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Original article

The safety and applicability of synthetic pyrethroid insecticides for aircraft disinsection: A systematic review

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ABSTRACT

Background: Air travel contributes to the global spread of vectors and vector-borne infections. Although WHO provides guidance on methods for disinsection of aircraft, there is currently no harmonized or standardized decision-making process to decide when disinsection of an aircraft should be conducted. It is however compulsory for flights arriving in certain countries. Concerns have been expressed about the usefulness of disinsection for preventing the international spread of vectors and vector-borne diseases via air travel and possible toxicity for passengers and flight crew.

Methods: We performed a systematic literature review using the databases PubMed, Embase, Medline, Scopus and CINAHL to evaluate all research findings about the applicability and safety of chemical-based, aircraft disinsection. Official reports from the WHO were also screened. This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and meta-analysis (PRISMA) statement. The literature search strategy included "disinsection, airplane/plane/aviation/aircraft" and several other search items including d-phenothrin, permethrin, insecticide. Papers in English, French and German were reviewed. Reports of adverse events attributed to the disinsection of aircraft were also searched. AMP and PS screened all papers of relevance and agreed on a final selection.

Results: Our search resulted in 440 papers of possible relevance. After screening, we included a total of 25 papers in this systematic review. Ten papers reported possible human toxicity and 17 papers addressed the applicability of disinsection and 2 papers addressed both topics. Chemical disinsection at recommended insecticide concentrations was found to be highly effective against a broad range of arthropods. Three papers reported passenger or crew illness possibly associated with insecticide spraying in passenger cabins – one describing a single passenger, the other two papers describing occupational illness of 12 and 33 aircrew members respectively, possibly due to aircraft disinsection. Another paper evaluating exposure of flight attendants to permethrin found higher levels of urinary metabolites in those working in planes that had recently been sprayed but this could not be linked to adverse health outcomes.

Conclusion: Our analysis confirmed that disease vectors are carried on international flights and can pose a threat particularly to island populations and certain airport hub areas. Disinsection with permethrin or d-phenothrin was shown to be highly effective against vectors. Despite several hundred million passenger and crew exposures to chemical disinsection, very few proven cases of toxicity have been reported. There is limited evidence linking exposure to insecticide spraying with negative health impact.

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Abbreviations

A.i	Active ingredient
DDT	Dichlorodiphenyltrichloroethane
DOT	US Department of Transportation
EPA	United States Environmental Protection Agency
FAO	Food and Agriculture Organization of the United Nations
FEV1	Forced Expiratory Volume in 1 second
IPCS	International Programme on Chemical Safety
SRA	Standard Reference Aerosol Spray
US	United States of America
WHO	World Health Organization

1. Introduction

Aircraft disinsection is the application of insecticides in aircraft as a public health measure to prevent the importation of insect/arthropod vectors and thus minimize the spread of vectors and vector-borne diseases to non-endemic areas [1]. Air travel has been identified as an important factor in the global spread of infectious and vector-borne diseases [2]. Of major concern are vectors of malaria (*Anopheles.* spp.); dengue, chikungunya and Zika (*Aedes.* spp.), and yellow fever (*Ae. aegypti*). Importation of vectors and cases to a country that lacks autochthonous transmission could cause high costs in terms of surveillance and epidemiological investigations; diagnosis and treatment including hospitalization; lost working time and wages; and a delay of diagnosis and treatment, with concomitant morbidity and mortality. Gratz et al. describe in their review several cases of airport malaria, some of which were fatal often due to a lack of suspicion of malaria [3]. Many authorities consider disinsection to be an effective and important measure for the reduction of mosquito importation [4]. Guillet et al. mentioned in their review that, compared to other years, no cases of airport malaria were reported in 1995, 1996 and 1997 where flights at risk were selected and a strict disinsection conducted [5]. According to the US Department of Transportation (DOT), there are 20 countries which require a strict disinsection of all in-bound flights (Table 1) and another 16 countries which have special regulations (Table 2). The US, however, discontinued their aircraft disinsection practices in 1979 because of health concerns and because of doubts regarding the effectiveness of disinsection [6–8]. In Australia and New Zealand, strict guidelines ensure that a systematic and effective disinsection of arriving aircraft is carried out due to an increasing risk of importing vectors [4,9]. The practicalities and logistics of this aircraft disinsection lie in the responsibility of each airline company [5]. The Zika outbreak led to a paradigm change in guidelines for aircraft disinsection. WHO and other authorities publish lists of countries with Zika risk which are updated ion accordance with the ever-changing epidemiology of this vector-borne virus [10].

Insecticidal aerosols have been used since before World War II to prevent spread of vector-borne diseases via air travel [11]. As early as in 1930s, India required insecticidal treatment of incoming aircraft to prevent importation of mosquito vectors [3]. Disinsection methods have been established by the World Health Organization (WHO) with recommendations published mainly in 1987 and 1995 [12–14] and currently include four methods i.e. “blocks-away”, “pre-flight”, “top-of-descent” spraying, and “residual treatment” as depicted in Fig. 1 and described in Table 3. Following the recommendation of a WHO expert consultation in 2018, the methods are currently under revision [9].

The insecticides d-phenothrin and permethrin belong to the synthetic pyrethroids Type I [15]. In 1970, pyrethroids began to be manufactured [16]. D-phenothrin has been used since 1977, for the control of human lice, for household spraying and now for aircraft disinsection. The use of synthetic pyrethroids for vector control was introduced in the 1990s [17]. Pyrethroids pose relatively low-risk to humans, have a high potency at low dosages and a rapid knock-down effect against mosquitoes. For aircraft disinsection, the two afore-mentioned insecticides – permethrin for residual treatment and d-phenothrin for a rapid knock-down effect, are recommended by the WHO. WHO considers the residual effect to be of 8 weeks duration for permethrin on aircraft surfaces [9]. The mechanisms of pyrethroids causing death in insects is based on muscular paralysis due to repetitive nerve impulses in sensory nerve fibers [18]. The application of pyrethroids in aircraft at WHO recommended levels is not considered to pose undue risk to humans [1,12].

Thus, on one hand, there is a clear public health rationale supporting the disinsection of aircraft in order to restrict and curtail the international spread of arthropods and arthropod-borne infections and to protect areas and territories from invading species. On the other hand, concerns have been expressed about possible adverse effects of aircraft disinsection on crew members and passengers [3,19–21].

The goal of this systematic review is to collate and evaluate all published research findings about the usefulness in the reduction of international spread of vectors and vector-borne diseases, and the safety of chemical aircraft disinsection using the currently recommended insecticides as a basis for a risk/benefit analysis.

2. Methods

2.1. Literature extraction

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews (PRISMA) statement [22]. Our systematic review is registered on PROSPERO to avoid duplication. We performed a systematic literature review using the databases PubMed, EMBASE, Medline, Scopus and CINAHL to evaluate all research findings about the applicability and safety of chemical-based aircraft disinsection. The cut-off date for searches was December 31, 2018. Articles in English, French and German were reviewed.

The literature search strategy (Appendix 1) included “disinsection,

Table 1
Countries with clear regulations for aircraft disinsection [8].

Countries with clear regulations		
n	Country	Regulation
13	Ecuador (only Galapagos and Interislands), Grenada, Guyana, India, Kiribati, Madagascar, Panama, Seychelles, Tanzania, Timor-Leste, Trinidad and Tobago, Uruguay, Zimbabwe	All in-bound flights must be sprayed while passengers are on board
7	Australia and New Zealand[a], Barbados, Chile, Cook Islands, Fiji, Jamaica	All in-bound flights must be sprayed either while passengers are on board or using a residual method

[a] Australia and New Zealand require the aircraft to have been disinsected using either pre-embarkation, residual or the pre-flight method (see Fig. 1). If none of these have occurred then the aircraft is sprayed on arrival. The use of the pre-embarkation or residual option is encouraged, which is in the absence of passengers.If the cabin spray on arrival is required there is a procedure where passengers with medical concerns over aerosol spraying can exit the aircraft without their hand luggage and wait until the disinsection has been completed. After the other passengers have disembarked they can reboard to collect their hand luggage.

Table 2
Countries with special regulations with regard to aircraft disinsection, updated: 09/2018 [8].

Countries with special regulations		
n	Country	Regulation (flights from/to)
16	France	Flights from areas, where malaria, yellow fever or dengue fever are endemic must be sprayed
	Italy	All incoming flights from areas affected by Zika virus transmission and areas, where the *Ae. aegypti* vector is present must be sprayed
	Switzerland	All incoming flights from tropical Africa must be sprayed
	United Kingdom	Flights incoming from malaria endemic countries or areas with confirmed transmission of Zika must be sprayed
	South Africa	Flights from areas either affected by malaria or affected by yellow fever must be sprayed
	Thailand	All incoming flights coming from yellow fever affected areas must be sprayed
	Egypt	Incoming flights from Zika-infected countries must be sprayed
	Taiwan	Flights from areas where the *Ae. aegypti* and *Ae. albopictus* vectors are present must be sprayed
	Hong Kong	All incoming flights coming from Zika virus affected areas (WHO category 1 or 2) must be sprayed
	Republic of Korea	All flights going to or arriving from 30 defined countries (US excluded) must be sprayed
	Czech Republic	All flights coming from areas of vector-borne diseases must be sprayed
	Peru	Some inland flights must be sprayed
	Macau	All flights coming from major infectious disease affected areas/Zika-infected countries must be sprayed
	Mauritius	All incoming flights from the African continent, Asia and sub-regions, the Middle East, islands of the Indian Ocean and all flights coming from any country where mosquito borne diseases are prevalent must be sprayed
	Indonesia	All incoming flights from contagious diseases infected areas must be sprayed
	Palau	All non-US carriers coming from Korea, Hong Kong, Macau and Thailand must be sprayed

airplane/plane/aviation/aircraft/airline" and one of the following search items: d-phenothrin, permethrin, insecticide, pre-flight and top-of-descent spraying, residual disinsection, safety, toxicity, landing regulation, pacific islands, passenger, cabin crew, insects, mosquito, arthropods, malaria, dengue, mosquito borne infections, airline regulation, Australia, New Zealand, wind curtains method, new methods. We also searched for reports of cases of adverse events of disinsection of aircraft on humans.

The following data were extracted: concentrations of insecticides sprayed, methods of spraying, modelled projections of exposure, markers of insecticide exposure in body fluids and urine, adverse events and demographics of persons with adverse events severity of adverse events reported in research papers that used structured questionnaires for investigations; impact on work, knock-down and killing rates of vectors in aircraft by spraying method and insecticide type, models of introduction of disease by "stow away" vectors and impact of insecticide use on airport malaria.

2.2. Screening, inclusion and exclusion criteria

AMP and PS screened studies for the systematic review according to the titles of the articles retrieved in the database searches, and the abstracts for possible suitability (Step 1). AMP and PS screened all full texts papers and agreed on a final selection and resolved any discrepancies with regard to the choice of papers from Step 1. WHO authors provided the full text of all WHO documents pertinent to the topic.

Excluded were all duplicates. Reports of adverse effects of pesticides used historically such as DDT and articles about the toxicity and effectiveness of mosquito ground control spraying were excluded for the final selection ("excluded with reasons").

Finally, 10 articles about safety and toxicity of insecticides used for aircraft disinsection and 17 articles concerning the usefulness and effectiveness of aircraft disinsection (two papers were included in both subgroups) were included in this systematic review (Prisma flow chart is shown in Fig. 2).

3. Results

Some 10 papers reported possible human toxicity and 17 papers addressed the applicability/usefulness of disinsection (two papers were used in both subgroups). Chemical disinsection at recommended insecticide concentrations was found to be highly effective against a broad range of arthropods.

Three papers (among the 10 papers about toxicity) reported illness of passengers or crew possibly associated with insecticide spraying – one paper describing a single passenger and the other two papers detailing occupational illness of 12 and 33 crew members, respectively. Another paper evaluating occupational exposure of flight attendants to permethrin found higher levels of urinary metabolites in those working

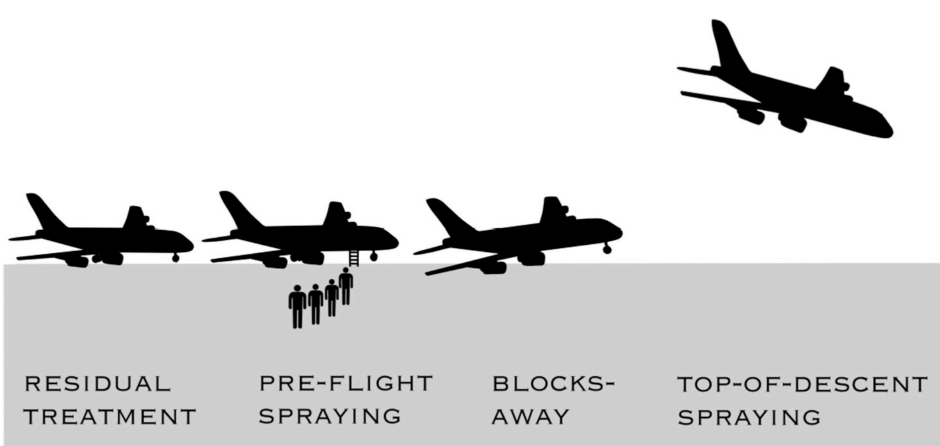

Fig. 1. Methods of aircraft disinsection.

Table 3
Description of WHO recommended cabin disinsection methods [9].

Methods	Insecticide	Applied by whom	Applied when	Additional comments	Air conditioning
Residual treatment	Permethrin EC applied at 0.2 g a.i. per m^2 dose for internal surfaces 0.5 g a.i. per m^2 on floors	Carried out by professional pest-control operators	Before the passengers embark the aircraft	The entire internal surfaces of the passenger cabin and cargo hold are sprayed (excluded are food preparation areas). Frequency of spraying should not exceed two months	After spraying air-conditioning must run for at least one hour before the aircrew and passengers are allowed to embark
Pre-flight spraying	Permethrin 2% aerosol applied at 35 g per 100 m^3	Applied by ground staff	Before passengers embark the aircraft (no more than one hour before the doors are closed). Aircrew often on board	Followed by the pre-flight spraying is an in-flight spraying to guarantee an effective disinsection (as "top-of-descent" spraying)	During spraying and for 5 min after, the air-conditioning should be switched off
Blocks-away	d-phenothrin 2% aerosol Applied at 35 g per 100 m^3	Carried out by crew members	When passengers are already on board, before the flight takes off (passengers and aircrew on board)	Every incoming flight has to be sprayed	During spraying, the air-conditioning system must be switched off
Top-of-descent spraying	D-phenothrin 2% aerosol applied at 35 g per 100 m^3	Carried out by crew members	While the aircraft starts its descent to its destination (passengers and aircrew on board)	Every incoming flight has to be sprayed	The air-conditioning should be set from high to normal flow during disinsection

in planes that had recently been sprayed.

3.1. Safety of chemical insecticides in passengers and aircrew

3.1.1. Reported symptoms

One case report and two case series reported possible toxicity among passengers and aircrew caused by chemical disinsection of aircraft [21,23,24]. The first case report describes a 20-year-old woman who suffered anaphylaxis symptoms (swelling of lips and eyelids, breathing difficulty) immediately after blocks away application of d-phenothrin. The causality could be confirmed after re-exposure to pyrethroids (electric anti-mosquito vaporizer (transfluthrin) and flea powder (containing a non-defined pyrethroid)) [23].

The first case series describes 17 flight attendants, who reported illness after insecticide exposure in aircraft. Among these, 12 reports met the definition of a "work-related pesticide illness" (i.e. occurred during work, exposure and adverse health effect were documented, and a causal relationship was established from the published literature). Of these, 11 cases were reported to have been associated with a residual treatment with permethrin (spraying the cargo hold and aircraft cabin with 34.4 L of 2.2% permethrin aerosol) immediately preceding the flight. All flight attendants were working on a 747–400 aircraft, all flying from Australia to the US and the symptoms were reported on three different occasions (in three different flights). The most common symptoms were respiratory problems ($N = 12$); effects on the central nervous system (headache, anxiety/irritability, tingling of hands and/or feet, dizziness) ($N = 11$); dermatological ($N = 9$); eye irritation ($N = 9$); cardiovascular ($N = 5$), and gastrointestinal ($N = 6$). Four of the 12 flight attendants reported noticing a bad odour upon entry in treated cabins. All of the 12 flight attendants reported to a medical care facility within 48 h of exposure [21,25].

In another case series, adverse effects among 33 self-selected flight attendants, who were regularly exposed to pesticides on flights (synthetic pyrethroids, the product was not specified), were compared with 202 non-exposed persons. Using a series of questionnaires and a test battery, an association between occupational exposure to pyrethroid insecticides and changes in moods and in balance could be observed [24].

3.1.2. Elevated urinary level of metabolites in aircrew

One of the included papers reported elevated urinary levels of certain primary metabolites of permethrin in flight attendants working in treated aircraft cabins. Analysis of urine samples collected from 11 flight attendants, who had worked in planes that had received permethrin residual treatment, showed significantly elevated levels of 3-PBA and cis- and trans-C12CA, as compared with levels in 17 non-exposed flight attendants. In the former group, the metabolite concentrations were higher in the immediate post-flight samples than those collected 24 h following flight duties. In flights originating from Australia, where permethrin residual treatment was carried out, higher urinary levels of the above described metabolites in aircrew were documented compared to those working in the domestic or international flights from Asia, Europe and North America. The time lag between the date of disinsection and start of the exposure (i.e. flight or exposure date) had a significant impact on the urinary metabolite levels in the exposed subgroup [26].

3.1.3. Role of formulations

In one paper, insecticide formulations that included solvents to enhance the solubility of the insecticide were evaluated. Although low concentrations of volatile organic compounds were found in the tested sprays, the authors suggested that there could be a health risk associated with chronic exposure of the persons working in confined and unventilated spaces [20].

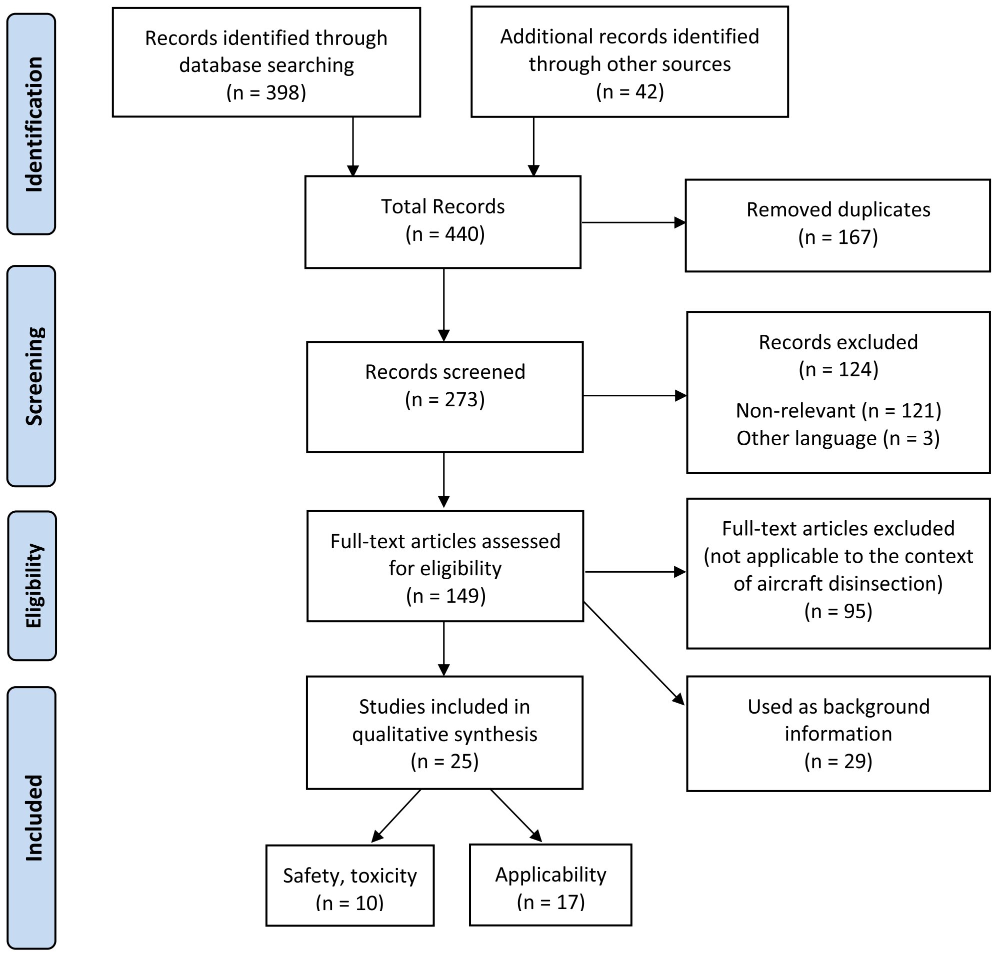

Fig. 2. Methods used for identification and screening of research papers and the criteria used for the determination of eligibility and exclusion of studies in the present systematic review.

3.1.4. Models of insecticide exposure of passengers and aircrew

In five of the selected papers, two models and three experimental studies described the chronic exposure of aircrew to pesticides associated with routine disinsection of aircraft. One of the models was a physiologically based pharmacokinetic model of permethrin exposure in flight attendants. Through the model, it was observed that dermal exposure was the predominant route to permethrin exposure under residual treatment scenario, whereas in preflight spraying the predominant exposure route was inhalation. These predominant routes also resulted in the highest impact on the urinary levels of 3-PBA [27].

In another model (exposure of flight attendants to insecticide in disinsected aircraft cabins modelled using virtual aircraft cabins) preflight spraying resulted in a 2–3.1 times higher pesticide exposure risk level for flight attendants compared to those exposed during top-of-descent spraying or residual spraying [28].

One experimental study described a new pre-embarkation method where negligibly low dermal and inhaled doses of pesticides were described. Therefore, it is assumed to be very unlikely that passengers would experience adverse health effects after the pre-embarkation spraying method [17]. In another experiment, in-flight spraying methods such as blocks-away, pre-flight and top-of-descent were tested. The applied aerosol spray was the SRA spray-Standard Reference Aerosol (Graichen GmbH, Bensheim, Germany) (consists of 1.25% pyrethrum extract (containing 25% pyrethrins, active ingredients), the synergist piperonyl butoxide (2.6%) and the propellants butane and propane). The highest calculated inhaled concentration of permethrin was found when the air conditioning was turned off. Because most of the study participants wore a face mask, no adverse health effects/irritant effect could be reported [29]. In a third experiment, the irritant effects of two insecticides (a SRA spray (1.6% pyrethrum extract (25% pyrethrins) and 3% DDT at a dosage of 35 g/100 m^3) and a G-1480 formulation (3.4% pyrethrum extract (of a 20% pyrethrins) and 1.17% DDT at a dosage of 48–64 g/100 m^3) in blocks-away spraying were compared.

More irritant effects were reported in the formulation with the higher pyrethrum extract content [11].

A more detailed description of the afore-mentioned studies is given in Table 4.

3.2. Applicability of aircraft disinsection

3.2.1. Reports of insects in aircraft/airport malaria

Four reviews have described airport malaria cases [3,5,6,30]. Gratz et al. produced a detailed list of mosquito species found in aircraft and a list of confirmed airport malaria cases reported during the period 1969 to 1999 [3]. These malaria cases were reported in Australia, Belgium, France, Germany, Israel, Italy, Luxembourg, Netherlands, Spain, Switzerland, United Kingdom and USA [3]. Later, another review reported four airport malaria cases in Tunisia in 2013 [31]. Most of the airport malaria cases were reported during the warmer periods in Europe (late June to September) and predominantly in very warm years [5,30,32,33], and were caused by *Plasmodium falciparum* [5,30,31].

3.2.2. Mosquito invasion on islands

Fiji and Hawaii are two good examples of how new mosquito species can be introduced to island settings. In 1988, *Ae. albopictus,* the

Table 4
Summary of human safety issues associated with aircraft disinsection

Lead author	Location, country	Type of paper	Insecticide/Method	Key findings	Toxicity of insecticide	Pro/contra disinsection
Vanden Driessche et al., 2010 [23]	Netherlands (Nijmegen)	Case report	1.) First exposure: D-Phenothrin, tetrafluoroetane, C11-15-isoalkanes, methoxypropxypropanol and peach perfume (blocks-away spraying method) 2.) First re-exposure: Electric anti-mosquito vaporizer (transfluthrin, kerosene, butylated hydroxytoluene) 2. Re-exposure: Flea powder (non-defined pyrethroid).	A 29-year old woman developing an anaphylactic reaction on the exposure with pyrethroids. Documented symptoms: dyspnea, swelling of lips and eyelids, feeling of losing consciousness, diarrhea. Improvement of symptoms after inhalation with albuterol and oral corticosteroids. In a following examination a provoked immediate drop of the FEV1 could be observed.	Yes. Anaphylactic reaction caused by pyrethroids.	Importance of the awareness of a possible allergic potential. Passengers should be informed in advance when exposed to insecticides during a flight to be able to cover their face or take an exposure prophylaxis.
Sutton et al., 2007 [21]	USA	Case series	11 out of 12 cases: Permethrin 2.2% (25:75 cis:trans) 34.4 L for aircraft cabin and cargo hold (residual treatment).	Documentation of 12 work-related insecticide illnesses of flight attendants after spraying the aircraft with permethrin (11 out of 12 cases). Reported symptoms: respiratory (runny nose, upper respiratory pain/irritation, wheezing) (N = 12), nervous system (headache, anxiety/irritability, tingling hands/feet, dizziness) (N = 11), dermatological (pruritus, irritation/pain, erythema) (N = 9), eye (irritation/pain/inflammation) (N = 9), cardiovascular (palpitations) (N = 5), and gastrointestinal (nausea, anorexia, diarrhea, vomiting) (N = 6). 4 out of 11 flight attendants detected an odour.	Yes. Occupational illness of flight attendants caused by permethrin.	Pro disinsection: The elimination of vector-borne diseases remains essential. Passengers should be informed about possibly toxic effects. Disinsected aircraft should be scheduled to countries that require disinsection. Active illness surveillance among exposed workers and passengers should be done.
Kilburn, 2003 [24]	California	Observational study	Pyrethroid exposure (not clearly defined). 33 flight attendants (self-selected) regularly exposed to pyrethroids (not clearly described) were tested and filled out questionnaires 48 h or more after their last shift. The results were compared with 202 residents, non-exposed to insecticides.	The 33 flight attendants exposed to chemical disinsection were found to have changes in moods and in balance. A higher frequency (twice as frequent as in the control group) of extreme fatigue, loss of memory and concentration, loss of libido, dry mouth, somnolence, swollen stomach, Mucous membrane irritation, memory loss, and dizziness, decreased alcohol tolerance could be observed.	Study design weak	Findings speak against chemical disinsection.
Wei et al., 2012 [26]	USA	Observational study	Permethrin (residual treatment). Urinary samples were analyzed (three different samples: pre-flight sample, post-flight sample and 24 h-post-flight sample). Measurement of 3-PBA (3-phenoxybenzoic acid), cis- and trans-C12CA, primary metabolites of permethrin and d-phenothrin.	Elevated body burden (urine) of 3-PBA, cis-and trans-C12CA (was measured in urine samples of flight attendances exposed to permethrin. The creatinine adjusted concentrations of 3-PBA ranged from 2.18 to 71.0 μg/g. All collected samples of the exposed flight attendants had significant higher concentrations of the mentioned metabolites compared to those working on non-disinsected planes and compared to the regular U.S. population.	Health risk of the elevated concentrations remain unclear. No correlation for urinary metabolites and toxicity.	Further studies should be done (evaluation of the potential health risk of elevated body burden of primary metabolites of permethrin and d-phenothrin). Residual treatment should be practiced more frequently but in a less concentrated formulation.

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Table 4 (*continued*)

Lead author	Location, country	Type of paper	Insecticide/Method	Key findings	Toxicity of insecticide	Pro/contra disinsection
Wei et al., 2013 [27]	USA (New Jersey)	Experimental study (model)	Permethrin, residual treatment	Dermal exposure is the predominant route to permethrin exposure under residual treatment scenarios. In pre-flight spraying the predominant exposure route is through inhalation. These predominant routes also resulted in the highest effect on the urinary levels of 3-PBA.	Not described	Not defined. In the future PBPK models[3] could be used for more specific exposure questions.
Zhang et al., 2013 [28]	USA	Experimental study (model using a virtual aircraft and virtual aircrew)	A modelling system was used with a virtual aircraft cabin and virtual flight attendants using their estimated body weights. Pre-flight spraying, top-of-descent spraying and residual treatment.	In their model they found that pre-flight spraying results in a 2–3.1 times higher insecticide exposure risk level for flight attendants compared to top-of-descent spraying or residual spraying. Insecticide surface loading on the floor: residual application the highest. Air concentration: pre-flight the highest. Surface loadings on seat top and exposed surface of human body: top-of-descent the highest. Exposure of insecticide was comparable for women and men.	Not described	Not defined
Berger-Preiss et al., 2006 [17]	Germany (Berlin, Hannover)	Experimental study (non randomized)	2% d-phenothrin (Denka or Arrow[4]), pre-embarkation method compared to top-of-descent spraying.	Negligible exposure for passengers was found for the pre-embarkation method (collected filter paper and urine samples). A higher dermal exposure was found in top-of-descent method compared to the pre-embarkation method.	No. Very unlikely that passengers would experience adverse health effects (pre-embarkation).	Pro disinsection. Better methods should be developed. Pre-embarkation method is a good and effective method resulting in lower concentrations in the resting area for passengers and aircrew.
Berger-Preiss et al., 2004 [29]	Germany (Hannover)	Experimental study (non randomized)	Pyrethrin (a SRA[5] spray was used containing 1.25% pyrethrum extract (containing 25% pyrethrins, active ingredients), the synergist piperonyl butoxide (2.6%) and the propellants butane and propane), simulated in-flight spraying (in parked planes), measurement of inhalation exposure with Respicon TM 3-F[6], dust with a vacuum cleaner and the dermal exposure with pads (filter paper). The experiment was performed six times with six people involved all wearing masks.	Big differences were found between the sprayers, which could be due to a different handling of the insecticide. For passengers a concentration of 120–300 µg pyrethrins/person and a concentration of 1080–4040 µg piperonyl butoxide per person especially on the head and thighs could be seen. For passengers the dermal exposure was about a factor of two lower compared to the sprayers. The highest inhaled dose was found while the air conditioning was not working.	Not defined. No adverse health effect/irritant effect could be reported because all the involved participants were wearing mask.	Not defined. Further studies are needed to measure health effects (all pexposed had masks on).
Sullivan et al., 1962 [11]	USA (WHO)	Experimental study	Two insecticides were compared. A SRA spray (1.6% pyrethrum extract (25% pyrethrins) and 3% DDT at a dosage of 35 g/100 m^3) and a G-1480 formulation[7] (3.4% pyrethrum extract (of a 20% pyrethrins) and 1.17% DDT at a dosage of 48–64 g/100 m^3) in blocks-away spraying.	G-1480: more irritant effects were reported due to higher pyrethrum content compared to the SRA formulation.	Yes. Irritant effects occurred in the G- 1480 formulation (higher pyrethrum extract content). Irritant effect not closer defined.	Pro disinsection; against the spread of vector-borne diseases.

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Table 4 (*continued*)

Lead author	Location, country	Type of paper	Insecticide/Method	Key findings	Toxicity of insecticide	Pro/contra disinsection
Van Netten, 2002 [20]	Canada (Vancouver)	Observational study/ Analysis of lab data	Spray insecticide" (2% phenothrin as the active ingredient) 2.) "Callington 1-shot aircraft insecticide" an aerosol Insecticide for cargo holds (2% phenothrin and 2% permethrin) 3.) "AIROSOL aircraft insecticide" which was manufactured in Australia (2% phenothrin) 4.) Residual disinsectant formulation: "Pestgard" and "Pestgard low odour" 5.) Residual disinsectant formulation: "Airez" and "Airez low odour".	Volatile organic solvents (such as hexane, cyclopentane, cyclohexane, octane derivatives) were found in the examined sprays. The "Callington aircraft formulation" as well as the "AIROSOL" insecticide appeared to have lower levels of volatile organic compounds compared to "Callington 1-shot aircraft insecticide".	Not described. But a possible hazard when sprayed in confined and unventilated spaces due to a cumulative effect is suspected.	Pro disinsection; against the spread of vector-borne diseases.

[3] Physiologically based pharmacokinetic modelling.
[4] Insecticide brands.
[5] Standard Reference Aerosol Spray.
[6] Measuring system for size segregated dust.
[7] Insecticide formulation.

vector of dengue and other arboviral infections, was reported for the first time in Fiji [34]. Since then, it has spread widely on the archipelago's main island, Viti Levu.

In 2003, *Ae. japonicus japonicus* (Theobald) were collected on the island of Hawaii and it was assumed that they were imported via air travel [35]. This is the eighth invasive mosquito species reported to have been established in Hawaii.

3.2.3. Applicability of insecticides applied in aircraft

One paper compared the pre-embarkation/pre-flight and top-of-descent method in different experiments and in different planes and applied two different formulations (Denka and Arrow spray; two 2% d-phenothrin containing aerosols). Both methods and both spray formulations produced 100% mortality in arthropods (*Ae. aegypti.*, *A. stephensi*, *Culex pipiens molestus* and houseflies; *Musca domestica*) at 24 h post-exposure [17]. Another study reported 100% mortality in arthropods (*A. gambiae* and *Culex quinquefasciatus*) exposed at 57% of the recommended dose of d-phenothrin aerosol in aircraft [32].

Various experiments evaluated the efficacy of different pesticides applied by blocks-away method. In one study, the efficacy of two insecticides (1. SRA: 1.6% pyrethrum extract (25% pyrethrins) and 3% DDT, 2. G-1480: 3.4% pyrethrum extract (of a 20% pyrethrins) and 1.17% DDT) were compared. The higher efficacy was found with the use of the formulation with the higher pyrethrum extract content [11]. In another study comparing the efficacy of two d-phenothrin formulations (1.1.20% d-phenothrin, 2.2.00% d-phenothrin) mortality in *A. quadrimaculatus* and *Ae. aegypti* was found to be 100% but none of the exposed house flies, *Musca domestica,* died [36]. In yet another study, two different formulations of 2% (+)-phenothrin were analyzed (1.2% (+)-phenothrin in a 3:17 ratio of Freon 11 to Freon 12, 2.2% (+)-phenothrin in a 1:1 ratio of Freon 11 to Freon 12). One hundred percent mortality could be achieved in all experiments with mosquitoes (*Ae. aegypti, Ae. taeniorhynchus, A. quadrimaculatus, A. stephensi* and *Culex pipiens fatigans*), houseflies (*Musca domestica*), stable flies (*Stomoxys calcitrans*), Caribbean fruit flies (*Anastrepha suspensa*), and blackflies (*Simulium vittatum*) while no offensive odour or skin/eye irritation were experienced by the crew or the investigators [37].

In a different experiment comparing in-flight treatments with blocks-away and top-of-descent with d-phenothrin 2% (35 g per 100 m^3) when air conditioning in the cabin was tuned on, complete mortality in mosquitoes (*Culex quinquefasciatus*) and houseflies (*Musca domestica*) was observed [38].

In a residual treatment experiment, the effectiveness of residual spraying was assessed for the knockdown of flies after two and four weeks after spraying. A 100% knockdown of flies even after two weeks could be found. Four weeks after spraying some locations failed to give a sufficient dose to achieve a 100% knockdown of flies [39].

Sharma et al. launched an experiment in aircraft parked on the ground in South India in 2004 to describe the effectiveness of commonly used insecticides against aquatic and adult stages of *Ae. aegypti* and *Ae. Albopictus*. Permethrin was found to be effective against *Ae. aegypti* and *Ae. Albopictus* in South India, although an increase of resistance in the future can be expected [40].

3.2.4. Importation of pathogens – infected mosquitoes versus infected travelers

A model was generated to describe the probability of an introduction of pathogens by mosquitoes compared to the introduction of a pathogen by infected humans. After analyses of the collated data (mosquitoes were counted on flights, particularly originating in highly endemic countries) the authors concluded that the introduction of malaria parasite, *P. falciparum,* via infected human travelers was 1000 times and for dengue viruses more than 200 times more likely compared to the introduction of these diseases via infected mosquitoes [41].

A more detailed description about the mentioned studies is given in Tables 5 and 6.

Table 5
Cases of airport malaria and modelling of introduction of vectors via infected vectors

Lead author	Source, location, country	Type of paper	Cases/Disease	Vectors/Pathogens	Seasonal Pattern	Pro/contra disinsection
Rayman, 2006 [6]	Aviation, space, and environmental medicine	Review	1930: outbreak of malaria in Brazil. Most probably the vector was imported by air. 1994: 6 cases of airport malaria in Roissy France Between 1969 and 1999: 89 cases of airport malaria were reports in 12 countries.	Different mosquito-vectors, not closer defined.	Not described	Pro disinsection. Against the spread of vector-borne diseases.
Gratz et al., 2000 [3]	WHO Bulletin	Review of case reports	List of reported airport malaria cases between 1969 and 1999. In the following countries, cases of airport malaria have been reported: France, Belgium, Switzerland, United Kingdom, Italy, USA, Luxembourg, Germany, Netherlands, Spain, Israel and Australia.	List of reported mosquitoes in different planes and in different countries between 1931 and 1983: *Ae. aegypti, Ae. vexans, A. gambiae, A. grabhami, A. pseudopunctipennis, A. neomaculipennis, A. vestipennis, A. superpictus, Culex quinquefasciatus, Culex annulirostris, Culex bitaenriorhynchus, Culiseta incidens.*	Some cases occurred during hot summer months. Due to global warming vectors and transmissions could increase.	Pro disinsection
Siala et al., 2015 [31]	Tunisia	Case series	During summer of 2013 four airport malaria cases were reported in Tunisia. All patients were living within 2 km of Tunis International Airport. Severe symptoms were observed due to a delay in diagnosis.	All cases caused by *P. falciparum*	All four cases occurred in summer 2013 (all in July on different days).	Pro disinsection. Considering malaria in febrile patient living close to an airport to reduce a delay in diagnosis.
Van den Ende et al., 1995 [33]	Belgium	Case series	In summer 1995 six cases of airport malaria were reported in Belgium. One death.	5× *P. falciparum,* 1× *P. ovale*	All cases occurred during hot summer months.	Pro chemical disinsection, recommended by WHO. Special attention should be paid to cargo holds/cargo flights.
Isaäcson, 1989 [30]	WHO Bulletin, Europe	Review of case reports	Between 1969 and 1988 29 cases of airport malaria were reported in Europe.	*P. falciparum, P. vivax, P. malariae*	Most cases occurred between late June and September (warmest part of the year in Europe).	Not defined. Against airport malaria. To reduce a delay of diagnosis and therapy of malaria, malaria should be supected
Guillet et al., 1998 [5]	France	Review of case reports	Between 1969 and 1996 63 cases of airport malaria were reported in Western Europe. 24 cases alone in France. Most of the flights came back from Sub-Saharan Africa.	Most reported airport malaria cases were due to *Plasmodium falciparum.*	Most of the cases were documented in the hot summer months, predominantly in very warm years.	Pro chemical disinsection to protect against airport malaria. Airports must be kept free from vectors.
Laird et al., 1990 [34]	New Zealand	Survey	In 1988, *Ae. albopictus* was reported for the first time in Fiji. Since that initial introduction, this vector has spread widely on the archipelago' s main island, Viti Levu.	*Ae. albopictus* the vector of dengue and other arboviral infections.	–	Pro disinsection. Prevent the introduction of medically and economically significant mosquitoes into New Zealand.
Larish and Savage, 2005 [35]	USA	Survey	In 2003, *Ae. japonicus japonicus* were collected for the first time on the island of Hawaii. Most probably imported via air travel. This species is described as the 8th mosquito species that has been newly introduced and established in Hawaii.	*Ae. japonicus japonicus* the vector of West Nile virus disease.	–	Pro disinsection. Disinsection of cargo holds.
Mier-y-Teran-Romero et al., 2017 [41]	Great Britain (Oxford)/Vietnam	Modelling Study	Introduction of pathogens by mosquitoes compared by humans.	Infected humans versus pathogen carrying mosquitoes.	Not defined	Little impact of disinsection procedures. Infection transmission via an imported, infected mosquito is, in general, unlikely compared to the introduction of pathogens via infected human travelers.

Table 6
Effectiveness of aircraft disinsection against arthropods

Lead author	Location, country	Type of paper	Insects	Insecticide/Method	Location	Key findings	Mortality	Pro/contra disinsection
Berger-Preiss et al., 2006 [17]	Germany (Berlin, Hannover)	Experimental study (non randomized)	Female mosquitoes (*Ae. aegypti.*, *A. stephensi* and *Culex pipiens molestus*) and houseflies (*Musca domestica*)	2% d-phenothrin (Denka and Arrow sprays), pre-embarkation method compared to top-of-descent spraying.	Airbus 310, Boeing 747-400	Concentration of d-phenothrin was sufficient to kill all mosquitoes and houseflies up to 24 h after spraying.	20 min after spraying: 99–100% mortality of houseflies and mosquitoes in most of the exposed groups.	Pro disinsection. Pre-embarkation method is an effective method.
Curtis et White, 1984 [32]	Great Britain (London)	Experimental study	Mosquitoes *(A. gambiae* and *Culex quinquefasciatus)*	2% d-Phenothrin	Boeing 747	57% of the recommended aerosol is enough to achieve 100% mortality.	240 g insecticide sprayed: 100% mortality of mosquitoes 160 g insecticide sprayed: 100% mortality for all mosquitoes 80 g insecticide sprayed: majority survived.	Pro chemical disinsection, further studies needed on human toxicity.
Sullivan et al., 1962 [11]	USA (Beltsville), Switzerland (Geneva)	Experimental study	Mosquitoes *(Ae. aegypti, Ae. aegypti* (DDT-resistant), *Culex fatigans)*	Two formulations were tested: 1.) SRA: 1.6% pyrethrum extract (25% pyrethrins) and 3% DDT 2.) G-1480: 3.4% pyrethrum extract (of a 20% pyrethrins) and 1.17%DDT, Blocks-away disinsection procedure.	Passenger aircraft of piston, prop-jet and turbo-jet types.	1.) SRA: satisfactory control of non-resistant mosquitoes 2.) G-1480: effective against resistant and non-resistant mosquitoes.	SRA: 90–100% mortality, no adequate kill of resistant mosquitoes. G-1480: 100% mortality of all mosquitoes.	Pro chemical disinsection; develop an aerosol formulation which is effective and acceptable to passengers.
Sullivan et al., 1974 [36]	USA	Experimental study	Mosquitoes *(Ae. aegypti, A. quadrimaculatus),* houseflies *(Musca domestica* (only females)), other insects (*Anastrepha suspense, Triatoma infestans* and *Xenopsylla cheopis)*	D-phenothrin: 1.) 1.20% d-phenothrin 2.) 2.00% d-phenothrin. Air exchange rate 3–5 min, blocks-away disinsection procedure.	Commercial jet aircraft: Boeing 707 (4.2 g) and Boeing 727 (5.7 g).	Satisfactory mortality occurred and no odour and no irritation were described.	100% kill up to 24 h post-exposure of *Anastrepha suspense, Ae. aegypti* *A. quadrimaculatus* (exposed to insecticides for 30 min).	Not defined
L. A. Liljedahl et al., 1976 [37]	USA	Experimental study	Mosquitoes (*Ae. aegypti, Ae. taeniorhynchus, A. quadrimaculatus, A. stephensi* and *Culex pipiens fatigans),* houseflies (*Musca domestica*), stable flies (*Stomoxys calcitrans*), Caribbean fruit flies (*Anastrepha suspensa*), and blackflies (*Simulium vittatum).*	(+)-phenothrin, two formulations: 1.) 2% (+)-phenothrin in a 3:17 ratio of Freon 11 to Freon 12 2.) 2% (+)-phenothrin in a 1:1 ratio of Freon 11 to Freon 12. Complete air exchange every 3–4 min. Blocks-away disinsection procedure.	In training flights. Boeing 727 (aircraft of Eastern, National, and Pan American Airlines), Boeing 707 (US Air Force passenger aircraft).	2% (+)-phenothrin aerosol against mosquitoes was highly effective against mosquitoes. A dosage of 35.3 g/100 m^3 (+)-phenothrin is needed to control houseflies. No odour or irritation noted.	Boeing 727 (17.7 g/100 m^3): 100% mortality of *A. quadrimaculatus*, *S.calcitrans*, 98–100% mortality of *A.taeniorhynchus*. Mortality of *M. domestica* were low. Boeing 707 (17.7 g/100 m^3): 100% mortality of *S. vittatum, S. calcitrans*, 90–100% mortality of *Ae. aegypti, A. stephens*i. 82–100% mortality for *C.pipiens fatigans*, 31–100% mortality of *M. domestica*.	Not defined. Caged mosquitoes are less susceptible to insecticides than free flying mosquitoes. Chemical insecticides might be even more effective against mosquitoes as described.
Russell et Paton, 1989 [38]	Australia	Experimental study	Mosquitoes (*Culex quinquefasciatus*) and houseflies (*Musca domestica).*	2% d-phenothrin, 35 g per 100 m^3, blocks-away and top-of-descent disinsection procedure compared to the on-arrival methods.	Boeing 747, Boeing 767 (scheduled passenger flights).	In-flight disinsection procedures of Boeing 747 and 767 is efficacious. Satisfactory insect mortality for all the test positions could be shown.	100% mortality of *Culex quinquefasciatus* and *Musca domestica* for all the test positions with blocks-away or top-of-descent method with air conditioning on.	Pro disinsection. In-flight disinsection is an efficacious procedure.

(*continued on next page*)

Table 6 (*continued*)

Lead author	Location, country	Type of paper	Insects	Insecticide/Method	Location	Key findings	Mortality	Pro/contra disinsection
Dale et al., 1982 [39]	New Zealand	Experimental study	Houseflies (*Musca domestica* L.)	Permethrin	Air New Zealand DC-10 aircraft	Permethrin has a good effectiveness and remains effective for up to 4 weeks.	After 2 weeks: 100% knockdown and 100% mortality rate (exposure for 15–20 min). After 4 weeks: 1 out of 15 locations in the cabin, 2 out of 12 on the carpet, 1 out of the 5 of the hold failed to give a complete kill of flies (exposure for 15–20 min).	Pro chemical disinsection. Permethrin (residual treatment) is a good and effective alternative to the widely used d-phenothrin aerosol.
Sharma et al., 2004 [40]	India (Delhi)	Experimental study, survey	Mosquitoes (*Ae. aegypti* and *Ae. Albopictus*)	0.25% permethrin and other insecticides as DDT, dieldrin, malathion, deltamethrin, lambdacyhalothrin, fenitrothion, propoxur. Top-of-descent (high ventilation) and blocks-away (low ventilation) disinsection procedures.	Laboratory, not in planes	Permethrin is effective against *Ae. aegypti* and *Ae.albopictus.*	100% mortality of *Ae. aegypti* and *Ae.albopictus* (adults) when exposed for one or two hours to permethrin.	Pro disinsection

4. Discussion

Considering the risk of transportation of vectors carrying disease pathogens and/or invasion of non-native species to new territories [42,43], disinsection of passenger and cargo aircraft has long been required by many countries. WHO has issued guidelines for aircraft disinsection in 1987 and in 1995. More non-chemical, practical and low-risk methods and operational procedures such as wind curtains[1] are likely to become available in the coming decade, but until then, aircraft disinsection is required by many countries.

Insecticides used for disinsection have sometimes been linked to certain adverse health events in passengers and aircraft crew who were exposed in the aircraft cabins. However, despite several hundred million passenger and crew exposures to chemical disinsection, very few proven cases of toxicity have been published. This systematic review examines both the benefits and the possible adverse health effects of aircraft disinsection and updates our knowledge on the scientific evidence underpinning the use of chemical disinsection in aircraft.

4.1. Effectiveness of aircraft disinsection in knock-down and kill of vectors

The residual treatment method showed the highest insecticide loading on the floors [17]. Residual treatment is described as an effective good alternative to d-phenothrin in-flight spraying. It is more effective against a greater range of arthropods and less susceptible to organizational failure. It is assumed that residual treatment causes less inconvenience to passengers and crew members [39].

The pre-flight spraying method resulted in the highest insecticide exposure risk level for aircrew and the highest air concentration level. Pre-flight spraying showed a 2–3.1 times higher insecticide exposure risk level for air crew compared to top-of-descent spraying or residual treatment [28]. The pre-flight/pre-embarkation method with d-phenothrin is described as resulting in lower concentrations of d-phenothrin in the potential resting area for passengers and the aircrew compared to in-flight methods with d-phenothrin [17]. This method appears safe and is still very effective against arthropods. To reduce complaints from passengers, the aircrew prefer, in general, the pre-embarkation method. The method of choice appears to be the pre-embarkation method as there are many advantages and the lowest potential health risk [9,17]. A major challenge is the unavailability in Europe of the recommended permethrin 2% aerosol for pre-flight/pre-embarkation disinsection procedures due to new EU regulations [9,17]. In-flight spraying methods, as blocks-away and top-of-descent spraying, are described as leading to a markedly higher exposure of insecticides compared to residual treatment [18]. The highest, inhaled dose was found to occur while the air conditioning was not working [29]. The mortality rate of arthropods should be evaluated while the air conditioning is not running also in the blocks-away methods to reduce the exposure of passengers and aircrew.

In all the described experimental studies, aircraft spraying of any form showed high effectiveness (approaching 100% mortality of arthropods) for all recommended methods [11,17,32,36–40]. Despite these finding, it is still recommended to use the standard dosage recommended by WHO.

4.2. Applicability of aircraft disinsection

The fact that vectors are transported by aircraft and that airport malaria is a real problem for humans living or working close to an airport has been documented in several papers [3,5,6,30,31,33]. The

[1] Wind curtains or air curtains can prevent mosquitoes and flies from entering an aircraft when passengers do. Their action relies on fast-moving, outwardly directed currents of air to keep insects from flying into the aircraft. Their usefulness requires further evaluation.

effectiveness of chemical insecticides and the presence and carriage of vectors in planes can be used as a proxy for the potential usefulness/applicability of insecticide spraying in aircraft. The importation of mosquito vectors could result in infections such as airport malaria, autochthonous transmission by a local vector of diseases such as dengue or in an establishment of the introduced mosquitoes especially in semi- or tropical areas. New introduction of arthropods to islands via air, have been shown in the examples of Fiji and Hawaii [34,35]. Due to introduction of new vector mosquitoes, dengue fever spread on the Solomon Islands, in Fiji and in Bolivia. Australia's and New Zealand's concerns regarding the introduction of vectors goes back to an introduction of *A. indefinitus* in Guam and Saipan, islands of the South Pacific [3,30,33,34]. Most cases of documented airport malaria in Europe described in our systematic review occurred during the hot summer months from late June to September [3,5,30,31,33]. Especially in very warm years, more airport malaria cases could be observed. To reduce spraying of insecticides, one possible approach would be to limit disinsection to hot summer months. Furthermore, more detailed studies and evaluations of the exact number of stowaway arthropods on aircraft should be done, especially comparing hot months with colder month and different airport hubs.

One paper we included in our analysis compared the introduction of pathogens by mosquitoes (malaria and dengue) with the introduction of pathogens by infected humans using a model [41]. The introduction of pathogens via infected travelers was shown to be much more likely than through infected arthropods. The conclusion of that paper stated that the spread of mosquito-borne pathogens could not be mitigated using aircraft disinsection alone. On the other hand, disinsection may reduce the threat of vector invasion via aircraft to areas where these mosquitoes did not hitherto exist. Although the importation of infected travelers is likely more frequent than the importation of infected mosquitoes, imported mosquitoes might be much more efficient in spreading the pathogen in the arrival country [41]. Furthermore, imported arthropods such as mosquitoes may also spread drug resistant pathogens [44]. The importation of infected mosquitoes by air is documented as described and is a challenge for many countries [3,5,6,30]. It is not appropriate to compare strategies to reduce travel of infected travelers to disinsection strategies protecting against the spread of arthropods. A greater effort should be invested in the prevention and identification of returning pathogen-infected human travellers.

4.3. Limited toxicity associated with aircraft disinsection

Our systematic review examines evidence both of the toxicity or adverse reactions in passengers and aircrew attributed to the application of chemical insecticides. Although general concerns have been expressed about possible human toxicity of disinsection, we have come across just two reports i.e. one case report and one case series that have documented toxic effects of these procedures in passengers and aircrew. Overall, only one case of anaphylactic reaction due to aircraft disinsection was reported among over 81 million passengers flying back in disinsected aircraft to their home country Australia in 2018, not counting the global, large number of exposed passengers and aircrew [45]. No case of asthmatic reactions due to application of synthetic pyrethroids has been reported in the aircraft setting. In background papers describing other non-aircraft environments, we found one report of a child who suffered a fatal allergic reaction when she applied a pyrethroid (0.2% concentration) containing shampoo on her dog [46]. Again in 2000, a case of a non-asthmatic person, an insect control worker, is described who became sensitized after exposure to tetramethrin. While having strong reactions by being exposed to insecticide spraying he had to change his job [47]. Aerosolized pesticides could trigger a non-specific asthmatic response as documented by the WHO [12]. WHO does not rule out a possibility of an asthma attack after the contact with pyrethrin but indicates a low health risk related to modern pyrethroid exposure [18].

A review about the safety of pyrethroids for public health use was published by WHO in 2005 where pyrethroids are described as insecticides with moderate acute toxicity and no evidence for long-term toxicity in humans. Permethrin was evaluated several times by the FAO/WHO and WHO/IPCS (1979, 1987, 1999, 2002, 2013), and reviewed by the US EPA in 2006, 2007 and 2009 [48]. In 2013, an IPCS report on the risk assessment of aircraft disinsection was published by WHO. The extrapolated results showed a 25–50% lower exposure of passengers and aircrew to insecticides than the accepted safety threshold for the substances permethrin and d-phenothrin. This might only be correct if the insecticides are used as recommended [14]. One case series and one uncontrolled experimental study of documented occupational illness could be found in our literature research. Symptoms as fatigue, dizziness and skin irritations could be found in both papers. He et al. (1989) suggests that only paresthesia could clearly be attributed to exposure to pyrethroids. Nausea, headache and dizziness could rather be induced by organic solvents [49].

Berger-Preiss et al. mentioned a significant number of reports, which were filled out by flight attendants or by airlines personnel describing symptoms in aircrew and passengers after in-flight spraying [17]. According to Murawski [19], government agencies, labor unions, airlines and environmental groups have received reports of occupational illness from passengers and aircrew caused by aircraft disinsection. Symptoms like rashes as well as anaphylaxis were reported [19]. These reports were never published in the scientific literature [17] for unknown reasons. Due to several complaints of aircrew and passengers the U.S. department of transportation appealed to more than 20 different governments to discontinue disinsection methods with chemical insecticides [24]. According to the review of WHO 2005, there is an unproblematic recovery from an acute occupational exposure with pyrethroids, which is without any lasting health sequelae. Pyrethroids do not accumulate in the human body [18].

Elevated urine levels of metabolites of insecticides after the exposure to pyrethroids were documented, but no correlates of the levels of urinary metabolites and toxic effects could be found. The post-disinsection duration (time between disinsection date and flight date/exposure date) has a significant impact on the urinary metabolite levels. The longer the interval between the time of disinsection and the time of working in the disinsected plane, the lower were the levels of urinary metabolites measured [26]. The documented half-life of permethrin in the human body is 12.3 h in the plasma and 9–23 h in neuronal tissue. Permethrin may persist in fatty tissue with a half-life time of 4–5 days in body fat and brain [50,51]. No correlation could be found between body burden and the amount of pesticide sprayed. No evaluation of symptoms took place related to the higher body burden of the metabolites. One study has recommended more frequent use of less concentrated insecticide formulations in the residual treatment of aircraft [26]. This systematic review showed that there are specific methods used and recommended by WHO which result in a lower exposure or concentration of insecticides compared to others.

4.4. Strength and limitations

A strength of our paper is the wide range of screened databases and WHO documentation and adherence to PRISMA guidelines. A limitation is the paucity of papers addressing the topic of synthetic pyrethroid aircraft disinsection and their effect on humans. There were many articles about older aircraft disinsection strategies but our remit was to focus on aircraft disinsection with permethrin and d-phenothrin and the safety and effectiveness of these currently used products. Only a small number of case reports and case series describing toxicity due to aircraft disinsection procedures could be found, which was unexpected considering the millions of exposed passengers and crews. Mention of possible toxicity reported by government agencies, labour unions, airlines and environmental groups which are not published in scientific literature could not be included [17,19] and this may be a bias, but we referred to these reports in our discussion. A selection bias may be our inclusion only of studies published in English, French or German languages. Another limitation is that the studies we could find, did not or could not correlate pesticide exposure, body burden of pesticides or amount of urinary pesticide metabolites to possible toxicity. No studies were found that showed evaluated plasma levels after exposure to pesticide spraying in aircraft.

5. Conclusion

Our review found that the synthetic pyrethroids permethrin and d-phenothrin are very effective insecticides when used for aircraft disinsection, regardless of the application method used. Our analysis confirmed that disease vectors are carried on international flights and pose threats particularly to the island populations and airport hubs. All recommended insecticide spraying methods were identified as being particularly effective against vectors but disinsection treatment of aircraft in the absence of crew and passengers was more acceptable. Elevated urinary levels of metabolites of pesticides after the exposure with permethrin was observed but could not be linked to adverse health outcomes. Despite large numbers of exposures, we identified few cases of reported toxicity, including an allergic reaction in one passenger, attributed to aircraft disinsection, and a case series describing diverse health issues that fit the definition of work-related pesticide exposure in 12 flight attendants. We found no evidence of an association between repetitive aircrew exposure to insecticide and negative health impact. More research is needed to clarify the pathways of the international spread of vectors and vector-borne pathogens, the range of vectors carried in aircraft and alternative, non-chemical methods for disinsection.

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Declaration of competing interest

None of the authors report any conflicts of interest with this paper. Carmen Dolea, Corrine Poncé, Rajpal Yadav and Raman Velayudhan are WHO employees. Andrea Grout is a retired airline crew member.

Appendix 1

Electronic database searching (last search on 27.11.18)

1.) PubMed/Medline: “disinsection” searched in all fields retrieved 60 hits, “disinsection AND airplane/plane/aviation/aircraft” 40, “disinsection plane/aircraft” AND “d-phenothrin” 5, “permethrin” 5, “insecticide” 29, “Pre-flight/preflight” 3, “top-of-descent” 3, “residual” 5, “safety” 4, “toxicity” 5, “landing regulation” 1, “pacific islands” 3, “passengers” 8, “cabin crew” 2, “insects” 16, “mosquito” 11, “arthropods” 9, “malaria” 5, “dengue” 2, “mosquito borne infections” 1, “airline regulation” 0, “Australia” 2, “New Zealand” 1, “wind curtains method” 0, “new methods” 6. “Airplane/Plane/aviation/aircraft/airline” AND “insecticide” AND “d-phenothrin” 6, “permethrin” 13, “safety” 6, “toxicity” 43.Disinsection plane/aircraft cross-referenced with each of these terms resulted in 238 relevant hits.

2.) Medline: “disinsection” searched in all fields retrieved 60 hits, “disinsection AND airplane/plane/aviation/aircraft” 40, “disinsection plane/aircraft” AND “d-phenothrin” 2, “permethrin” 5, “insecticide” 26, “Pre-flight/preflight” 1, “top-of-descent” 3, “residual” 5, “safety” 3, “toxicity” 5, “landing regulation” 0, “pacific islands” 0, “passengers” 1, “cabin crew” 3, “insects” 21, “mosquito” 4, “arthropods” 0, “malaria” 2, “dengue” 0, “mosquito borne infections” 1, “airline regulation” 0, “Australia” 1, “New Zealand” 0, “wind curtains method” 0, “new methods” 1. “Airplane/Plane/aviation/aircraft/airline” AND “insecticide” AND “d-phenothrin” 2, “permethrin” 6, “safety” 9, “toxicity” 20.Disinsection plane/aircraft cross-referenced with each of these terms resulted in 54 relevant hits.

3.) EMBASE: “disinsection” searched in all fields retrieved 71 hits, “disinsection AND airplane/plane/aviation/aircraft” 44, “disinsection plane/aircraft” AND “d-phenothrin” 3, “permethrin” 8, “insecticide” 21, “Pre-flight/preflight” 1, “top-of-descent” 1, “residual” 6, “safety” 6, “toxicity” 8, “landing regulation” 0, “pacific islands” 0, “passengers” 5, “cabin crew” 3, “insects” 8, “mosquito” 11, “arthropods” 0, “malaria” 6, “dengue” 3, “mosquito borne infections” 0, “airline regulation” 0, “Australia” 2, “New Zealand” 1, “wind curtains method” 0, “new methods” 5. “Airplane/Plane/aviation/aircraft/airline” AND “insecticide” AND “d-phenothrin” 77, “permethrin” 14, “safety” 15, “toxicity” 38.Disinsection plane/aircraft cross-referenced with each of these terms resulted in 33 relevant hits.

4.) Scopus: “disinsection” searched in all fields retrieved 87 hits, “disinsection AND airplane/plane/aviation/aircraft” 50, “disinsection plane/aircraft” AND “d-phenothrin” 3, “permethrin” 10, “insecticide” 30, “Pre-flight/preflight” 1, “top-of-descent” 4, “residual” 6, “safety” 6, “toxicity” 2, “landing regulation” 0, “pacific islands” 0, “passengers” 15, “cabin crew” 3, “insects” 23, “mosquito” 15, “arthropods” 4, “malaria” 6, “dengue” 3, “mosquito borne infections” 0, “airline regulation” 1, “Australia” 2, “New Zealand” 2, “wind curtains method” 0, “new methods” 4. “Airplane/Plane/aviation/aircraft/airline” AND “insecticide” AND “d-phenothrin” 2, “permethrin” 13, “safety” 11, “toxicity” 14.Disinsection plane/aircraft cross-referenced with each of these terms resulted in 70 relevant hits.

5.) CINAHL: “disinsection” searched in all fields retrieved 3 hits, “disinsection AND airplane/plane/aviation/aircraft” 2, “disinsection plane/aircraft” AND “d-phenothrin” 1, “permethrin” 1, “insecticide” 0, “Pre-flight/preflight” 0, “top-of-descent” 0, “residual” 6, “safety” 6, “toxicity” 2, “landing regulation” 0, “pacific islands” 0, “passengers” 1, “cabin crew” 0, “insects” 0, “mosquito” 0, “arthropods” 0, “malaria” 1, “dengue” 0, “mosquito borne infections” 0, “airline regulation” 0, “Australia” 0, “New Zealand” 0, “wind curtains method” 0, “new methods” 0. “Airplane/Plane/aviation/aircraft/airline” AND “insecticide” AND “d-phenothrin” 2, “permethrin” 2, “safety” 1, “toxicity” 3.Disinsection plane/aircraft cross-referenced with each of these terms resulted in 3 relevant hits.

From the eligible 149 full-text articles, 25 provide original research data on the subject of disinsection of aircraft, applicability and safety.

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