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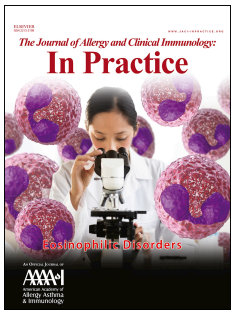

How common are allergic reactions during commercial flights? A systematic review and meta-analysis

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Title:

How common are allergic reactions during commercial flights? A systematic review and meta-analysis

Short Title: Allergic reactions during commercial flights

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Author Contributions:

PJT conceived the study. JL and PJT designed the protocol. Data extraction was undertaken by JM, JL, AB and PJT, and analyzed by NP and PJT. The manuscript was drafted by PJT, and then reviewed and the final version approved by all authors.

Conflicts of Interest:

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Abstract:

Background: Global passenger demand for air travel has increased by over 7% annually since 2006, with a strong recovery following the COVID-19 pandemic. Prior to COVID-19, individuals with food allergies reported significant concern and anxiety over the risk of reactions when travelling by air. However, published data of in-flight medical events (IMEs) due to allergic reactions are limited.

Objective: To undertake a systematic review with meta-analysis to estimate the incidence of in-flight medical emergencies (IMEs) due to allergic reactions on commercial flights.

Methods: We searched MEDLINE, Embase, PsycINFO, TRANSPORT databases and the Cochrane Register of Controlled Trials for relevant studies reporting IMEs of allergic etiology, published since 1980. Data were extracted in duplicate for meta-analysis, and risk of bias assessed. Study registration: PROSPERO CRD42022384341.

Results: 17 studies met the inclusion criteria. At meta-analysis, a pooled estimate of 2.2% (95%CI 1.6%-3.1%) of IMEs are coded as being due to allergic reactions. This may be higher in children (3.1%, 95%CI 1.5%-6.7%). The incidence of allergic IMEs at meta-analysis was 0.7 events per million passengers (95%CI 0.4 to 1.1). Reassuringly, the rate of allergic IMEs has been stable over the past 30 years, despite increasing passenger numbers and food allergy prevalence.

Conclusion: Allergic reactions coded as IMEs during commercial air travel are uncommon, occurring at an incidence around 10-100 times lower than that reported for accidental allergic reactions to food occurring in the community. Despite increasing passenger numbers and food allergy prevalence, the rate of allergic IMEs has not changed over the past 3 decades.

Keywords: allergic reaction; anaphylaxis; epinephrine; food; in-flight medical event.

Abbreviations:

CI Confidence Interval

IME In-flight medical event

HIGHLIGHTS

1. What is already known about this topic?

Global demand for commercial air travel has increased by over 7% annually since 2006, along with prevalence of food allergy. However, data relating to the reported rates of in-flight medical events (IMEs) due to allergic reactions are limited.

2. What does this article add to our knowledge?

We undertook a systematic review and meta-analysis, which found that around 2-3% of IMEs are due to allergic reactions, equivalent to an incidence of around 0.7 reactions per million passengers.

3. How does this study impact current management guidelines?

Allergic reactions coded as IMEs during commercial air travel are uncommon, occurring at an incidence around 10-100 times lower than that reported for reactions in the community. This incidence has been stable over the past 30 years, despite a significant increase in passenger numbers and food allergy prevalence.

INTRODUCTION

There is a perception amongst many individuals with food allergies that the risks of accidental allergic reactions are increased when travelling on commercial aircraft.[1-3] A particular concern is whether there is potential for allergic reactions occurring due to inhalation of airborne particles of food allergens, particularly with respect to peanut and tree nut allergy.[2-5] A further problem is that airline policies with respect to food-allergic individuals are not always readily available,[6,7] and there can be significant differences in terms of policy specifics between air carriers, as well as how these policies might be implemented by cabin crew and ground staff.[1-3,8]

Global passenger demand for commercial air travel has increased by over 7% annually since 2006, and is now recovering to pre-COVID levels following the very significant impact of the COVID-19 pandemic.[9] The increase in passenger numbers has been associated with an increase in the number of in-flight medical events reported by airlines and ground-based medical services (GBMS).[10] However, published data relating to the reported rates of in-flight medical events (IMEs) due to allergic reactions are limited. We therefore undertook a systematic review and meta-analysis to estimate the incidence of in-flight medical emergencies (IMEs) due to allergic reactions on commercial flights, and evaluate for any trends in incidence over time.

METHODS

This systematic review was registered at inception with PROSPERO (CRD42022384341) and the study is reported in accordance with PRISMA Statement 2009 and MOOSE recommendations.[11,12]

Search Strategy and Eligibility Criteria

We searched MEDLINE, Embase, PsycINFO, TRANSPORT databases and the Cochrane Register of Controlled Trials, from 1 January 1980 and 31 December 2022. The search strategy can be found in the online supplement. We included all primary research reporting either the proportion of IMEs due to "allergy" or the estimated incidence (events per person years) of unintended IgE-mediated food-induced allergic reactions while travelling on commercial aircraft. We also reviewed reference lists of included studies and review articles to identify other relevant studies. There were no language restrictions. Abstracts were independently screened by at least two authors to identify relevant studies. We included only published, peer-reviewed full papers or research letters, and excluded conference abstracts. Where repeated reports of the same study were identified, we included the most up-to-date or detailed report. All studies were assessed for risk of bias by two independent authors, using the approach of Hoy et al.[13] Studies deemed at high risk of bias were excluded. Data were extracted in duplicate (AB, JM, JL) and any discrepancies identified were resolved by discussion and consensus with a third reviewer (PJT). Authors were contacted for clarifications, where needed.

Data Analysis and Statistical Methods

Meta-analysis was performed using Meta Package, R project, version 4.0.3a (random-effects model, REML). Study heterogeneity was assessed using the I2 statistic. Tests for small study effects were performed using Funnel plots to assess asymmetry.

RESULTS

The PRISMA diagram for this systematic review is shown in Figure 1. 17 studies were eligible for inclusion (Table 1).[10,14-29] All studies were assessed as being at low-moderate risk of bias (Table E1), and there was no evidence of publication bias (Figure E1).

At meta-analysis, a pooled estimate of 2.2% (95%CI 1.6%-3.1%) of IMEs were coded as due to allergic reactions (Figure 2A). Limiting the analysis to those studies reporting data in children, the rate of IMEs due to allergic reactions was 3.1% (95%CI 1.5%-6.7%) (Figure E2). Most studies reported IMEs across a range of ages (both children and adults), thus these data should be interpreted accordingly. Analyzing studies where data relating to the number of flights taken (revenue passengers) was also available, the rate of IMEs due to allergic reactions was 0.66 (95%CI 0.38-1.14)) per million passengers (Figure 2B).

We then assessed whether the rate of IMEs due to allergic reactions had changed over time. There was no evidence that either the absolute number or proportion of IMEs due to allergic reactions had increased over the past two decades, despite a documented increase in passenger numbers (Figure 3).

Finally, we determined how the incidence of IMEs due to allergic reactions compared to the estimated incidences of food anaphylaxis incidents in food-allergic people in general, using data from a previously published systematic review and meta-analysis.[30] Incidence of comparator risks using US data were also included, as previously described.[31] In estimating the annual incidence of IMEs due to food allergy, we made the following assumptions:

i. One flight per day per passenger
ii. A population average of 4.2 flights per person per annum,[32] and a rate of 52 flights per year for “frequent flyers”
iii. Food-allergic passengers fly at the same frequency as those without food allergies.
iv. Food allergy related IMEs are only reported around 50% of the time,[3,8] thus the true incidence of food-induced allergic reactions on board commercial aircraft will be double that reported in the literature, and thus estimated rates at meta-analysis must be doubled.

On this basis, we estimated that the annual incidence of a food-induced allergic reaction is 2.7 (95%CI 1.6-4.8) per 10,000 person-years, equivalent to 1 reaction per 3600 food-allergic passengers travelling in any one-year period. In food-allergic individuals who fly once per week, this increases to 34 (95%CI 20-59) per 10,000 person-years (Figure 4).

DISCUSSION

In this systematic review, we estimated at meta-analysis that the incidence of in-flight allergic reactions was 0.66 (95%CI 0.38-1.14) events per million passengers. This is similar to the estimated incidence of 0.64 (95%CI 0-1.74) events per million passengers reported by Borges do Nascimento et al, who undertook a broader meta-analysis of the incidence of all IMEs (irrespective of etiology) but included a sub-analysis of 8 studies reporting allergic IMEs.[33] This means that in a food-allergic person flying at a frequency equivalent to the population average, the incidence of an unintended allergic reaction while on a commercial flight is around 100 times less than that for self-reported anaphylaxis when "on the ground", and 10 times less frequent than that for medically-coded anaphylaxis. Reassuringly, this risk seems to be stable over the past 30 years, despite an increase in passenger numbers and increasing prevalence of food allergy. However, this needs to be interpreted in the context of the vast majority of food-allergic individuals taking a number of significant precautions when travelling, ranging from avoiding flying in the first place, to wiping down their seat area and bringing their own food to consume during the flight.[3,8]

There has been significant growth in growth in low-cost short haul routes over the past two decades, where complementary food/snacks are no longer provided. At the same time, many airlines have stopped serving peanuts as in-flight snacks. It is therefore interesting to note that despite this, the rate of IMEs due to allergy had not significantly changed over time, (although we could not assess changes in the frequency at which some passengers purchase nut-based snacks prior to flying, to consume in-flight). We were also unable to obtain data relating to whether the allergic IMEs might have occurred as a result of consumption of a food product provided by the airline or brought along by the passenger themselves. At least one prospective survey has identified that a significant proportion of in-flight allergic reactions occur due to consumption of food brought along by allergic

individuals themselves as a “safe” alternative, either purchased in the airport or made at home.[34] This highlights the risk of human error in preparing for travel.

Ideally, our analysis would have analyzed the rate of IMEs, normalized according to flight duration (and also whether flights were domestic or international), but most studies included in this analysis did not provide these data. This may explain the high rate of heterogeneity as determined by the I^2 statistic at meta-analysis. We did perform a sensitivity analysis which demonstrated a high level of heterogeneity irrespective of the data source (GBMS database versus airline records). Similarly, the studies did not, in general, report the assumed cause of the reported IME (trigger allergen, route of exposure) nor whether epinephrine was used to treat the reaction. In a retrospective analysis of a GBMS database (2017-2019), Kodoth et al reported an incidence for allergic IMEs of 0.91 cases per million passengers, while the incidence of allergic IMEs for which epinephrine was recommended by the GBMS was 0.08 (interquartile range 0.02-0.16) cases per million passengers.[29] The authors concluded that IMEs requiring epinephrine treatment are rare, equivalent to a rate of 1 event per 12.5 million passengers. Thus, it is likely that the rate of anaphylaxis as an IME is much less common than the reported incidence of allergic IMEs reported in the current analysis.

In summary, we found that the rate of in-flight medical events due to food-induced allergic reactions is low: for a typical food-allergic passenger, the risk of an accidental reaction is 1 reaction per 3600 food-allergic passengers travelling on board an aircraft in any one year period. This is 10-100 times lower than the equivalent incidence in food-allergic individuals when not travelling. This needs to be interpreted in the context of the majority of food-allergic passengers taking precautions when travelling on aircraft, which is likely to reduce the risk of their having an in-flight allergic reaction.

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References

1. Barnett J, Botting N, Gowland MH, Lucas JS. The strategies that peanut and nut-allergic consumers employ to remain safe when travelling abroad. Clin Transl Allergy. 2012 Jul 9;2(1):12. doi: 10.1186/2045-7022-2-12.
2. Beaumont P, Renaudin J-M, Dumond P, Drouet M, Moneret-Vautrin D.A. Sécurité aérienne pour les allergiques alimentaires : données actuelles et recommandations. [Flight safety for food-allergic travellers: Current data and recommendation]. Rev Fr Allergol 2015;55:463-9. doi: 10.1016/j.reval.2015.08.004.
3. Warren C, Mandelbaum L, Nowak-Wegryzn A, Herbert L, Sicherer S, Sampson H, et al. Understanding experiences, barriers, & facilitators of safe airline travel—A global survey of food allergy patients and caregivers. J Allergy Clin Immunol. 2023; 151 (2 Suppl), AB341. doi: 10.1016/j.jaci.2022.12.799.
4. Comstock SS, DeMera R, Vega LC, Boren EJ, Deane S, Haapanen LA, et al. Allergic reactions to peanuts, tree nuts, and seeds aboard commercial airliners. Ann Allergy Asthma Immunol. 2008 Jul;101(1):51-6. doi: 10.1016/S1081-1206(10)60835-6.
5. Sicherer SH, Furlong TJ, DeSimone J, Sampson HA. Self-reported allergic reactions to peanut on commercial airliners. J Allergy Clin Immunol. 1999 Jul;104(1):186-9. doi: 10.1016/s0091-6749(99)70133-8.
6. Stojanovic S, Zubrinich CM, O'Hehir R, Hew M. Airline policies for passengers with nut allergies flying from Melbourne Airport. Med J Aust. 2016 Sep 19;205(6):270. doi: 10.5694/mja16.00384.
7. Seidenberg J, Stelljes G, Lange L, Blumchen K, Rietschel E. Airlines provide too little information for allergy sufferers! Allergo J Int 29, 262–279 (2020). doi: 10.1007/s40629-020-00147-1.

8. Greenhawt M, MacGillivray F, Batty G, Said M, Weiss C. International study of risk-mitigating factors and in-flight allergic reactions to peanut and tree nut. J Allergy Clin Immunol Pract. 2013 Mar;1(2):186-94. doi: 10.1016/j.jaip.2013.01.002.
9. Statista. Coronavirus: impact on the aviation industry worldwide. 2021. Available at: https://www.statista.com/study/71610/coronavirus-impact-on-the-aviation-industry-worldwide/
10. Ceyhan MA, Menekşe İE. In-flight medical emergencies during commercial travel. J Travel Med. 2021 Oct 11;28(7):taab094. doi: 10.1093/jtm/taab094.
11. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000;283(15):2008-2012.
12. Preferred Reporting Items for Systematic Reviews and Meta-Analyses available at: http://www.prisma-statement.org/
13. 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. J Clin Epidemiol. 2012;65(9):934-939.
14. Donaldson E, Pearn J. First aid in the air. Aust N Z J Surg. 1996 Jul;66(7):431-4. Doi: 10.1111/j.1445-2197.1996.tb00777.x.
15. DeJohn CA, Véronneau SJH, Wolbrink AM, Larcher JG, Smith DW, Garrett J; US Department of Transportation Federal Aviation Administration. The Evaluation of In-Flight Medical Care Aboard Selected U.S. Air Carriers: 1996 to 1997. 2000. Available at: www.faa.gov/data_research/research/med_humanfacs/oamtechreports/2000s/media/00_13.pdf

16. Szmajer M, Rodriguez P, Sauval P, Charetteur MP, Derossi A, Carli P. Medical assistance during commercial airline flights: analysis of 11 years experience of the Paris Emergency Medical Service (SAMU) between 1989 and 1999. Resuscitation. 2001 Aug;50(2):147-51. Doi: 10.1016/s0300-9572(01)00347-1.

17. Sirven JI, Claypool DW, Sahs KL, Wingerchuk DM, Bortz JJ, Drazkowski J, et al. Is there a neurologist on this flight? Neurology. 2002 Jun 25;58(12):1739-44. Doi: 10.1212/wnl.58.12.1739.

18. Delaune EF, Lucas RH, Illig P. In-flight medical events and aircraft diversions: one airline's experience. Aviat Space Environ Med. 2003 Jan;74(1):62-8.

19. Moore BR, Ping JM, Claypool DW. Pediatric emergencies on a US-based commercial airline. Pediatr Emerg Care. 2005 Nov;21(11):725-9. Doi: 10.1097/01.pec.0000186424.84764.94.

20. Baltsezak S. Clinic in the air? A retrospective study of medical emergency calls from a major international airline. J Travel Med. 2008 Nov-Dec;15(6):391-4. Doi: 10.1111/j.1708-8305.2008.00233.x.

21. Sand M, Bechara FG, Sand D, Mann B. Surgical and medical emergencies on board European aircraft: a retrospective study of 10189 cases. Crit Care. 2009;13(1):R3. Doi: 10.1186/cc7690.

22. Mahony PH, Myers JA, Larsen PD, Powell DM, Griffiths RF. Symptom-based categorization of in-flight passenger medical incidents. Aviat Space Environ Med. 2011 Dec;82(12):1131-7. Doi: 10.3357/asem.3099.2011.

23. Peterson DC, Martin-Gill C, Guyette FX, Tobias AZ, McCarthy CE, Harrington ST, et al. Outcomes of medical emergencies on commercial airline flights. N Engl J Med. 2013 May 30;368(22):2075-83. Doi: 10.1056/NEJMoa1212052.

24. Kesapli M, Akyol C, Gungor F, Akyol AJ, Guven DS, Kaya G. Inflight Emergencies During Eurasian Flights. J Travel Med. 2015 Nov-Dec;22(6):361-7. Doi: 10.1111/jtm.12230.
25. Kim JH, Choi-Kwon S, Park YH. Comparison of inflight first aid performed by cabin crew members and medical volunteers. J Travel Med. 2017 Mar 1;24(2). Doi: 10.1093/jtm/taw091.
26. Alves PM, Nerwich N, Rotta AT. In-Flight Injuries Involving Children on Commercial Airline Flights. Pediatr Emerg Care. 2019 Oct;35(10):687-691. Doi: 10.1097/PEC.0000000000000993.
27. Pauline V, Camille B, Philippe B, Vincent F, Charles-Henri HC, Isabelle AC. Paediatric and adult emergencies on French airlines. J Travel Med. 2020 Mar 13;27(2):taz094. Doi: 10.1093/jtm/taz094.
28. Rotta AT, Alves PM, Nerwich N, Shein SL. Characterization of In-Flight Medical Events Involving Children on Commercial Airline Flights. Ann Emerg Med. 2020 Jan;75(1):66-74. Doi: 10.1016/j.annemergmed.2019.06.004.
29. Kodoth SM, Alves P, Convers K, Davis K, Chang C; Infectious Diseases and International Travel Committee of the ACAAI. The frequency and characteristics of epinephrine use during in-flight allergic events. Ann Allergy Asthma Immunol. 2023 Jan;130(1):74-79. Doi: 10.1016/j.anai.2022.08.004.
30. Umasunthar T, Leonardi-Bee J, Turner PJ, Hodes M, Gore C, Warner JO, et al. Incidence of food anaphylaxis in people with food allergy: a systematic review and meta-analysis. Clin Exp Allergy. 2015 Nov;45(11):1621-36. doi: 10.1111/cea.12477.
31. Umasunthar T, Leonardi-Bee J, Hodes M, Turner PJ, Gore C, Habibi P, et al. Incidence of fatal food anaphylaxis in people with food allergy: a systematic review and meta-analysis. Clin Exp Allergy. 2013 Dec;43(12):1333-41. doi: 10.1111/cea.12211.

32. GALLUP. US Air Travel Remains Down as Employed Adults Fly Less. January 2022. Available at: news.gallup.com/poll/388484/air-travel-remains-down-employed-adults-fly-less.aspx.

33. Borges do Nascimento IJ, Jerončić A, Arantes AJR, Brady WJ, Guimarães NS, Antunes NS, et al. The global incidence of in-flight medical emergencies: A systematic review and meta-analysis of approximately 1.5 billion airline passengers. Am J Emerg Med. 2021 Oct;48:156-164. doi: 10.1016/j.ajem.2021.04.010.

34. Crealey M, Byrne A. Going on vacation increases risk of severe accidental allergic reaction in children and adolescents. Ann Allergy Asthma Immunol. 2022 Dec 24:S1081-1206(22)02009-9. Doi: 10.1016/j.anai.2022.12.026.

340 **TABLES**

Study	Data source	Location	Study period	No. of revenue passengers	Number of IMEs		Incidence of IMEs due to allergy		Risk of Bias
					Overall	Allergy	% overall	per million passengers	
Donaldson 1996[14]	Airline records	Australia	1993	4 million	454	5	1.1%	1.25	Low
DeJohn 2000[15]	Ground-to-air provider	USA	1996-1997	N/A	1132	27	2.4%	–	Low
Szmajer 2001[16]	Ground-to-air provider	France	1989-1999	70 million	374	9	2.4%	0.13	Low
Sirven 2002[17]	Ground-to-air provider	USA	1995-2000	312.1 million	2,042	71	3.5%	0.23	Moderate
Delaune 2003[18]	Airline records	Unknown	1999-2000	100.8 million	2,279	63	2.8%	0.62	Low
Moore 2005[19]	Ground-to-air provider	USA	1995-2002	N/A	165	15	9.1%	–	Moderate
Baltsezak 2008[20]	Ground-to-air provider	China	2006	N/A	191	7	3.7%	–	Moderate
Sand 2009[21]	Airline records	Europe	2002-2007	N/A	10,189	222	2.2%	–	Moderate
Mahony 2011[22]	Airline records	Oceania	1996-2004	71.4 million	11,326	257	2.3%	3.60	Low
Peterson 2013[23]	Ground-to-air provider	Global	2008-2010	744 million	11,920	265	2.2%	0.36	Low
Kesapli 2015[24]	Airline records	Eurasia	2011-2013	10.1 million	1,312	10	0.76%	0.99	Low
Kim 2017[25]	Airline records	Asia	2009-2013	115 million	2,818	132	4.7%	1.15	Low
Alves 2019[26]	Ground-to-air provider	Global	2009-2013	N/A	114,222	1052	0.92%	–	Low
Pauline 2020[27]	Airline records	Europe	2017	N/A	581	5	0.86%	–	Moderate
Rotta 2020[28]	Ground-to-air medical	Global	2015-2016	N/A	11,719	647	5.5%	–	Low
Ceyhan 2021[10]	Airline records	Unknown	2018-2020	177.4 million	19,313	138	0.71%	0.78	Low
Kodoth 2022[29]	Ground-to-air provider	Global	2017-2019	6313 million	140,579	4230	3.0%	0.67	Low

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342 **Table 1**: Summary of included studies. Full risk of bias evaluation is shown in Table E1.

343 **FIGURE LEGENDS**

344

345 **Figure 1**: PRISMA Flow Diagram

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348 **Figure 2**: Forest plots for (**A**) the proportion of IMEs coded as being due to allergic reactions
349 and (**B**) and incidence of IMEs due to allergic reaction per million passengers.

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352 **Figure 3**: Time trends for in-flight medical events (IMEs) due to allergic causes over the last 3
353 decades, by study period.

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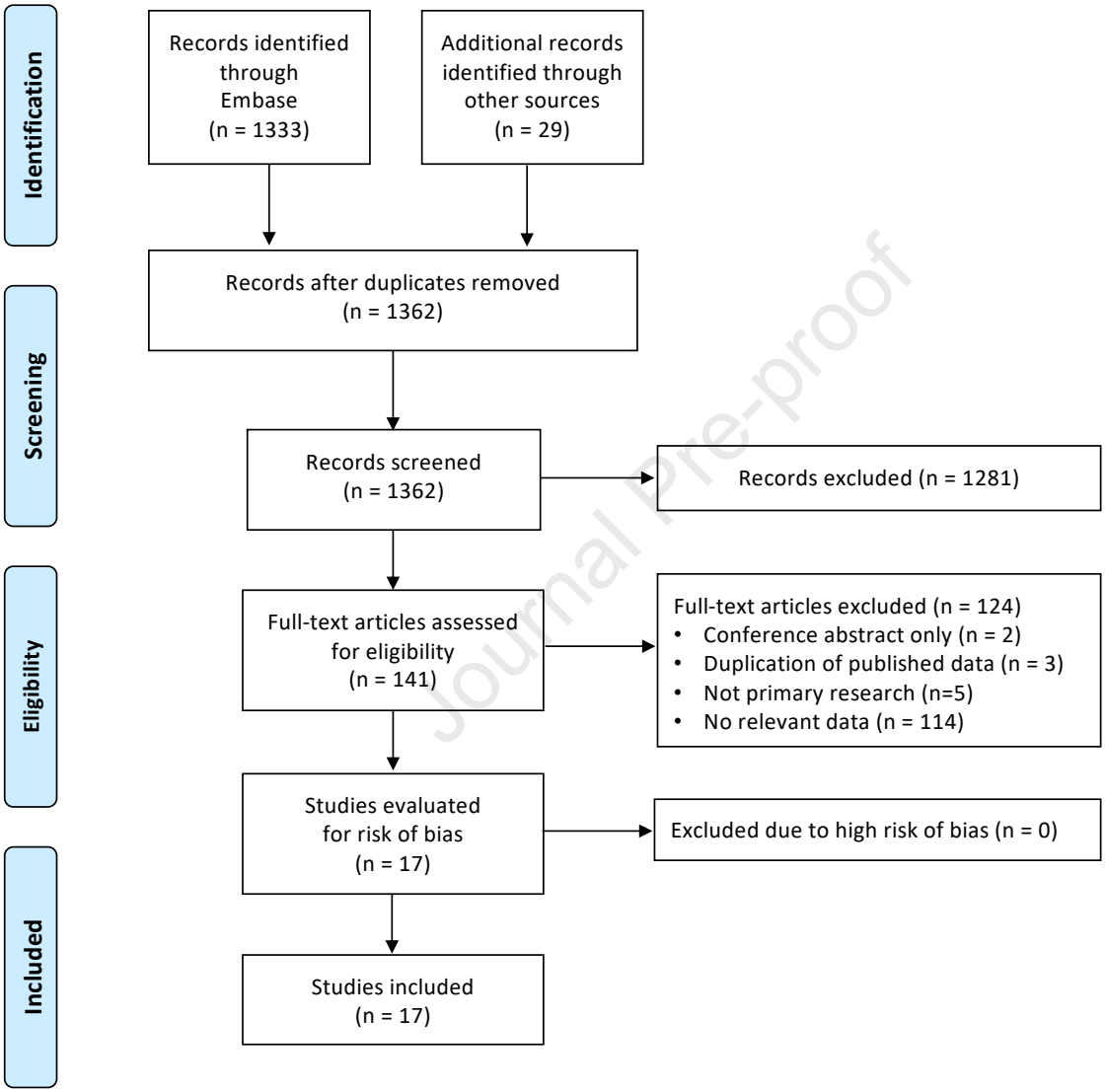
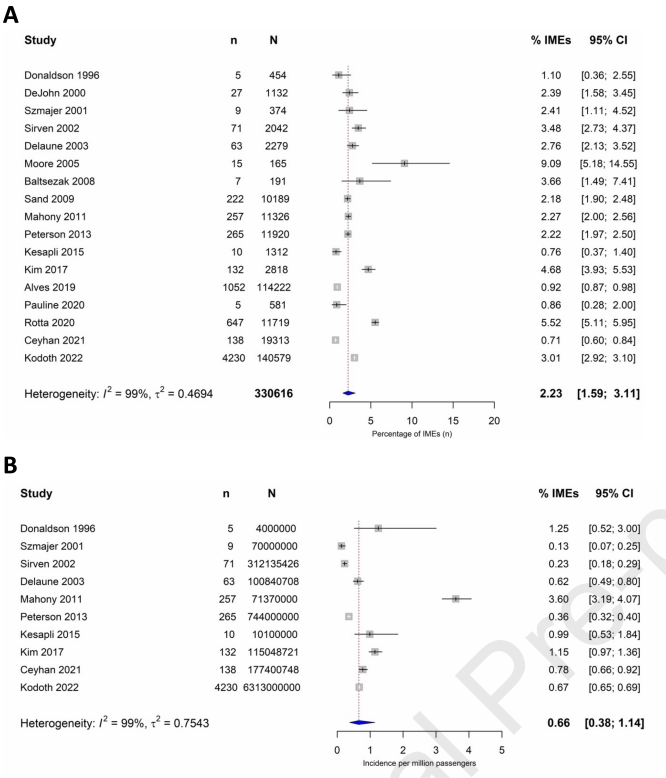
355

356 **Figure 4**: Estimated rates of food-induced allergic reactions in people with known food
357 allergy during commercial flights, assuming a 2% prevalence of food allergy. Comparison is
358 made to equivalent rates reported in food-allergic individual when not flying, together with
359 reference risks (US population, unless otherwise stated). Data are shown as 95% confidence
360 intervals for risk of food-induced allergic reaction, derived from the systematic review of
361 Umasunthar et al.[30]

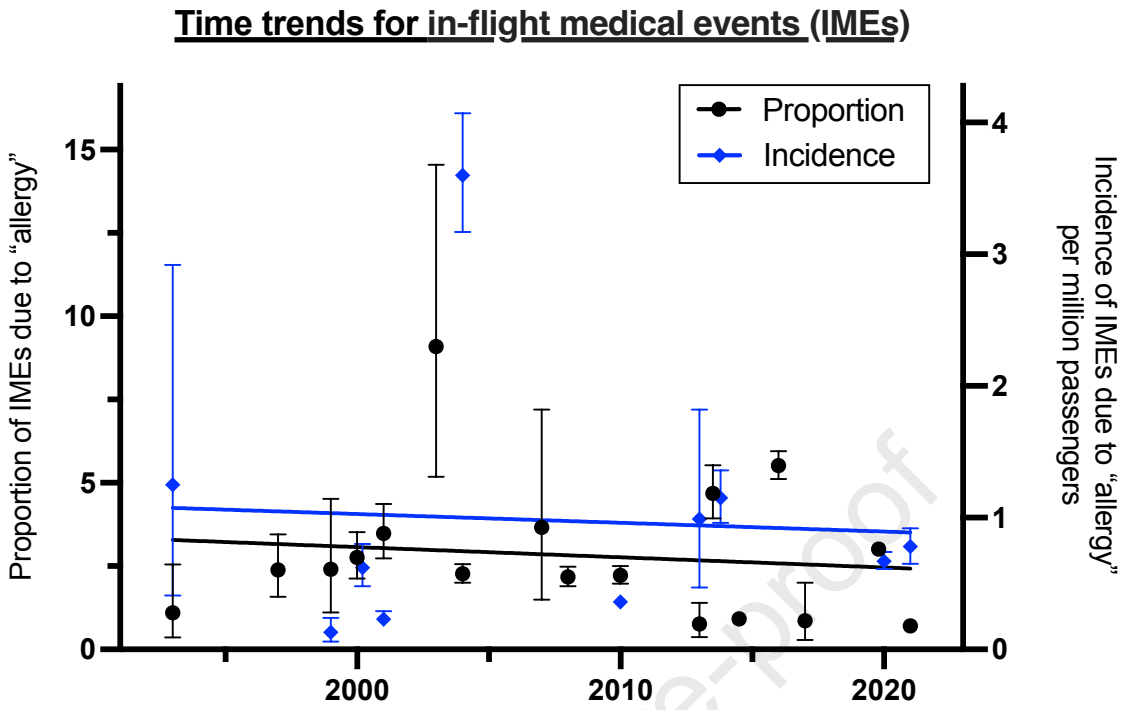
Table E1: Risk of bias for included studies describing the incidence of in-flight medical events due to allergy, evaluated using the approach of Hoy et al.[13]

Study	Study population	Sampling frame	Selection	Nonresponse bias	Data collection	Case definition	Evaluation	Consistent data collection	Recall bias	Numerator(s) / denominator(s)	**OVERALL RISK OF BIAS**
Donaldson 1996[14]	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Low
DeJohn 2000[15]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Szmajer 2001[16]	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Low
Sirven 2002[17]	Low	Low	Low	Low	Low	Unclear	Unclear	Low	Low	Low	Moderate
Delaune 2003[18]	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Low
Moore 2005[19]	Low	low	Unclear	Low	Low	Unclear	Low	Low	Low	Low	Moderate
Baltsezak 2008[20]	Low	Low	Low	Low	Low	Unclear	Unclear	Unclear	Low	Low	Moderate
Sand 2009[21]	Low	Low	Unclear	Moderate	Low	Unclear	Unclear	Unclear	Low	Low	Moderate
Mahony 2011[22]	Low	Low	Low	Low	Low	Low	Low	Unclear	Low	Low	Low
Peterson 2013[23]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Kesapli 2015[24]	Low	Low	Low	Low	Low	Unclear	Unclear	Low	Low	Low	Low
Kim 2017[25]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Alves 2019[26]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Pauline 2020[27]	Low	Low	Low	Low	Low	Unclear	Unclear	Low	Low	Low	Moderate
Rotta 2020[28]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Ceyhan 2021[10]	Low	Low	Low	Unclear	Low	Low	Low	Low	Low	Low	Low
Kodoth 2022[29]	Low	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low





362 **Figure 2**: Forest plots for (**A**) the proportion of IMEs coded as being due to allergic reactions
363 and (**B**) and incidence of IMEs due to allergic reaction per million passengers.



Annual incidence rate for different events in food-allergic people