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How Common Are Allergic Reactions During Commercial Flights? A Systematic Review and Meta-Analysis

Paul J. Turner, FRCPCH, PhD[a], Jelena Mamula, MD[a,b], Jeremiah Laktabi, MD[a,c], and Nandinee Patel, MD, PhD[a] *London, United Kingdom; Madrid, Spain; and Eldoret, Kenya*

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.

What does this article add to our knowledge? We undertook a systematic review and meta-analysis, which found that approximately 2% to 3% of IMEs are due to allergic reactions, equivalent to an incidence of approximately 0.7 reactions per million passengers.

How does this study impact current management guidelines? Allergic reactions coded as IMEs during commercial air travel are uncommon, occurring at an incidence approximately 10 to 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.

BACKGROUND: Global passenger demand for air travel has increased by over 7% annually since 2006, with a strong recovery following the coronavirus disease 2019 (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 IMEs due to allergic reactions on commercial flights.

METHODS: We searched MEDLINE, Embase, PsycINFO, and 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: Seventeen studies met the inclusion criteria. At meta-analysis, a pooled estimate of 2.2% (95% confidence interval [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%−6.6%). The incidence of allergic IMEs at meta-analysis was 0.7 events per million passengers (95% CI 0.4−1.1). Reassuringly, the rate of allergic IMEs has been stable over the past 30 years, despite increasing passenger numbers and food allergy prevalence.

CONCLUSIONS: Allergic reactions coded as IMEs during commercial air travel are uncommon, occurring at an incidence approximately 10 to 100 times lower than that reported for

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Abbreviations used
COVID-19- Coronavirus disease 2019
GBMS- Ground-based medical services
IME- In-flight medical event
MOOSE- Meta-analysis Of Observational Studies in Epidemiology
PRISMA- Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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. **(J Allergy Clin Immunol Pract 2023;11:3400-6)**

Key words: *Allergic reaction; Anaphylaxis; Epinephrine; Food; In-flight medical event*

INTRODUCTION

There is a perception among 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 owing 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-19 (coronavirus disease 2019) 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 (IMEs) reported by airlines and ground-based medical services (GBMS).[10] However, published data relating to the reported rates of IMEs due to allergic reactions are limited. We, therefore, undertook a systematic review and meta-analysis to estimate the incidence of IMEs due to allergic reactions on commercial flights and to 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 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement 2009 and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) recommendations.[11,12]

Search strategy and eligibility criteria

We searched MEDLINE, Embase, PsycINFO, and TRANSPORT databases and the Cochrane Register of Controlled Trials, from January 1, 1980 to December 31, 2022. The search strategy can be found in the Online Repository (available at www.jaci-inpractice.org) We included all primary research reporting either the proportion of IMEs due to allergy or the estimated incidence (events/person-years) of unintended immunoglobulin E–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. When 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 (J.M. and J.L.) and any discrepancies identified were resolved by discussion and consensus with a third reviewer (P.J.T.). 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 I^2 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. Seventeen studies were eligible for inclusion (Table 1).[10,14-29] All studies were assessed as being at low-moderate risk of bias (Table E1; available in this article's Online Repository at www.jaci-inpractice.org), and there was no evidence of publication bias (Figure E1; available in this article's Online Repository at wwwjaci-inpractice.org)

At meta-analysis, a pooled estimate of 2.2% of IMEs (95% confidence interval [95% CI] 1.6%–3.1%) were coded as due to allergic reactions (Figure 2, *A*). 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%–6.6%) (Figure E2; available in this article's Online Repository at www.jaci-inpractice.org) Most studies reported IMEs across a range of ages (both children and adults); thus, these data should be interpreted accordingly. Analyzing studies in which data relating to the number of flights taken (revenue passengers) were also available, the rate of IMEs due to allergic reactions was 0.66 per million passengers (95% CI 0.38–1.14) (Figure 2, *B*).

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 the proportion of IMEs due to allergic reactions had increased over the past 2 decades, despite a documented increase in passenger numbers (Figure 3).

Finally, we determined how the incidence of IMEs due to allergic reactions compared with the estimated incidences of food anaphylaxis incidents in food-allergic people in general, using data from a previously published systematic review and meta-

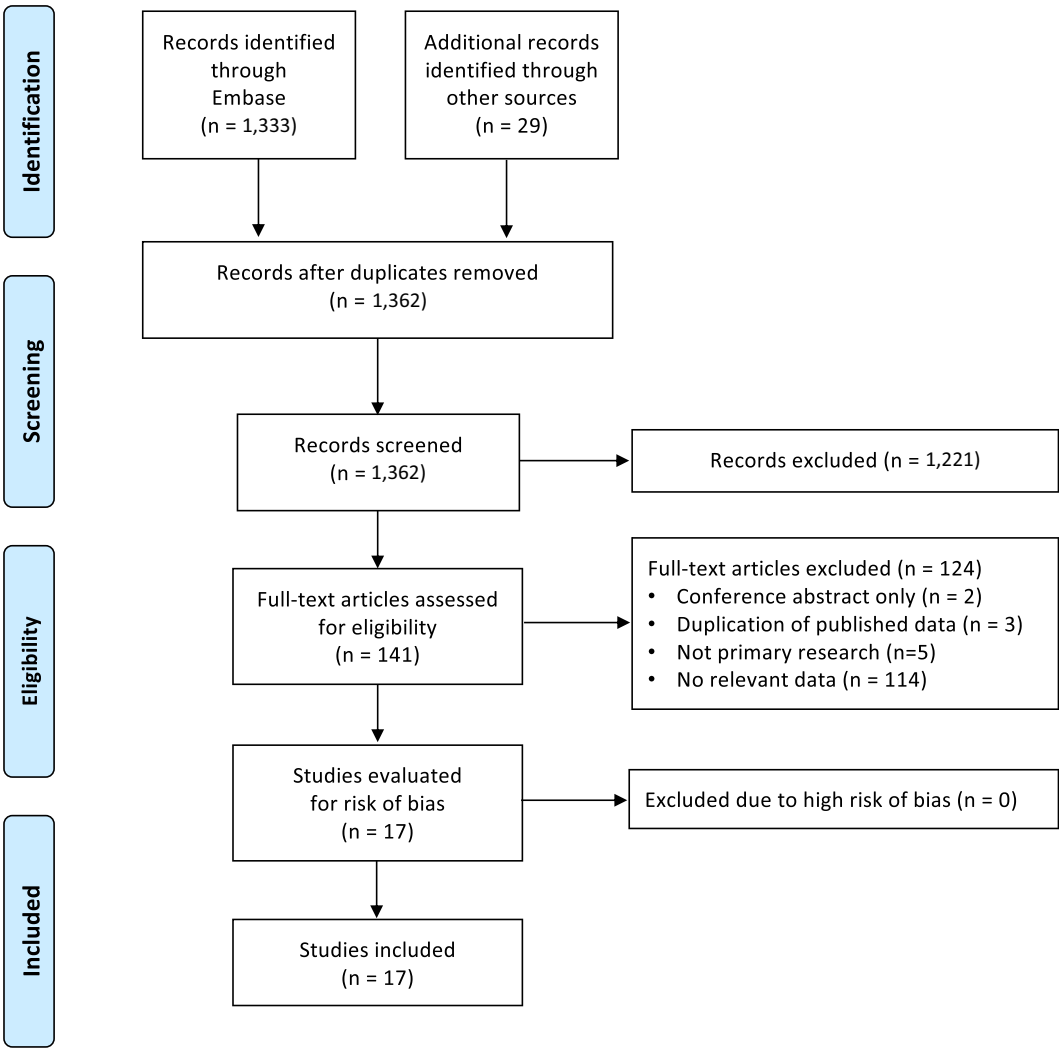

FIGURE 1. PRISMA flow diagram.

analysis.[30] Incidence of comparator risks using U.S. data were also included, as previously described.[31] In estimating the annual incidence of IMEs due to food allergy, we made the following assumptions:

1. One flight per day per passenger.
2. Population average of 4.2 flights per person per annum,[32] and a rate of 52 flights per year for frequent flyers.
3. Food-allergic passengers fly at the same frequency as those without food allergies.
4. Food allergy—related IMEs are only reported approximately 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 per 10,000 person-years (95% CI 1.6—4.8), equivalent to 1 reaction per 3,600 food-allergic passengers travelling in any 1-year period. In food-allergic individuals who fly once per week, this increases to 34 per 10,000 person-years (95% CI 20—59) (Figure 4).

DISCUSSION

In this systematic review, we estimated at meta-analysis that the incidence of in-flight allergic reactions was 0.66 events per million passengers (95% CI 0.38—1.14). This is similar to the estimated incidence of 0.64 events per million passengers (95% CI 0—1.74) reported by Borges do Nascimento et al,[33] who undertook a broader meta-analysis of the incidence of all IMEs (irrespective of etiology) but included a subanalysis of 8 studies reporting allergic IMEs. 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 approximately 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

TABLE I. Summary of included studies*

Study	Data source	Location	Study period	Revenue passengers (n)	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	United States	1996–1997	NA	1,132	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	United States	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	United States	1995–2002	NA	169	15	8.9	–	Moderate
Baltsezak, 2008[20]	Ground-to-air provider	China	2006	NA	191	7	3.7	–	Moderate
Sand, 2009[21]	Airline records	Europe	2002–2007	NA	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	NA	114,222	1,052	0.92	–	Low
Pauline, 2020[27]	Airline records	Europe	2017	NA	581	5	0.86	–	Moderate
Rotta, 2020[28]	Ground-to-air medical	Global	2015-2016	NA	11,719	643	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	6,313 million	140,579	4,230	3.0	0.67	Low

*Full risk of bias evaluation is shown in Table E1.

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 2 decades, on which 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 1 prospective survey has identified that a significant proportion of in-flight allergic reactions occur owing 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 vs airline records). Similarly, the studies did not, in general, report the assumed cause of the reported IMEs (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[29] reported an incidence for allergic IMEs of 0.91 cases per million passengers, whereas the incidence of allergic IMEs for which treatment with epinephrine was recommended by the GBMS was 0.08 cases per million passengers (interquartile range 0.02–0.16). 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 incidence of allergic IMEs reported in the current analysis.

In summary, we found that the rate of IMEs due to food-induced allergic reactions is low: for a typical food-allergic passenger, the risk of an accidental reaction is 1 reaction per 3,600 food-allergic passengers travelling on board an aircraft in any 1-year period. This is 10 to 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.

Acknowledgments

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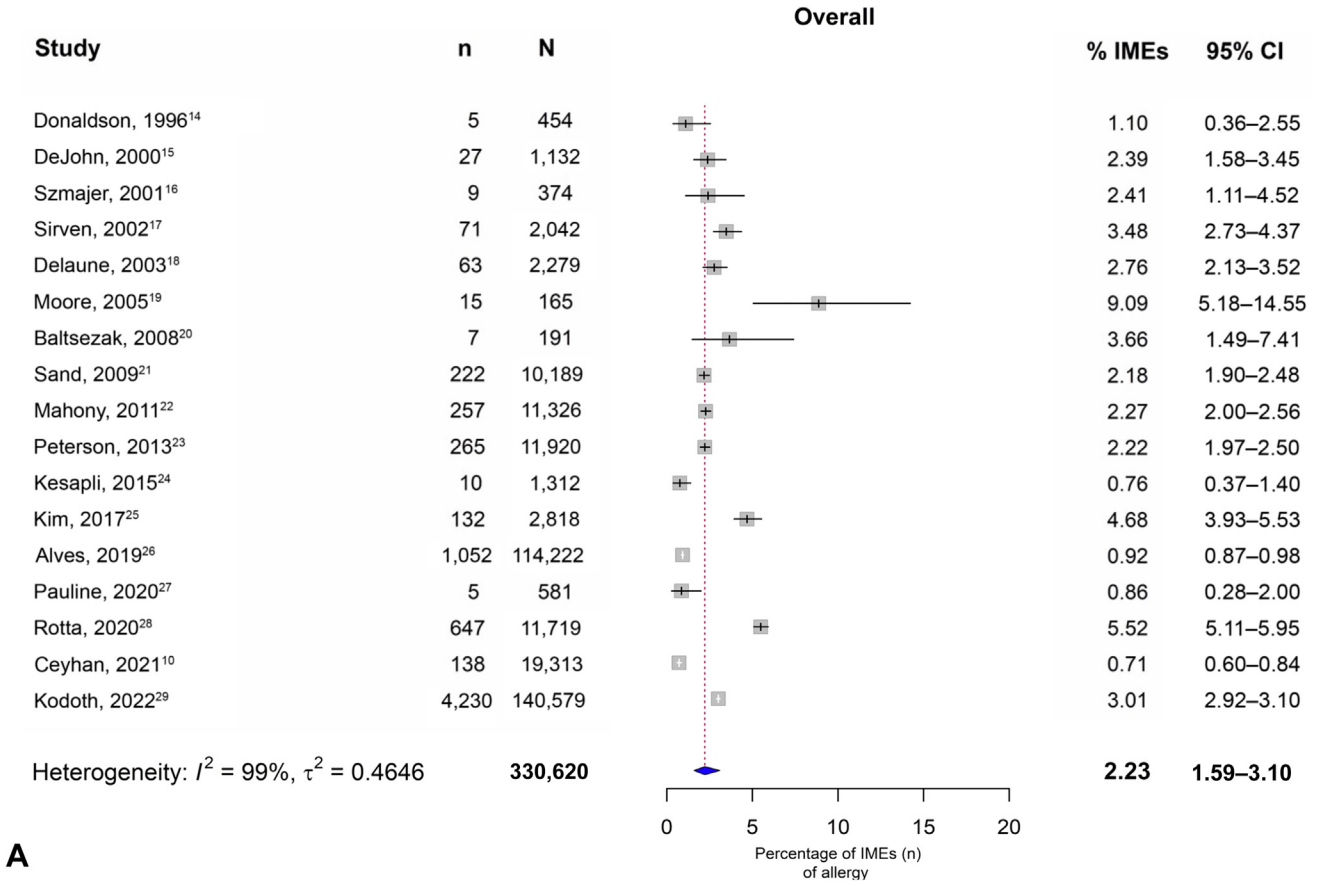
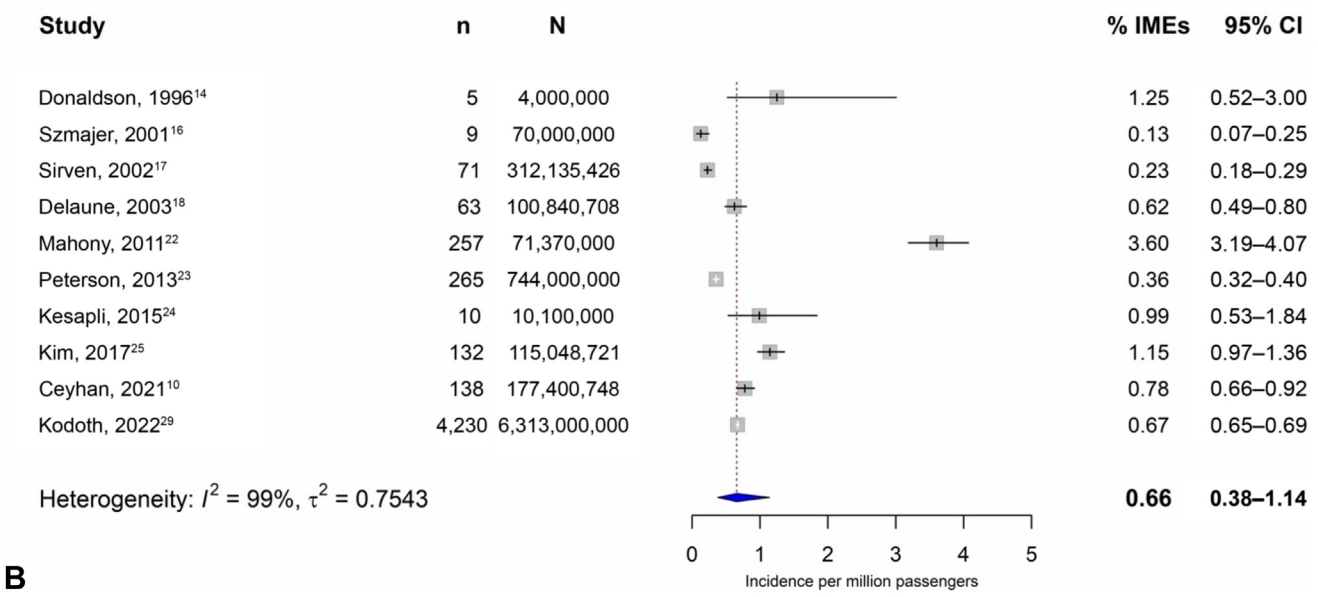
P. J. Turner conceived the study. J. Laktabi and P. J. Turner designed the protocol. Data extraction was undertaken by J. Mamula, J. Laktabi, and P. J. Turner and analyzed by N. Patel and P. J. Turner. The manuscript was drafted by P. J. Turner, and the final version was reviewed and approved by all authors.



A



B

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

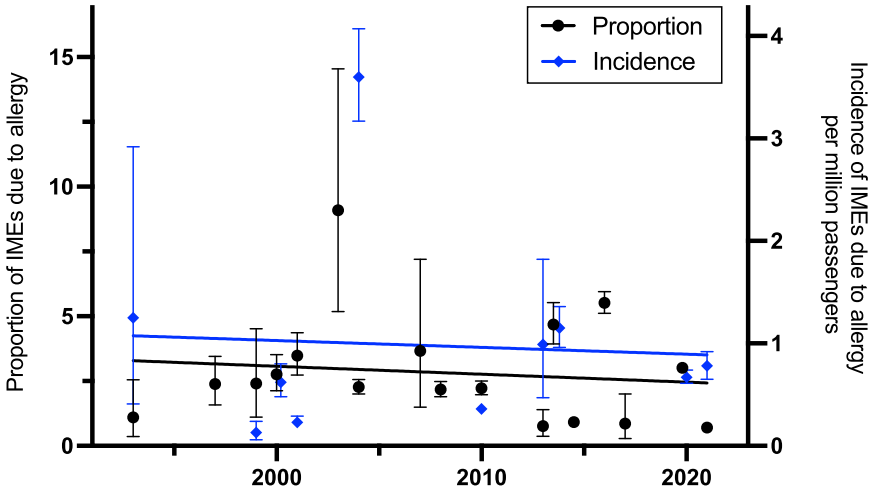


FIGURE 3. Time trends for IMEs due to allergic causes over the last 3 decades, by study period.

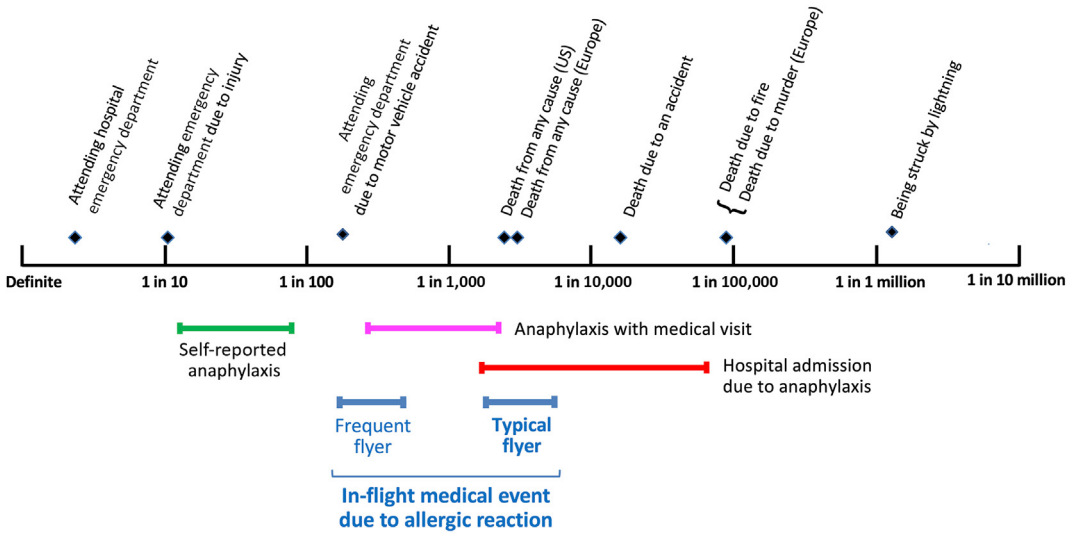


FIGURE 4. Estimated rates of food-induced allergic reactions in people with known food allergy during commercial flights, assuming a 2% prevalence of food allergy. Comparison is made with equivalent rates reported in food-allergic individual when not flying, together with reference risks (U.S. population,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

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ONLINE REPOSITORY

SEARCH STRATEGY

We systematically searched MEDLINE, Embase, PsycINFO, TRANSPORT, and the Cochrane Register of Controlled Trials, including all primary records from January 1, 1980 to December 31, 2022. We used the following search strategy:

1. (food or peanut or milk or egg or wheat or LTP or nut or fish or seafood or crustac*).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, tc, id, tm, an]
2. (allerg* or anaphyla*).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, tc, id, tm, an]
3. 1 and 2
4. limit 3 to human
5. (air* or flight*).mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kf, fx, dq, bt, nm, ox, px, rx, ui, sy, tc, id, tm, an] AND react*.af
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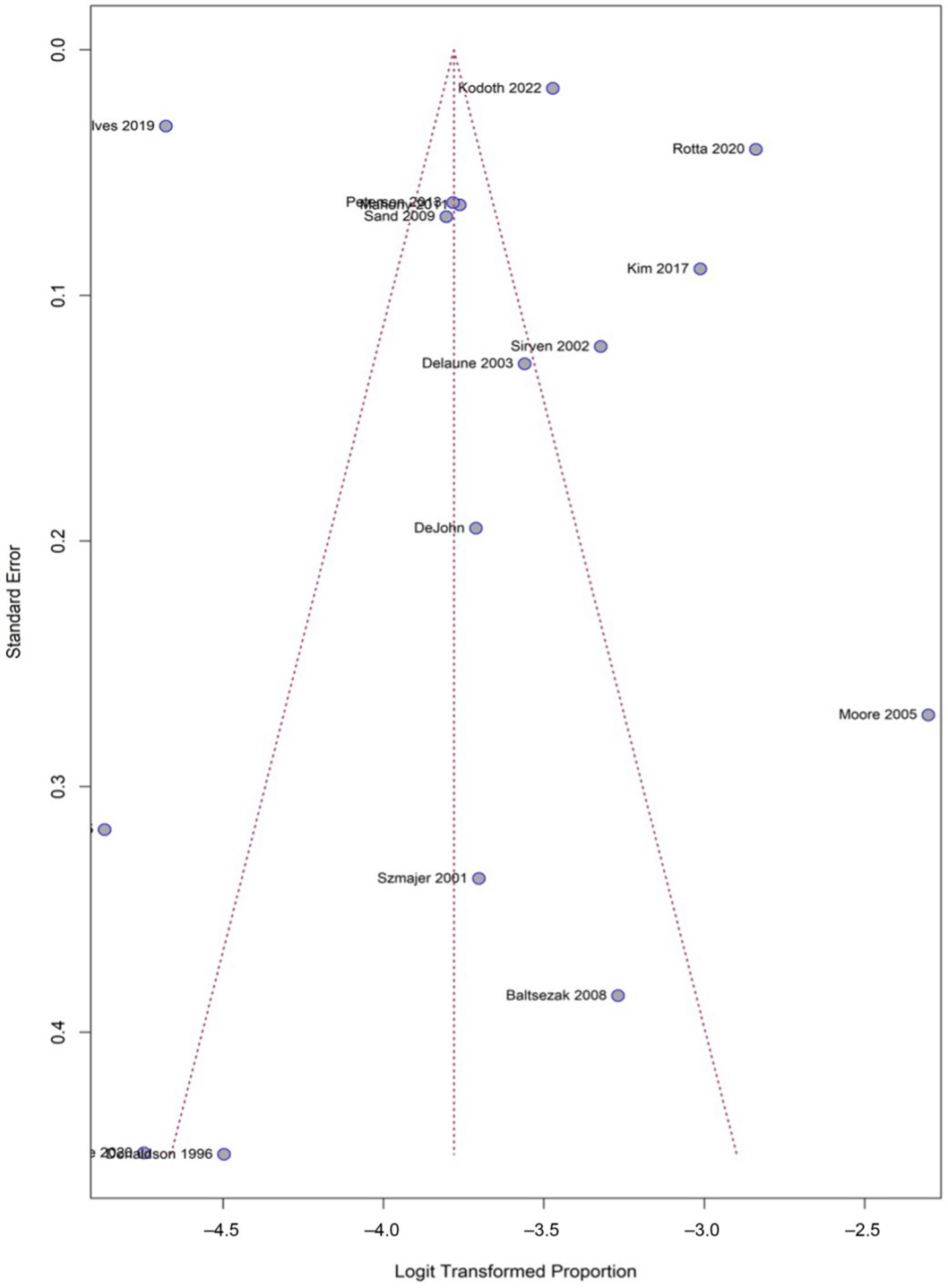

FIGURE E1. Funnel plot for studies describing the incidence of in-flight medical events (IMEs) due to allergic reactions.

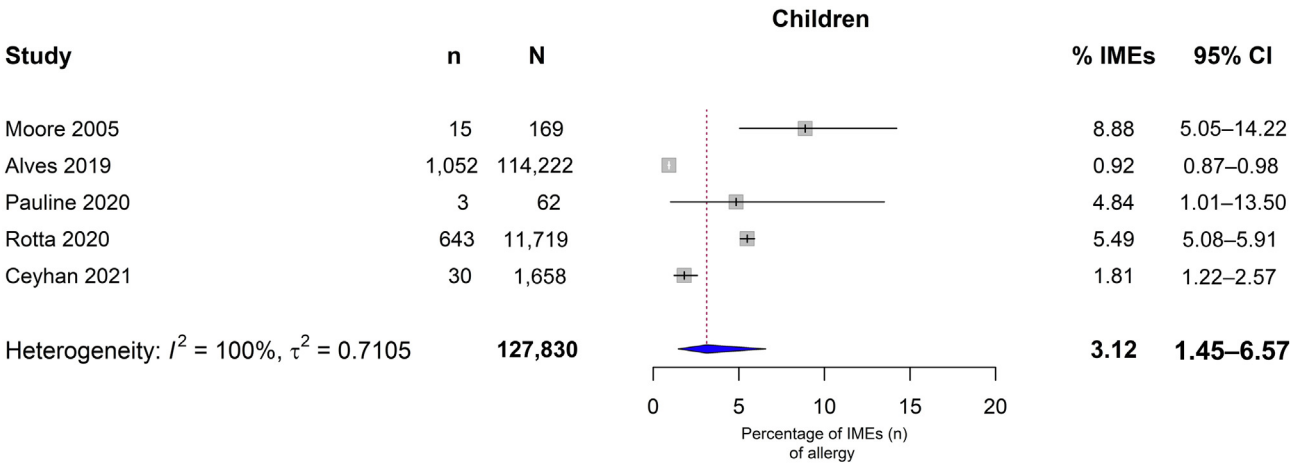

FIGURE E2. Forest plots for the proportion of in-flight medical events (IMEs) coded as being due to allergic reactions in children.

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