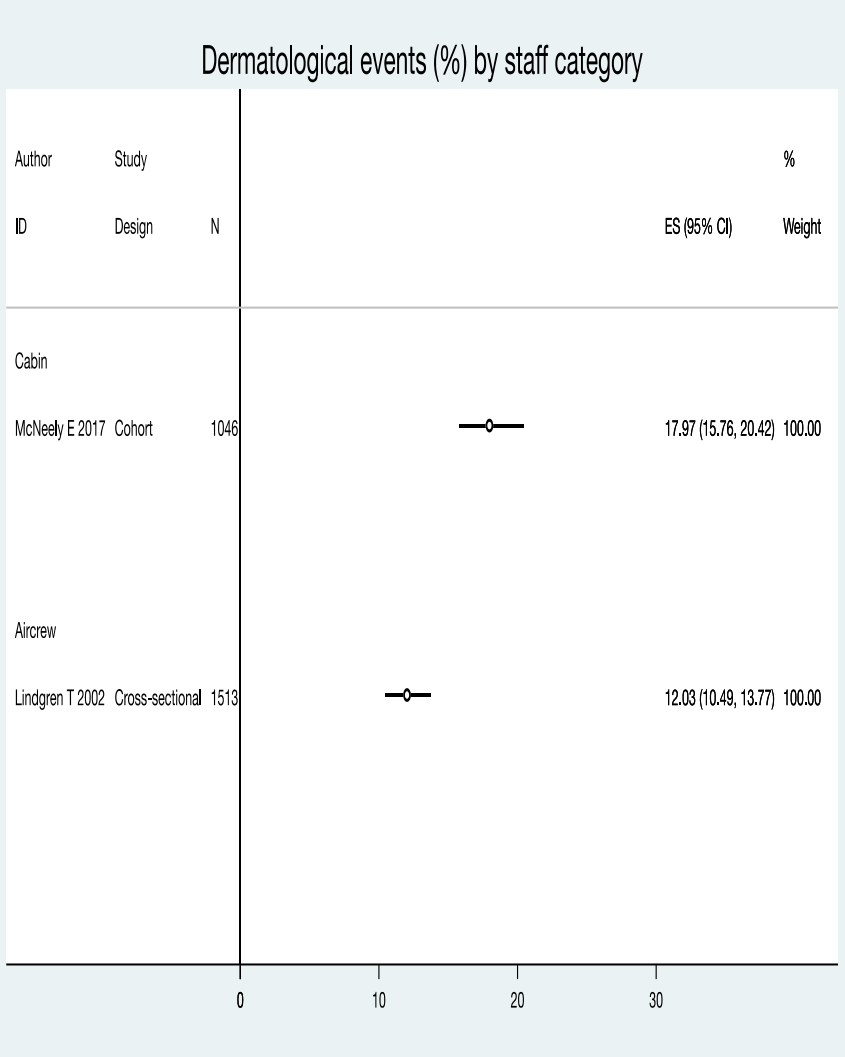

Figure 7: Forest plot of prevalence of having a dermatological diseases among ACMs

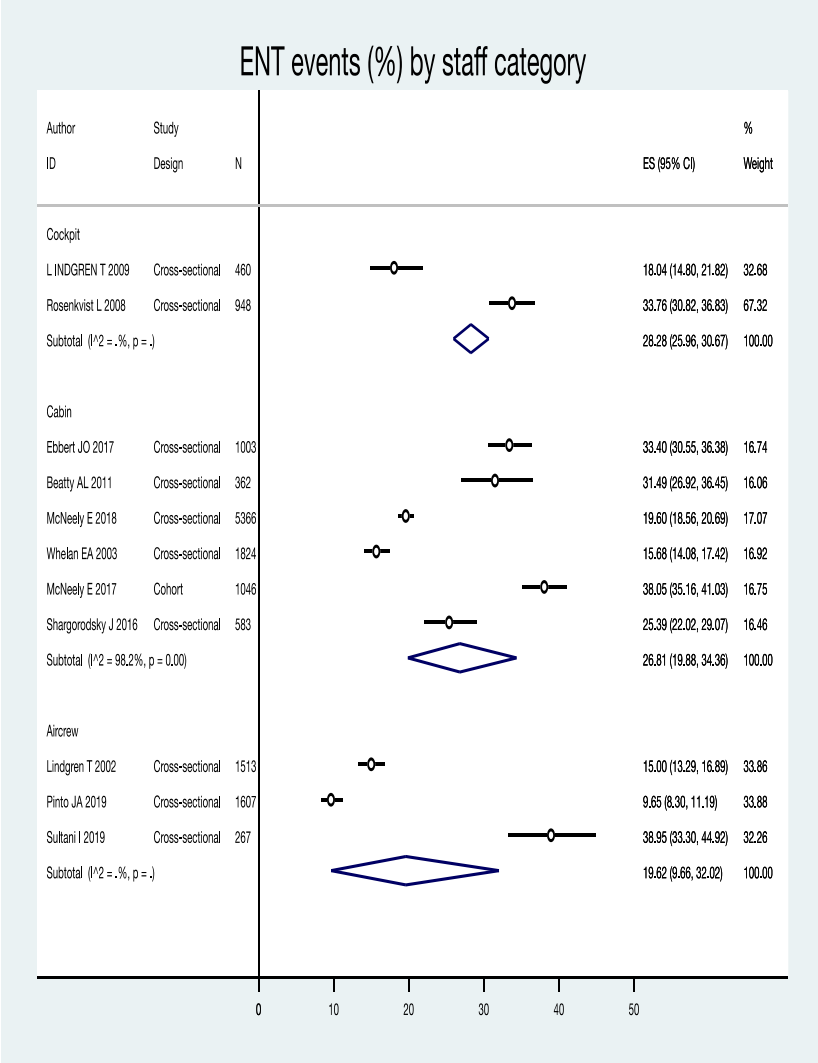

Figure 8: Forest plot of prevalence of having a ENT diseases among ACMs

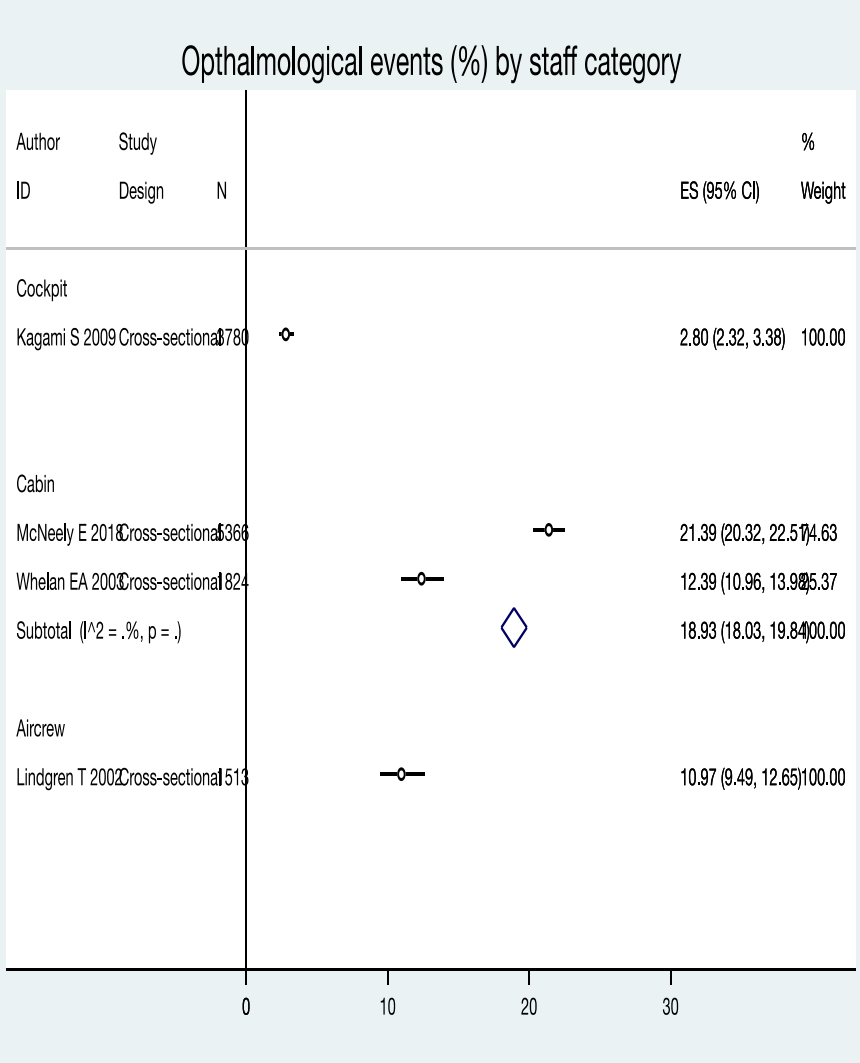

Figure 9: Forest plot of prevalence of having ophthalmological diseases among ACMs

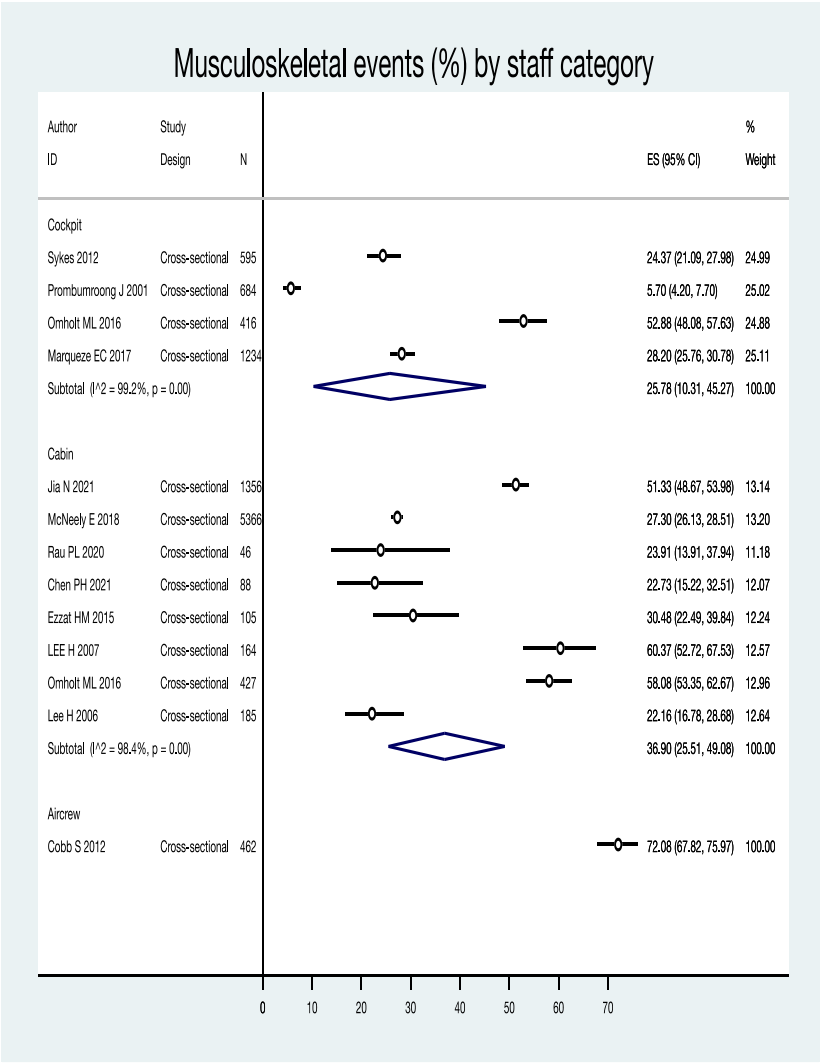

Figure 10: Forest plot of prevalence of having a musculoskeletal diseases among ACMs

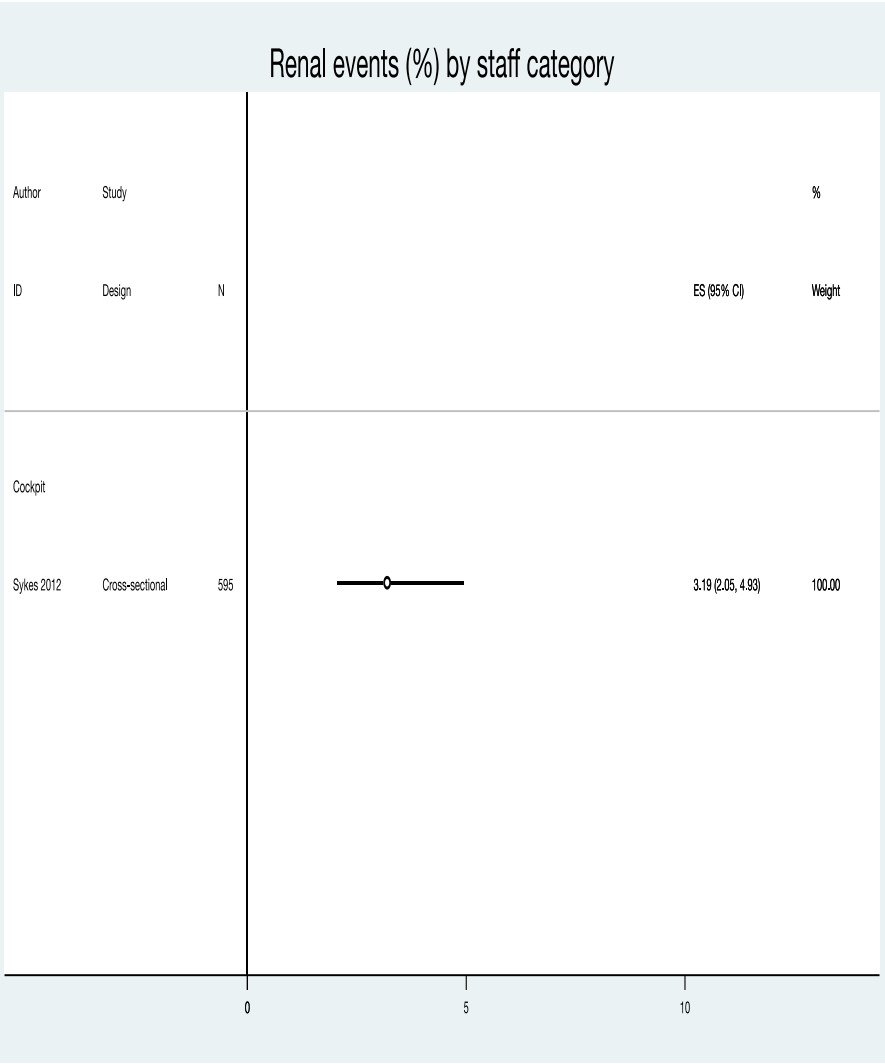

Figure 11: Forest plot of prevalence of having a renal diseases among ACMs

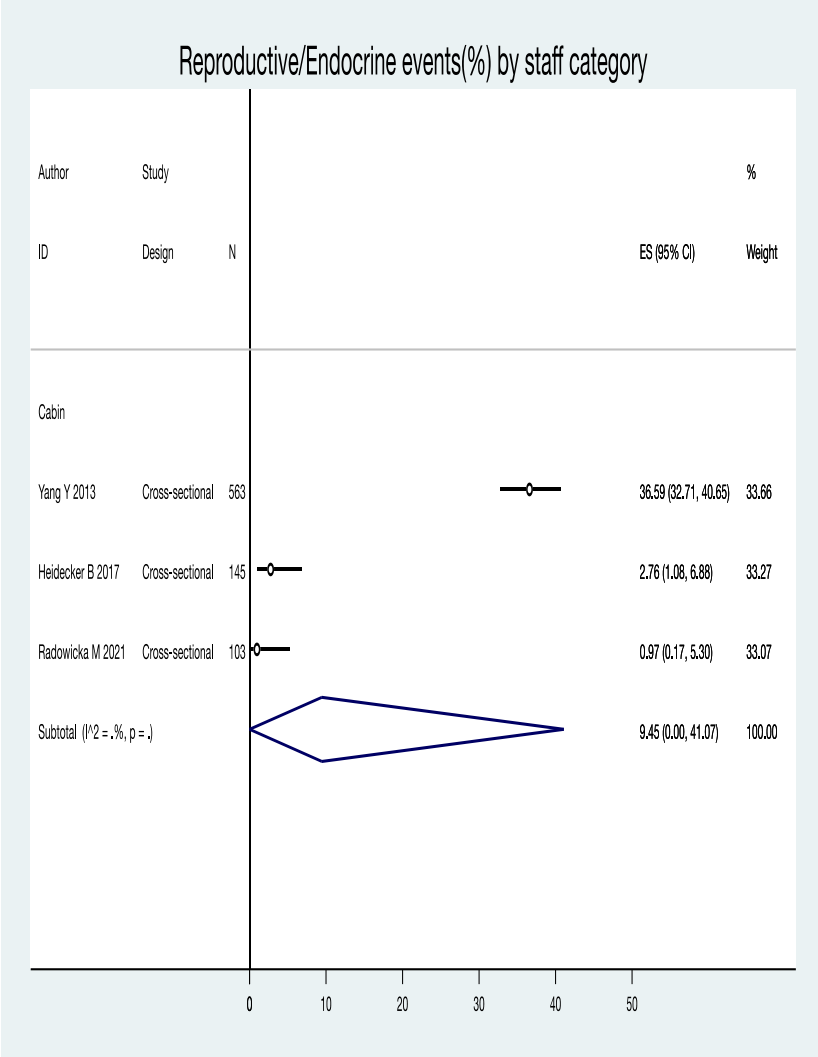

Figure 1: Forest plot of prevalence of having a reproductive/endocrine diseases among ACMs

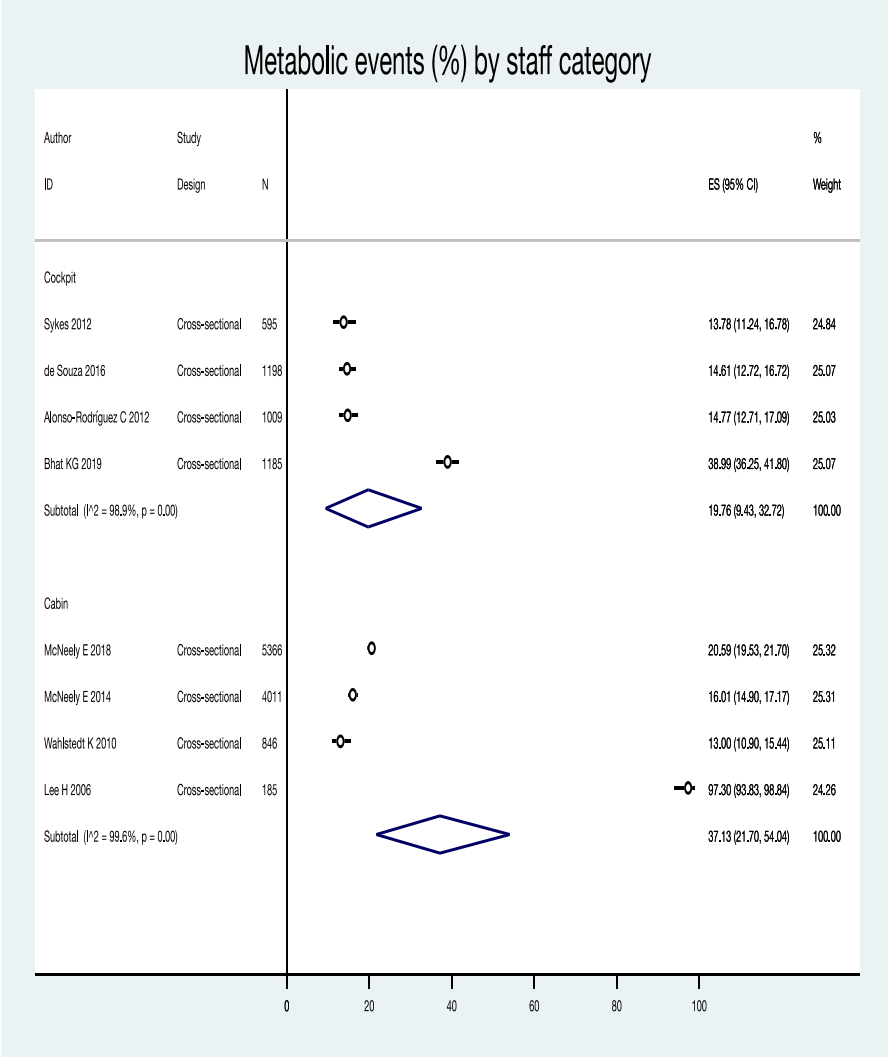

Figure 2: Forest plot of prevalence of having a metabolic diseases among ACMs

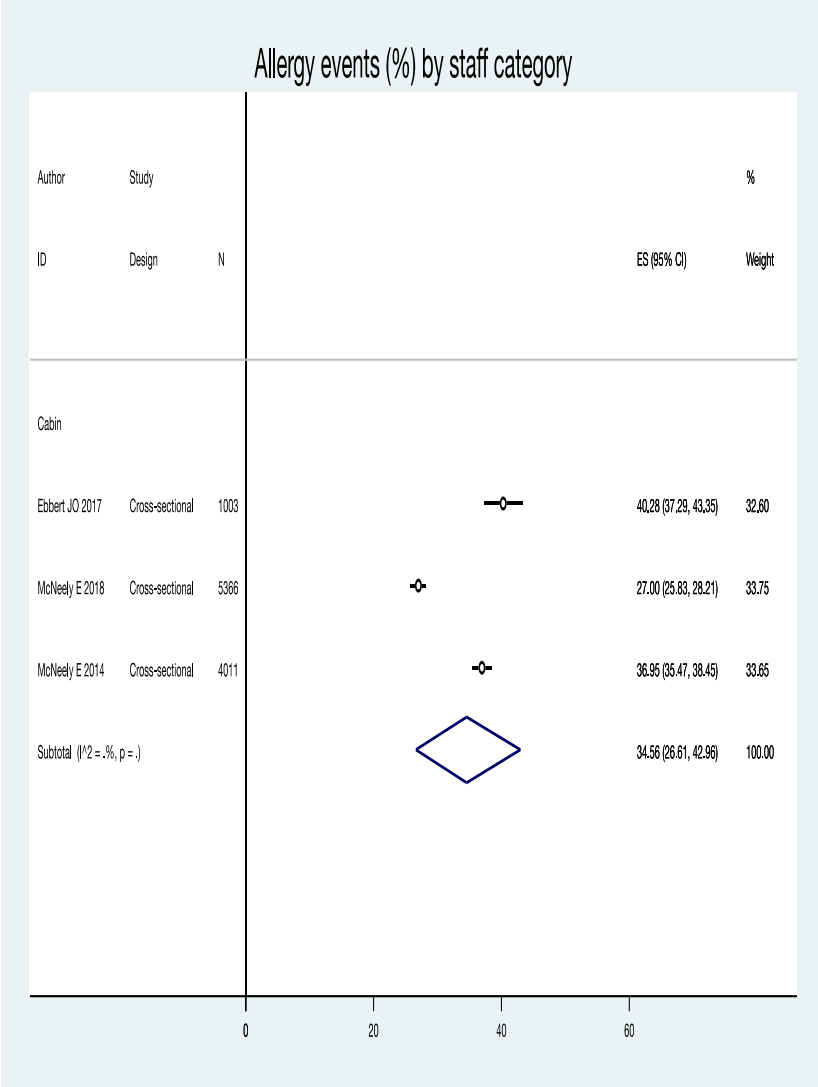

Figure 3: Forest plot of prevalence of having allergy diseases among ACMs

Figure 4: Forest plot of prevalence of having all site cancer among ACMs

Figure 5: Forest plot of prevalence of having reproductive cancer among ACMs

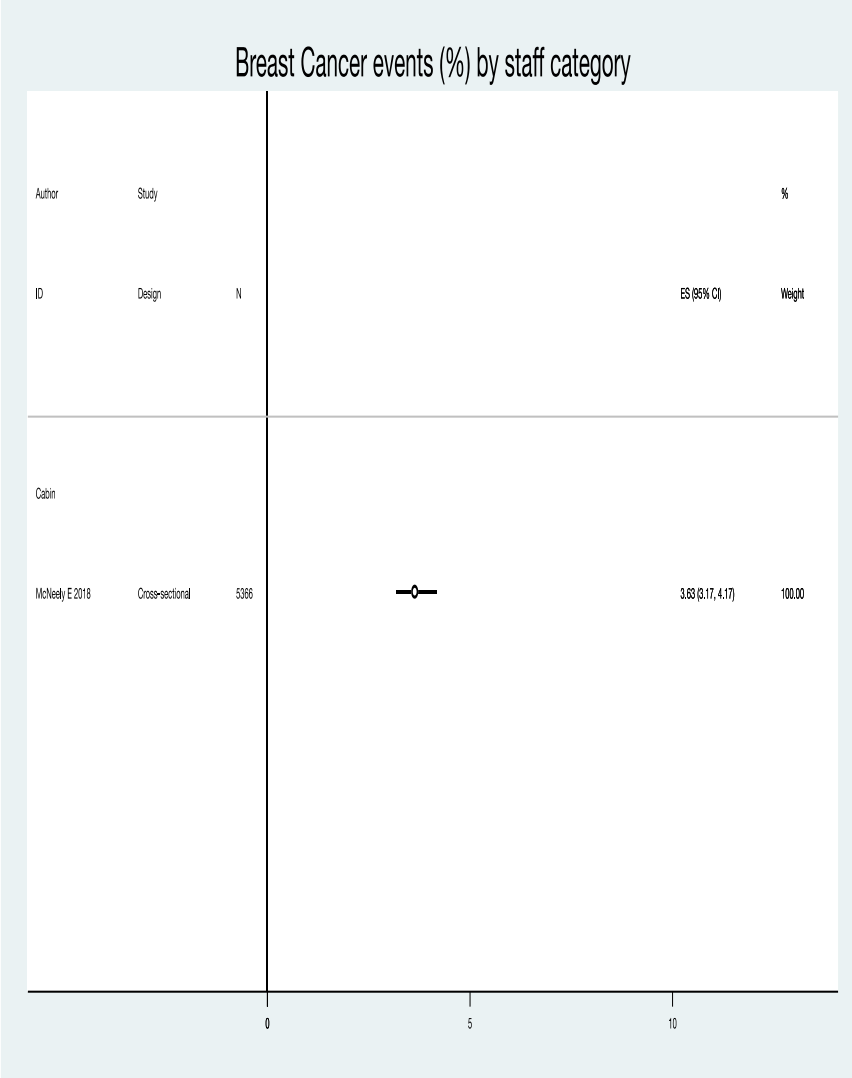

Figure 17: Forest plot of prevalence of having a breast cancer among ACMs

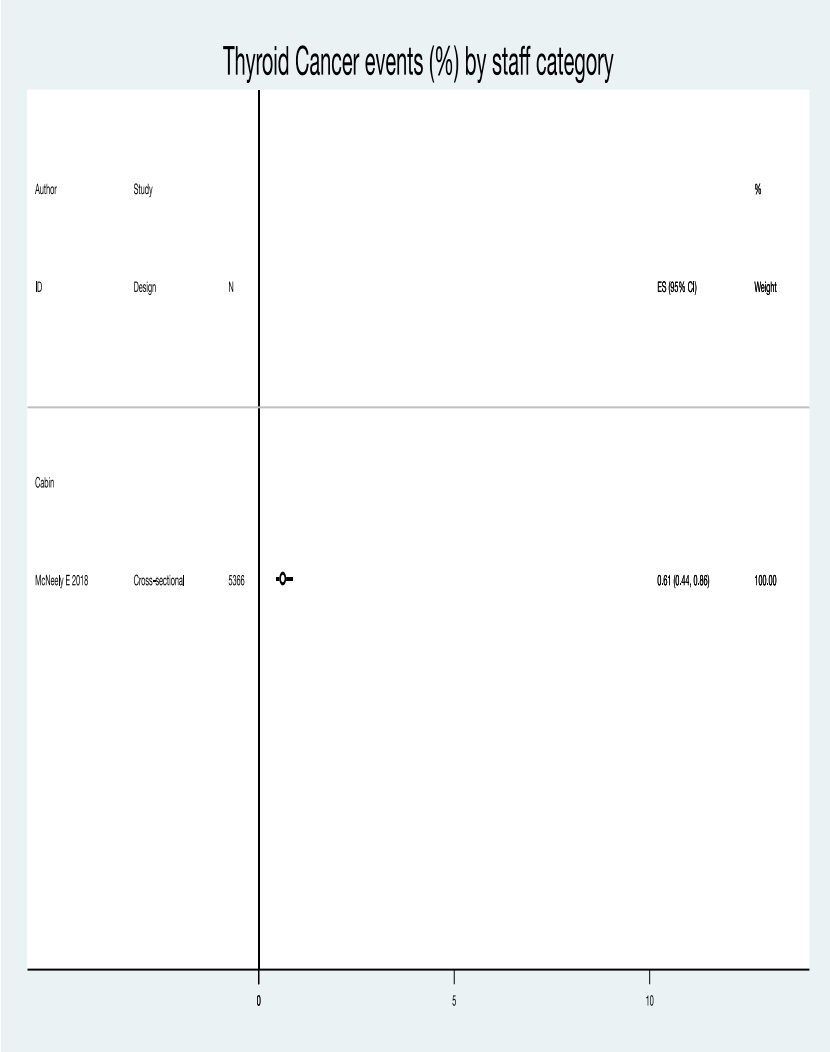

Figure 6: Forest plot of prevalence of having thyroid cancer diseases among ACMs

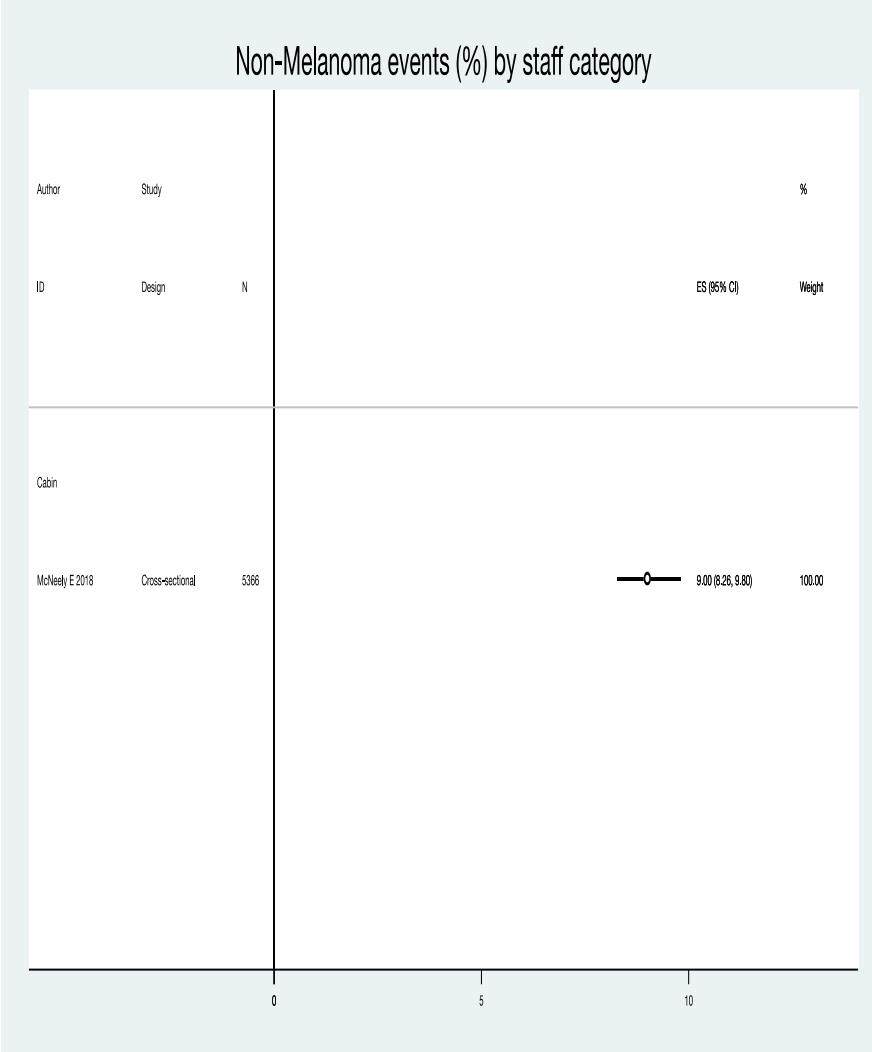

Figure 7: Forest plot of prevalence of having non-melanoma cancer among ACMs

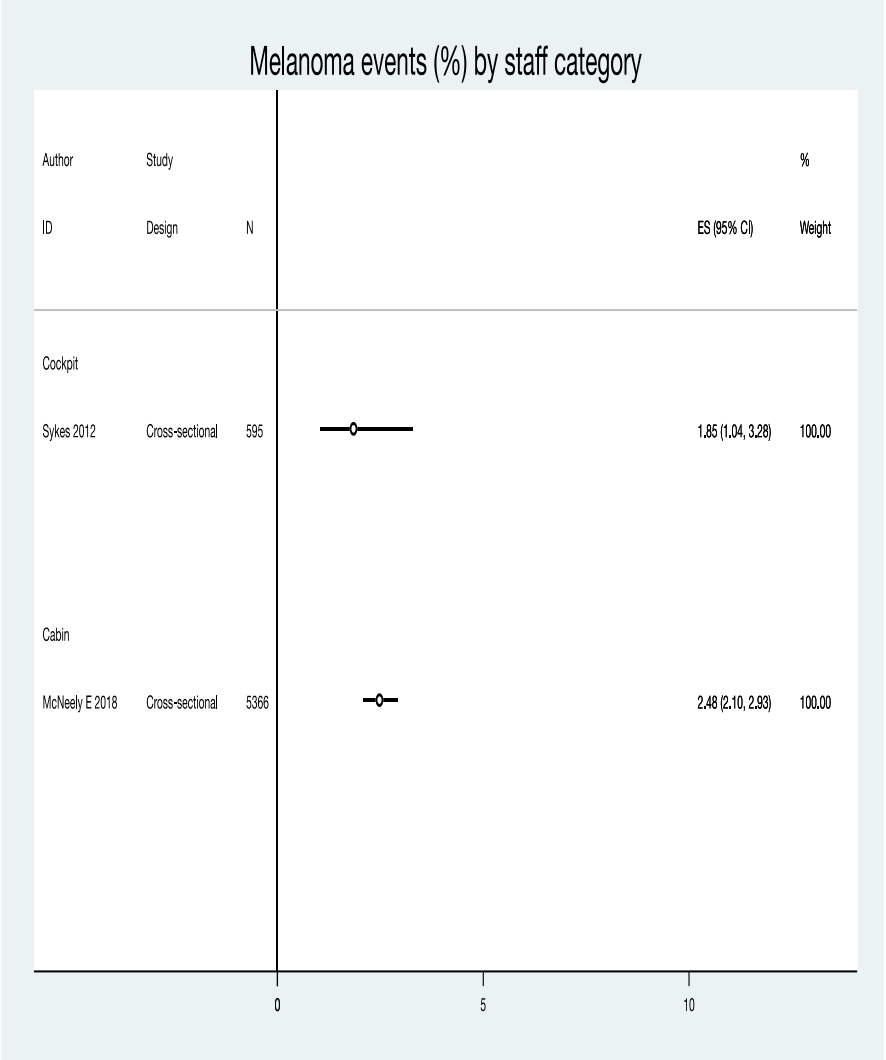

Figure 20: Forest plot of prevalence of having melanoma cancer among ACM

Figure 21: Forest plot of prevalence of having occupational injuries among ACMs

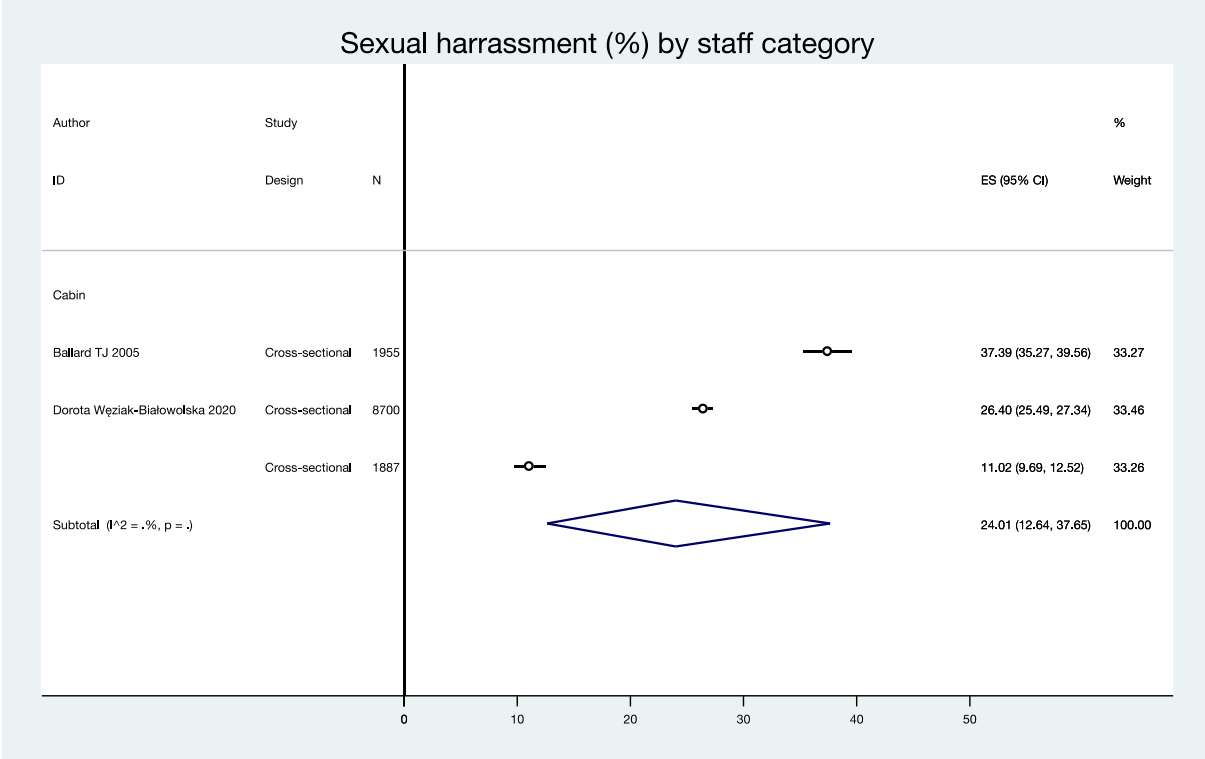

Figure 8: Forest plot of prevalence of having a sexual harassment among ACMs

Journal of Occupational and Environmental Medicine Author guidelines

Table: *JOEM* Article Types and Required Parameters

Manuscript Type	Word Count	Abstract*	Learning Outcomes †	Headings #	Key-word ^	Clinical Signifi-cance+	Figure & Tables~	Open Access Allow-ed □
Original Article	No Limit	Structured 135 Words	Yes	Structured	Yes	Yes	No Limit	Yes
Fast Track Article	No Limit	Structured 135 Words	Yes	Structured	Yes	Yes	No Limit	Yes
Editorial	No Limit	No	No	Descriptive	Yes	No	No Limit	No
Letter to the Editor	No Limit	No	No	Descriptive	No	No	No Limit	No
Book Review	No Limit	No	No	No	No	No	N/A	No
Occupational Medicine Forum	1,500-2,000	No	No	Descriptive	No	No	No Limit	No
ACOEM Article	No Limit	Structured	No	Structured & Descriptive	No	No	No Limit	Yes

* Structured abstracts consist of:

Objective: What is the problem being addressed?

Methods: How was the study performed?

Results: What are the findings?

Conclusions: What is the significance?

† Learning Outcomes are 2 to 3 conceptual bulleted statements encompassing SMART concepts (see section for more detail)

Headings are either structured (methods, results, discussion, conclusion) or descriptive (identify major areas of text in the document)

^ Manuscript require 5-7 keywords as part of the submission process

+ Requires a statement of 50 words or less describing the significance to clinical practice of the information being presented in a separate file

~ Supplemental Digital Content (SDC) is 'strongly recommended' for non-essential material. SDC appendices can be used to provide additional text, nonessential figures, supplementary tables, data collection instruments, details regarding study methods, statistical computing code, and other materials. The article should be able to stand without this supplemental material; if information is essential, it must be part of the manuscript main text. N/A is "Not Applicable".

□ Open Access (OA) Option requires selecting the OA Option during submission (screen pop-up) and submitting the License to Publish (LTP) along with the submission. Please download the LTP and submit an electronically signed copy: http://links.lww.com/LWW-ES/A49 as part of the submission.

EDITORIAL POLICIES

JOEM adheres to the editorial policies and best practices put forth by the Committee on Publication Ethics (COPE) and the International Committee on Medical Journal Editors (ICMJE). For additional information, please visit the *JOEM* Editorial, Legal, and Ethical Policies page at https://journals.lww.com/joem/Pages/editoriallegalethicalpolicies.aspx.

Author Responsibility

All submitted manuscripts must be original contributions, not previously published (except as an abstract and not under consideration for publication elsewhere). For manuscripts that have been posted in a recognized preprint archive, please review our Preprint Policy section below. Authors must include any closely related manuscripts (published, in press, or under review) as part of the online submission. Results from related manuscripts should be discussed in the submitted manuscript, providing readers with a synthesis of findings.

If any part of a manuscript is copied directly from another paper (even a paper by the same authors), set that text in quotation marks and provide the reference (including the page number of the quotation). The Editorial Office checks manuscripts for duplication with published papers with iThenticate.

Permissions

Authors must obtain written permission from the copyright owner (usually the publisher) for the use of tables, illustrations, or extensively quoted material that has previously appeared in another publication. That permission must be included with the submission within an Acknowledgements section on the title page for quoted material, in the legends of any figures/tables, and in the meta-data in the 'Notes" section of the submission.

Conflicts of Interest

Authors must state all possible conflicts of interest on the title page, including financial, consultant, institutional, and other relationships that might lead to bias or a conflict of interest. All relevant conflicts of interest should be included on the title page of the manuscript with the heading "Conflicts of Interest." If there is no conflict of interest, this should also be explicitly stated as "None Declared." Please be sure that the Conflict of Interests reported by every author on the title page of the submission matches the Conflicts of Interest reported by every Author on their individual COI/CTF form. For additional information on conflict of interest disclosures please consult the International