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TECHNICAL REPORT

Risk assessment guidelines for infectious diseases transmitted on aircraft

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This report was commissioned by the European Centre for Disease Prevention and Control (ECDC), coordinated by Katrin Leitmeyer at ECDC, and produced by Robert Koch Institute, Berlin, Germany.

Authors and main contributors

Karl Schenkel, Rahel Amorosa, Inge Mücke, Valentina Dias-Ferrao, Michaela Diercke, Katrin Leitmeyer, Gérard Krause, Tim Eckmanns

Contributors

Preben Aavitsland
Franz Allerberger
Paulo M. Alves
Peter Andersen
Thomas Bettes
Dounia Bitar
Bonita Brodhun
Udo Buchholz
Silke Buda
Neville Byrne
Marty Cetron
Jacques Chemardin
Miguel Dávila Cornejo
Annette Dietrich
Suzanne Cotter
Susan Courage
Roel Coutinho
Agnes Csohan
Jean-Claude Desenclos
Jozef Dlhý
Anou Dreyfus
Sabine Erne
Anthony Evans
Christina Frank
David Gamper
Helen Giamarella
Miguel Mínguez Gonzalo
Rene Gottschalk
Walter Haas
Danielle Hansen-Koenig
Wiebke Hellenbrand
Pierrette Huberty-Krau
Ansa Jordaan
Irena Klavs
Jan Klika
Judith Koch
Henry Kong
Ichiro Kurane
Kuulo Kutsar
Irina Lucenko
Tomohiko Makino
Patrick Mathys
Karen Marineau
Tanya Melillo Fenech
Kore Molbak
Maria Jose Sierra Moros
Ion Morrison
Howard Njoo
Joan O'Donnell
Darina O'Flanagan
Rose Ong
Maria Teresa
Avilez Paixao
Androula Pavli
Gabriele Poggensee
Jelena Rjabinina
Petri Ruutu
Daniel Sagebiehl
Stefania Salmaso
Kirsten Schubert
Anette Siedler
René Snacken
Gianfranco Spiteri
Klaus Stark
Robert Steffen
Arnaud Tarantola
Claude Thibeault
Thomas Tsang
Rolanda Valinteliene
Anneke van den Hoek
Cliff Webster
Brita Winje
Anne Witschi

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Contents

Abbreviations

ACI	Airport Council International
AFB	Acid-fast fast bacilli
APU	Auxiliary power unit (in passenger aircraft)
BCG	Bacille Calmette-Guérin
CDC	Centers for Disease Control and Prevention, Atlanta, Georgia, USA
CT	Contact tracing
DZK	German Central Committee against Tuberculosis
ECDC	European Centre for Disease Prevention and Control, Stockholm, Sweden
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
HEPA filter	High-efficiency particulate air filter (in passenger aircraft cabins)
HNIG	Human normal immunoglobulin
HPA	Health Protection Agency, UK
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization
IHR (2005)	International Health Regulations (year of becoming operative)
MDR TB	Multidrug-resistant tuberculosis; defined as resistance to at least isoniazid and rifampin
PEP	Post-exposure prophylaxis
PH	Public health
RKI	Robert Koch Institute, Berlin, Germany
SARS	Severe Acute Respiratory Syndrome
TB	Tuberculosis
TST	Tuberculin skin test
VHF	Viral haemorrhagic fever
WHO	World Health Organization
XDR TB	Extensively drug-resistant tuberculosis; resistance to at least isoniazid and rifampin (i.e. multidrug-resistant TB or MDR-TB) plus resistance to any fluoroquinolones and any one of the second-line anti-TB injectable drugs: amikacin, kanamycin or capreomycin

Introductory remarks by ECDC

In order to assist national authorities in Member States in the assessment of risks associated with the transmission of various infectious agents onboard airplanes, ECDC commissioned the production of an initial set of guidelines on infectious diseases and their transmission onboard aircraft. The guidelines presented here provide a comprehensive overview of the available evidence in this field and are based on a systematic review of scientific literature, disease-specific guidance material, and expert opinions. They provide an excellent basis for Member States to individually assess in-flight transmission events.

ECDC and the authors would like to point out that for some of the diseases covered in this guidance document, little event-based evidence of transmission exists. Consequently, these guidelines prefer to err on the safe side and therefore frequently recommend contact tracing.

In June 2009, ECDC will facilitate a technical expert workshop entitled 'Risk assessment guidelines for diseases transmitted on airplanes'. This workshop aims to critically review the compiled evidence and provide operational guidance for an evidence-based risk assessment, to be issued as an 'expert opinion'. In this first ECDC workshop on in-flight disease transmission, the following diseases/disease groups (as prioritised by ECDC's Advisory Forum) will be addressed: tuberculosis, meningococcal infections, and new airborne diseases such as SARS or new influenza strains. Further workshops on this topic are scheduled.

Executive summary

National and international commercial air travel has seen a steady increase in passenger numbers over the last years. International airports welcome millions of passengers every day, allowing individuals to travel around the globe in hours. At the same time, changing travel habits may give rise to new threats: in the closed cabin environment of modern airplanes, passengers may be exposed to various infectious diseases that afflict their fellow passengers.

The emergence of SARS in 2003 demonstrated the potential of a new disease to suddenly appear and spread globally via air travel. The early detection of infectious diseases on board aircraft, in conjunction with timely risk assessment, is crucial when initiating a public health response. When a public health risk is detected, contact tracing passengers who were exposed during a flight is an essential step towards containment — and a major challenge to public health experts worldwide.

RAGIDA ('risk assessment guidelines for infectious diseases transmitted on aircraft') combines evidence retrieved from scientific literature with expert knowledge in order to provide viable options for decision makers. RAGIDA can provide valuable help when determining triggers and when faced with having to make a decision on whether to contact trace air travellers and crew that were exposed to infectious diseases during a flight.

For the RAGIDA project, experts from Robert Koch Institute and ECDC agreed on 12 diseases: TB, influenza, SARS, meningococcal disease, measles, rubella, diphtheria, Ebola haemorrhagic fever, Marburg haemorrhagic fever, Lassa fever, smallpox, and anthrax. Over 3 700 peer-reviewed articles and grey literature sources were systematically reviewed in order to evaluate the exact circumstances that led to the transmission of these infectious diseases on board aircraft. In addition, we systematically searched guidelines on risk assessment and risk management of these infectious diseases from international aviation boards and national or international public health agencies. For additional input, 73 experts from 38 countries were contacted and asked for advice.

Our systematic literature search suggests that TB, influenza, SARS, meningococcal disease and measles are relatively frequently transmitted on board of airplanes. However, the number of articles reporting confirmed on-board transmission for any of these diseases was surprisingly low, especially when considering the large number of potential contacts. In the light of these results, the total number of events with on-board transmission is probably also quite low. Although it is difficult to draw any conclusions on the number of infections arising through on-board transmission, it seems likely that the potential for spreading infectious diseases on board is not higher than on the ground.

All in all, we remain convinced that risk assessment and the decision for contact tracing should be specific for each event and take into account factors such as the potential for epidemiological spread, infectivity and pathogenicity of index patients, functionality of on-board ventilation systems, intensity of contacts, and seating details — as suggested in this technical report.

1 Introduction

The recommendations given in this document are based on evidence from three sources: a systematic literature search, expert opinions, and established disease-specific parameters (e.g. incubation period, period of shedding, etc.). For some diseases, event-based evidence was poor or completely lacking, since there are no or only a few publications available concerning these diseases. In such cases (and to be on the safe side), we frequently opted for a comprehensive approach, i.e. contact tracing (CT). We are aware that contact tracing is not always feasible and may absorb a substantial amount of human and financial resources. Therefore, public health experts in charge of contact tracing should consider the algorithms in this document merely as a point of reference and not as a binding recommendation. Prior to making the decision to initiate contact tracing, clinicians or epidemiologist should take into account that the algorithms provided in this document cannot cover every aspect or factor, e.g. the epidemiological situation in the country of origin, the destination of a flight, the susceptibility of the affected passengers, vaccine coverage, pathogen type/subtype, and antibiotic resistance. The 'Question and answer (Q&A) sheets for contact tracing' (see Annex 1) provided in this document are intended to assist public health experts with the decision-making process.

This document focuses exclusively on the transmission of infectious diseases on airplanes. However, a more comprehensive risk assessment should also examine the possible transmission of diseases in airports and during airport transfers.

1.1 Background information

Over the last years, national and international commercial air travel has seen a steady increase in passenger numbers. Passenger forecasts by the International Air Transport Association (IATA) are predicting an increase of global commercial air traffic of + 3.0 % for 2009 [1]. International airports collectively welcome millions of passengers on a daily basis: in 2006, 4.4 billion people arrived at and departed from the world's airports. Long-term traffic forecasts predict that by 2025 this number will double to over nine billion passengers a year [2].

Passengers travelling on airplanes in a closed cabin environment may be exposed to infectious diseases afflicting fellow passengers. Contact tracing of passengers who were exposed during flight increasingly challenges public health experts worldwide.

The emergence of SARS illustrated a new disease's potential to suddenly appear and spread, threatening the health, economic well-being and social life of many people, including EU citizens. Early recognition of diseases and appropriate risk assessment is essential in order to initiate the most appropriate public health response when passengers and/or crew members become exposed to an infectious or potentially infectious passenger during a flight.

1.2 Aircraft ventilation and cabin air quality

The environmental control systems in modern passenger aircraft control the pressurisation, oxygen level, humidity and filtration of air in the passenger cabin. During flight, the cabin represents a closed environment that exposes passengers to environmental conditions different from those on ground: hypobaric hypoxia, relative low humidity and relative proximity to fellow passengers are tributes paid to the technical and economical necessities of flying. During flight, fresh air is usually supplied to the cabin from the outside through the intake of air by the aircraft engines. The outside air at flying altitude can be regarded as sterile, as it contains hardly any microorganisms and is heated by the aircraft engines to over 250 degrees Celsius [3]. The majority of modern passenger aircraft re-circulate about 50 % of the cabin air back into the cabin (see Figure 1). 85 % of the current American fleet of passenger planes carrying more than 100 passengers are re-circulating air [4]. The re-circulated air is usually filtered through high-efficiency particulate filter systems (HEPA) before re-entering the cabin [5]. In general, proper ventilation within confined spaces such as the cabin reduces the load of pathogens, and one air exchange removes about 63 % of airborne organisms [6,7]. Normally, cabin air exchange rates are 15–20 air changes/hour, while European-built aircraft have lower exchange rates of about 10 air changes/hour. In comparison, offices and private homes have exchange rates of 12 air changes/hour and five air changes/hour, respectively. [3] Aircraft built before 1980 and aircraft seating less than 100 passengers are often not equipped with HEPA systems.

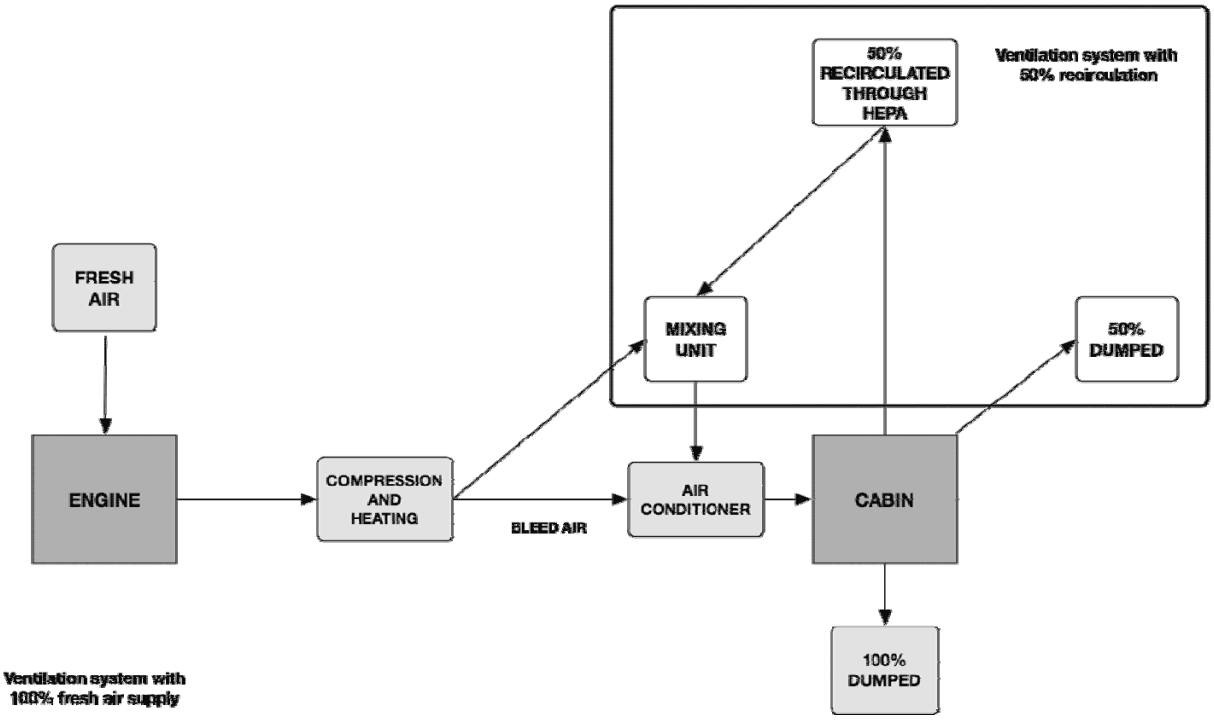
While the engine is off, e.g. during ground delay or while boarding, there are several ways in which air is supplied to the cabin. An air conditioning unit can be connected to the aircraft ventilation system and supply air from a preconditioned air source. Alternatively, a ground pneumatic source provides air, which is then conditioned and

distributed via the aircraft environmental control system. A third method to provide air to the cabin is by operating the aircraft ventilation system with energy supplied by an auxiliary power unit.

The least favourable method is to allow cross ventilation through the open aircraft doors [8,9]. This will distribute possibly harmful air pollutants such as pathogens throughout the cabin.

How important the ventilation system is was demonstrated by one incident in which passengers remained on board during a four-hour ground delay, with closed doors and no operating ventilation system. This contributed to an influenza outbreak among the passengers on board [10]. WHO therefore recommends that passengers should not be left on board longer than 30 minutes in an aircraft without proper ventilation [11].

Figure 1. Ventilation systems in aircraft



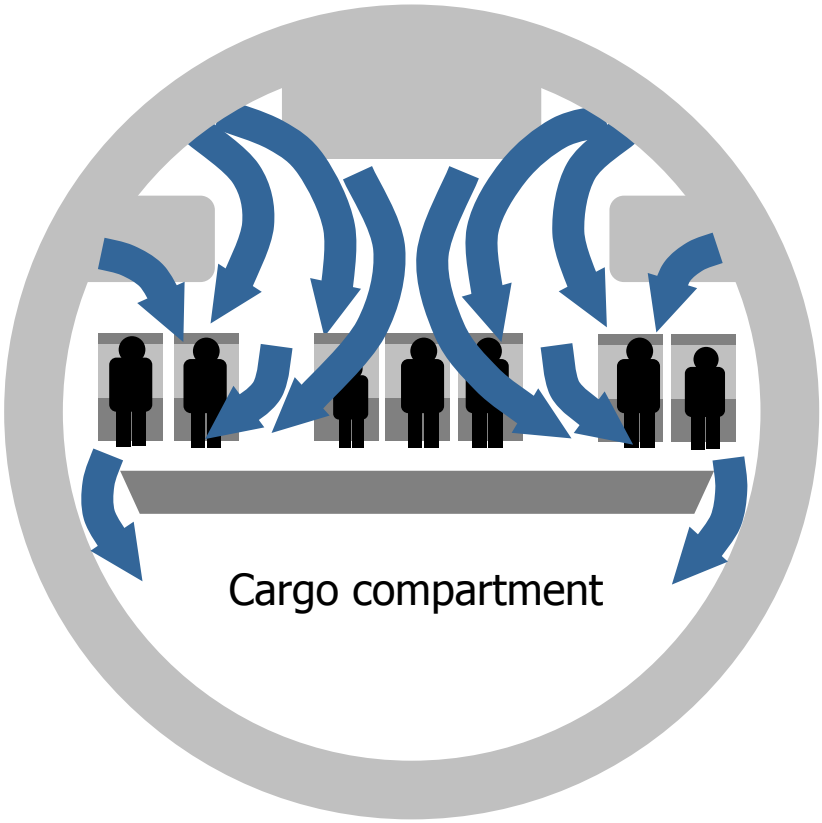
Source: Robert Koch Institute, Berlin

The air supplied to the cabin enters the cabin from overhead through outlets throughout the entire cabin, then flows downward towards outflow valves close to the floor, as shown in Figure 2 [8,12].

This divides the plane into ventilation zones in which air movement is mainly transverse. This system of distribution limits the number of seating rows sharing the same air before it gets evacuated or recirculated [13].

Understanding the ventilation system is of importance, not only for better risk assessment, but also because the WHO guidelines base their definition of 'close contact' on the zones created by the ventilation pattern. WHO recommends tracing passengers sitting +/- 2 rows from the index case.

Figure 2. **Cabin airflow**



Source: Illustration by ECDC, based on: WHO: Tuberculosis and air travel: Guidelines for prevention and control [8]

1.3 Legal and regulatory issues

The need for a timely risk assessment of infectious disease incidents with a possible public health impact has been expressed through several international legal regulations.

EU Decision 2119

According to this EU decision, Member States `… must provide information on communicable diseases through the appropriate designated structures and/or authorities, in accordance with Article 4 of Decision No 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community (3), which requires timely scientific analysis in order for effective Community action to be undertaken'.

International Health Regulations (IHR 2005)

On 15 June 2007, the International Health Regulations (2005) (IHR 2005) came into effect. This legally-binding agreement provides a new framework for the coordination and management of events that may constitute a public health emergency of international concern. It is meant to improve the capacity of all countries to detect, assess, notify and respond to public health threats.

Under IHR (2005), all WHO member states are expected to strengthen their public health capacities at designated airports, ports and ground crossings, both in routine circumstances and when responding to events that may constitute a public health emergency of international concern (PHEIC).

Articles 18 and 23 of the IHR 2005 address health measures regarding international air travel, including the necessity for contact tracing (CT) on the arrival or departure of international travellers. In Article 45, the treatment of personal data in the context of contact tracing is regulated. (The text of Articles 18, 23 and 45 IHR is quoted below).

'Article 18. Recommendations with respect to persons, baggage, cargo, containers, conveyances, goods and postal parcels

1. Recommendations issued by WHO to States Parties with respect to persons may include the following advice:

- no specific health measures are advised;
- review travel history in affected areas;
- review proof of medical examination and any laboratory analysis;
- require medical examinations;
- review proof of vaccination or other prophylaxis;
- require vaccination or other prophylaxis;
- place suspect persons under public health observation;
- implement quarantine or other health measures for suspect persons;
- implement isolation and treatment where necessary of affected persons;
- implement tracing of contacts of suspect or affected persons;
- refuse entry of suspect and affected persons;
- refuse entry of unaffected persons to affected areas; and
- implement exit screening and/or restrictions on persons from affected areas.'

'Article 23. Health measures on arrival and departure

1. Subject to applicable international agreements and relevant articles of these Regulations, a State Party may require for public health purposes, on arrival or departure:

(a) with regard to travellers:
  (i) information concerning the traveller's destination so that the traveller may be contacted;
  (ii) information concerning the traveller's itinerary to ascertain if there was any travel in or near an affected area or other possible contacts with infection or contamination prior to arrival, as well as review of the traveller's health documents if they are required under these Regulations; and/or
  (iii) a non-invasive medical examination which is the least intrusive examination that would achieve the public health objective;
(b) inspection of baggage, cargo, containers, conveyances, goods, postal parcels and human remains.

2. On the basis of evidence of a public health risk obtained through the measures provided in paragraph 1 of this Article, or through other means, States Parties may apply additional health measures, in accordance with these Regulations, in particular, with regard to a suspect or affected traveller, on a case-by-case basis, the least intrusive and invasive medical examination that would achieve the public health objective of preventing the international spread of disease.

3. No medical examination, vaccination, prophylaxis or health measure under these Regulations shall be carried out on travellers without their prior express informed consent or that of their parents or guardians, except as provided in paragraph 2 of Article 31, and in accordance with the law and international obligations of the State Party.

4. Travellers to be vaccinated or offered prophylaxis pursuant to these Regulations, or their parents or guardians, shall be informed of any risk associated with vaccination or with non-vaccination and with the use or non-use of prophylaxis in accordance with the law and international obligations of the State Party. States Parties shall inform medical practitioners of these requirements in accordance with the law of the State Party.

5. Any medical examination, medical procedure, vaccination or other prophylaxis which involves a risk of disease transmission shall only be performed on, or administered to, a traveller in accordance with established national or international safety guidelines and standards so as to minimise such a risk.'

'Article 45. Treatment of personal data

1. Health information collected or received by a State Party pursuant to these Regulations from another State Party or from WHO which refers to an identified or identifiable person shall be kept confidential and processed anonymously as required by national law.

2. Notwithstanding paragraph 1, States Parties may disclose and process personal data where essential for the purposes of assessing and managing a public health risk, but States Parties, in accordance with national law, and WHO must ensure that the personal data are:

(a) processed fairly and lawfully, and not further processed in a way incompatible with that purpose;
(b) adequate, relevant and not excessive in relation to that purpose;

(c) accurate and, where necessary, kept up to date; every reasonable step must be taken to ensure that data which are inaccurate or incomplete are erased or rectified; and
(d) not kept longer than necessary.

3. Upon request, WHO shall as far as practicable provide an individual with his or her personal data referred to in this Article in an intelligible form, without undue delay or expense and, when necessary, allow for correction.'

1.4 Objectives of the RAGIDA guidelines

The aim of these guidelines (RAGIDA: risk assessment guidelines for infectious diseases transmitted on aircraft) is to develop recommendations that assist EU Member States in the evaluation of risks related to the transmission of various infectious agents on board of aircraft and advise on appropriate public health measures for containment. The recommendations are intended to assist national public health authorities when determining triggers and making decisions on whether or not to contact trace air travellers and crew in case of exposure.

2 Methodology

Our aim was to gather as much information as possible on the likelihood of infectious diseases being transmitted during air travel. This information is essential when assisting Member States in case-to-case risk assessments or making recommendations regarding triggers for contact tracing. We obtained information through the following sources:

- a systematic literature review of the peer-reviewed literature;
- a systematic request and search of grey literature;
- standardised interviews with public health experts at EU public health agencies and on aviation boards; and
- a compilation of pathogen-specific epidemiological attributes such as incubation period, shedding, etc.

We also consulted our in-house experts on the respective pathogens and discussed these results and recommendations for contact tracing and risk assessment.

2.1 Disease selection

We identified several diseases relevant for transmission during air travel, using the following categories/criteria:

- potential transmissibility in the context of air travel (sexually transmitted diseases were excluded);
- person-to-person transmissibility;
- outbreak potential;
- pathogenicity;
- likelihood of starting a new transmission cycle when imported to the EU (if newly introduced);
- ability and justification for disease containment; and
- the frequency of mentionings in peer-reviewed literature obtained through a preliminary literature search.

Diseases were selected by calculating an accumulated score for all seven categories. The resulting disease list was ranked according to priority, with the high-priority diseases at the top of the list:

- TB, including MDR and XDR TB
- SARS
- Influenza, including new subtype influenza
- Measles
- Rubella
- Meningococcal disease
- Diphtheria
- Ebola haemorrhaegic fever
- Marburg haemorrhaegic fever
- Lassa fever
- Smallpox
- Anthrax

During a meeting with ECDC experts in February 2007, we agreed to not include food- and vectorborne pathogens.

2.2 Survey on the relevance of contact tracing for selected diseases

Using a 'quick-and-dirty' approach, we asked national public health experts from EU Member States for their personal opinions on the necessity of contact tracing for selected pathogens/diseases (3.1–3.12) and analysed their input separately.

2.3 Event search

Literature search

According to our definition, an 'event' is 'an incident in which transmission of an infectious disease from one or more index cases to contact person/s during air travel has been suspected, proven or ruled out'. Case-based information for events was obtained systematically from:

- a systematic literature search of peer-reviewed literature; and
- ProMed and non peer-reviewed literature obtained from public health experts and aviation board experts.

Literature databases searched for internationally published, peer-reviewed publications were Pubmed and DIMDI (the latter includes Medline, Global Health, Embase, Biosis Previews, Embase Alert SciSearch, Cochrane CDSR, and Cochrane CDTR).

Search terms for peer-reviewed literature were:

- (aircraft OR airplane OR flight OR flight crew OR air travel OR airline OR air passenger)

AND

- (epidemiology OR microbiology OR transmission)

In another search, we used the terms:

- (aircraft OR airplane OR flight OR flight crew OR air travel OR airline OR air passenger)

AND

- (infectious)

In a second step, we identified articles relevant to air-travel-related events that met our event definition by assessing title and abstract of each article yielded by the literature search.

We searched ProMed-based grey literature for air-travel-related events and systematically asked state epidemiologists to send us non-peer-reviewed literature or non-published notes related to events according to our case definition. For the ProMed search, terms used were 'airline' Or 'air travel' Or 'air passenger'.

Additionally, we systematically approached public health experts in EU countries, Japan, Hong Kong, the US, Canada and medical experts on major international aviation boards in order to acquire grey literature or notes of events involving infectious persons on board passenger aircraft.

Public health and civil aviation expert interviews

We designed a standardised questionnaire including more than 50 variables in order to systematically assess case-based information on events (see Annex 1). This questionnaire was used to interview national and international experts who regularly perform contract tracing (CT) or are otherwise involved in CT, risk assessment, or the development of guidelines.

We also conducted telephone interviews with experts that had consented to participate.

Analysis of event articles

We systematically analysed articles on events that were obtained from the peer-reviewed literature, grey literature, and expert interviews, using the categories established in our standardised questionnaire (see Annex 1). Consequently, every event article was reviewed for information taking into account more than 50 variables (Annexes 1 and 2).

The following key questions have been extracted from our questionnaire. Annotations were added for further explanation. The complete list of questions is given in Annex 1.

Key questions for contact tracing

1. Flight details and key information of event

Initial year of the event: ___

The year is used to identify the event in our analysis, but also provides information on historical facts, such as the time period between event and the implementation of guidelines, or the technical standard of the aircraft. If available, the exact date of an event should be noted as well.

Disease/pathogen found: ___

This information is crucial. Transmissibility, severity, public health threat, and necessity for action are all entirely dependent on disease/pathogen information.

Flight origin and destination: ___

The origin of the flight can provide information on the epidemiology of the suspected disease and can be used to obtain information regarding possible outbreaks in the originating country.

The country from which the flight originated should be informed of a possible public health threat if the index patient contracted the disease in the country or was already infectious prior to the flight.

The destination of the flight is important to alert public health authorities of possible public health threats and allows authorities to take further action. For our analysis, both variables provided us with a way to identify, and differentiate between, different events.

Total number of contacts/successfully traced contacts/crew members: ___

We identified the following flight and passenger information as indispensable:

- number of total passengers and crew on board;
- number of index cases (passenger/crew?);
- seating details (contacts' seat locations in relation to index case);
- number of contacts traced (passenger/crew?); and
- number of contacts successfully traced (passenger/crew).

The evidence for transmission on board depends on the number of successfully traced passengers. The more comprehensive the contact tracing, the less likely the possibility of missing infected contacts. The same is true for the evidence of non-infection: the possibility of missing infected contacts decreases with the proportion of successfully traced passengers

Flight duration: ___

The flight time is equivalent to the exposure time for fellow passengers and therefore important for estimating the risk of on-board transmission. 'Total flight duration' is defined as the combination of the period after boarding (including any ground delays), the actual flight time, and any ground delays after landing. When assessing the need for contact tracing, some guidelines specify a minimum flight duration. The WHO guideline on transmission of tuberculosis during air travel recommends contact tracing for flights that are eight hours or longer.

Major ground delays (hours): ___

Ground delays prolong the time during which passengers are exposed to an infectious person. Due to possibly altered ventilation conditions during ground time (when engines are generally off), the risk of disease transmission might multiply.

High-efficiency particulate air (HEPA) system fully functional during flight time: ___

Modern passenger aircraft are usually equipped with HEPA filter systems that filter recirculated cabin air as long as the engines or an auxiliary power source are running. About 99.97 % of particles > 0.3 ìm, including the majority of microbiological pathogens, are eliminated from the cabin air by these systems. Even viruses smaller than 0.3 ìm which tend to adhere to particles or form clumps are eliminated. In theory, non-functional or turned off HEPA filter systems may increase the risk of pathogen distribution throughout the cabin via the ventilation system.

2. Questions concerning contact tracing (CT) procedures

Most of the following questions are relevant for gathering information on the initiation, process, and outcome of contact tracing (CT) performed in different settings and involving different pathogens.

Country initiating CT: ___

How many seat rows before/after the index patient were considered for CT? ___

Comprehensive CT (entire passenger list traced)? ___

Cabin crew members contacted? ___

Were CT contact categories used? If so, which categories? Proximity of the contacts to the index cases: ___

A passenger's physical proximity to the index case is important when assessing the risk. If categories (such as 'close contact') are established, they can be combined with a specific priority level when tracing passengers. For scientific purposes, differentiating between contacts that were confirmed as infected (but asymptomatic) and contacts that were confirmed as infected *and* symptomatic can be useful.

CT method:

- Passenger manifest used for CT?
- Passenger locator card used for CT?
- Customs declaration used for CT?

Method of contacting passengers:

- Questionnaire used for CT?
- Telephone contacting used for CT?
- Other methods used for CT? (Please specify!)

3. Questions concerning the index patient/s

Age and gender: ___

Since certain diseases take a more severe course in different age groups or genders, age and gender are important epidemiological parameters for risk assessment. Other important factors (such as the spread of pathogens through coughing) can be influenced by age.

Nationality or country of residence: ___

The nationality is of importance in order to inform the health authorities of the country of origin, to conduct contact tracing if needed, and to inform the family. Moreover, the country of residence can provide valuable clues on the prevalence of a disease or the frequency of vaccination.

Symptoms of the index patient: ___

Information on the presence of symptoms is crucial in order to estimate the infectiousness of an index patient during flight. In addition, the number of contacts can vary, e.g. diarrhoea can lead to contact tracing of every passenger that used, or had access to, the lavatory (e.g. passengers, crew or cleaning personnel).

Level of infectiousness of the index case during the flight: ___

The index case's level of infectiousness should be evaluated based on all available information: the signs and symptoms of the index case, the stage of the disease, potential shedding, and the mode of transmission.

4. Information about actions taken

Actions may include:

- structured telephone interview with contacts;
- post-exposure prophylaxis (PEP) (recommended for all contact persons?); and
- if PEP was administered, exact information on how many contact persons actually received PEP.

Assessment of events, event articles, and entry in database

We assessed the event articles obtained from the literature search and expert interviews according to previously defined assessment criteria/definitions that had been set in order to systematically make use of the information. In the context of this study, the assessment criteria were defined as follows:

Index case/s

Person or persons identified as the initial case/s reported in a chain of infection, or single case with no known secondary cases. According to our definition, the index case/s represent/s the starting point for the process of contact tracing and may or may not have infected other persons (contacts).

Contact

Person with relevant exposure to an infectious or potentially infectious index case. The relevancy of exposure is assessed and described by referring to event-specific factors such as pathogen, infectiousness of index case, infectious period, availability and validity of information on on-board exposure, possible alternative exposures, risk factors for infection, vaccination status, and susceptibility of contacts.

Successfully traced contacts

The term 'successfully traced contacts' is used for contacts with clear evidence of infection/non-infection, e.g. laboratory evidence or clinical diagnosis. If laboratory tests were not available, the absence of symptoms after two incubation periods is considered as evidence of non-infection.

Technical information on contact tracing

Contact tracing (CT) is an investigation procedure aimed at acquiring contact information in order to approach contacts that were potentially exposed to pathogens. CT can be comprehensive (contacting all passengers and crew) or follow a more restrained approach: passengers will only be contacted when they meet certain criteria as published in existing guidelines, e.g. defined contact categories (close contact = +/- 2 rows in front of/behind the index case; highly exposed contact = coughed or sneezed at).

Event

An incident during which the transmission of an infectious disease from one or more index cases to contact person/s during air travel has been suspected, proven or ruled out.

Number of events: Generally, each flight is counted as one event. In the event dataset, flights are counted separately when the number of all traced contacts and other contacts are reported per flight (and not cumulative for all flights). In all other cases, the cumulative number of several traced flights should be regarded as one single event.

In the event dataset, flights were considered as separate events when the number of all traced contacts and other contacts were reported per flight (and not cumulative for all flights). If the total number of contacts was counted cumulatively (and not per flight), we considered those flights as one event.

Flight time

We define total flight duration as the sum of the actual flying time (total time spent in the air), time after boarding and ground delays before and after a flight. If no specific information on the flight time is available but the flight origin/destination suggests a (non-stop) long-haul flight of at least eight hours, flight time is set to eight hours. When the numbers of all traced contacts and other contacts were given per flight (and not cumulative), individual flight times were considered separately for analysis. In case of cumulative numbers given for several flights of unequal duration, individual flight time could not be considered.

TST conversion (tuberculosis only)

We define TST conversion as an initially negative tuberculin skin test (TST) that becomes positive after a second test. An initially TST-negative contact person (either as a result from previous medical records or a TST applied within the first three weeks after air travel-related exposure during a flight) who becomes TST positive in week 4–8 after air travel-related exposure during a flight is considered to have been infected by the index case. A negative TST within the first three weeks after exposure should elicit a second TST no later than eight weeks after the initial exposure. If the second TST is negative, no further investigation is needed, as there is no evidence for an infection during the flight. A positive TST within the three weeks after exposure is probably due to previous exposure or vaccination, and no further TST is indicated.

For each event we assessed whether or not on-board transmission occurred. In cases of confirmed transmission, we assessed the evidence of transmission according to the developed evidence criteria (see Box 1). In addition, we took into account disease-specific criteria, e.g. the validity of diagnostic tests, the validity of information for (alternative) exposures, and the susceptibility of the contacts.

In many events, only a single positive TST result was available. In these events, we assessed evidence according to the validity of retrievable information on susceptibility or alternative exposures.

Box 1. Criteria used for the assessment of evidence levels for onboard transmission, if information was available for analysis

We considered a high evidence for onboard transmission if
A)
index patient/s' and case/s' TB strains were either matching in molecular diagnosis AND the acquired information that contacts had no prior exposure was plausible;
— OR —
contacts had a proven TST conversion after in-flight exposure AND the acquired information that contacts had no prior exposure was plausible.

We considered a medium evidence for onboard transmission if
B)
index patient/s' and case/s' TB strains were either matching in molecular diagnosis AND the acquired information that contacts had no prior exposure was plausible, but less complete than in A) (Information about susceptibility less conclusive than in A);
— OR —
contacts had a proven TST conversion after in-flight exposure AND the acquired information that contacts had no prior exposure was less plausible, but less complete than in A) (Information about susceptibility less conclusive than in A);
— OR —
contacts had a single positive TST after in-flight exposure AND the acquired information that contacts had no prior exposure was plausible.

We considered a low level of onboard transmission if
C)
contact persons had a single positive TST after exposure, but information about susceptibility before and during the flight was either not available or inconclusive.

We concluded the likelihood for on-board transmission in events assigned to category A, B, C as high, probable and possible consecutive.

When there was no evidence of transmission, we assessed the evidence level of non-transmission by relating the successfully traced contacts of index cases to the number of all known contacts during a flight. We then calculated the percentage of successfully traced contacts.

Thus, we took into account the so-called beta error (error of the second kind). Many articles reported a comprehensive search of fellow passengers, i.e. all passengers on the flight — with the exception of the index case — were considered contacts. If contact tracing was restricted to close contacts or certain rows in the vicinity of the index case, we defined and traced contacts according to these specifications, as no other information was available.

We defined the relationship between evidence level and percentage rates of successfully traced contacts (of all contacted contacts of index cases) as follows:

- low evidence level for non-transmission: fewer than 35 % of contacts successfully traced;
- medium evidence level for non-transmission: between 35 % and 75 % of contacts successfully traced; and
- high evidence level for non-transmission: 75 % or more of contacts successfully traced.

'Medium evidence level' signifies that the evidence for the transmission of an infection is less compelling than at a high evidence level.

For each journal article describing an event, three scientific staff members completed a questionnaire and assessed the article, using our evidence criteria (see Box 1). Results were entered into an event database (Microsoft Access 2002). Later, discrepancies were identified and discussed in a meeting. A final version of each event was decided upon and then added to the database. The decision-making process was documented.

We assembled a final event dataset by merging data from the literature assessment with data from our interviews with external experts. A descriptive analysis of the event datasets was performed thereafter.

We analysed the dataset in SPSS for Windows, Version 15.0.

2.4 Guidelines

We systematically reviewed sources related to passenger air travel, such as guidelines on risk assessment or management of infectious diseases from international aviation boards, e.g. from Airport Council International (ACI), International Air Transport Association (IATA), and International Civil Aviation Organization (ICAO). In addition, web-based publications of national and international public health agencies such as WHO, CDC, ECDC, HPA, Health Canada, and Robert Koch Institute were systematically searched.

2.5 Pathogen-specific attributes

We collected peer-reviewed literature on disease-specific epidemiological parameters such as R_0, incubation period, period of shedding, duration of shedding, period of maximum and minimum infectiousness, signs and symptoms indicating increased transmissibility, and pre-vaccination immunity in order to consider them for our recommendations.

2.6 In-house experts' opinion

We presented the results of our literature search, expert interviews, pathogen-specific attributes, and guideline search to experts on the respective pathogens at Robert Koch Institute (RKI) and discussed disease-specific recommendations.

2.7 Delivered product

Evidence obtained through our literature search, guideline search, expert meetings, and literature search for pathogen-specific attributes was incorporated into a proposal for fact sheets for each pathogen, entitled 'Questions and answers for contact tracing' .

Whenever appropriate, we designed an algorithm that — for each disease and based on the collected information — included the triggers, procedures and recommendations for contact tracing. The results of our analysis of all available sources are presented in Section 3.

3 Disease-specific results

This section presents the results of our systematic literature review and our expert interviews. In addition, this section reviews existing guidelines and summarises our discussions with in-house experts at Robert Koch Institute in Berlin.

In collaboration with ECDC and based on our ranking of diseases mentioned in section 2.1, we chose the following diseases for further analysis: tuberculosis, influenza, SARS, meningococcal disease, measles, rubella, diphtheria, Ebola haemorrhagic fever, Marburg haemorrhagic fever, Lassa fever, smallpox, and anthrax.

A systematic search of peer-reviewed literature resulted in 3 711 hits. Of these, 421 suggested a possible link to 'risk assessment guidelines for infectious diseases transmitted on aircraft' in their titles. We were able to exclude 377 articles not meeting our definition of an 'event' by analysing the abstract and/or the full text. We finally identified 44 articles relevant for contact tracing. A further 14 articles were omitted since they only related to food-borne diseases. Five additional peer-reviewed articles were obtained through cross-references. Overall, 35 peer-reviewed event articles were found.

11 grey literature articles covering events were found through cross-references and a ProMed search.

We contacted 73 experts from 38 countries. Of these, 22 contributed either by telephone interview (14) and/or participated in our survey on the need for contact tracing (11).

3.1 Tuberculosis (TB)

Results from the survey

When asked about the need for contact tracing for TB-related events, the 11 experts from the EU, Japan and Switzerland that responded to our survey considered contact tracing indispensable if there was a suspected or confirmed case of infectious disease on board aircraft. All together, 12 EU countries and Switzerland have traced contacts in connection with more than 80 events between 2001 and 2007. The majority of these events were not recent, and none of them have been covered in either peer-reviewed or grey literature articles, nor was there any information available for our expert interviews.

Results from literature search and event article analysis

Overall, we identified 28 TB-related events between 1992 and 2008.

A literature search identified 18 events in 11 peer-reviewed event articles where index cases with tuberculosis had travelled on board airplanes [14–24]. In addition to peer-reviewed literature, we identified another four events in four event articles in the grey literature. All four events concerned index cases with multidrug-resistant (MDR) TB. Moreover, we found another six events through six expert interviews.

We analysed information on reasons/motivations for contact tracing, which was only available for six telephone interviews. The most important criteria for initiating contact tracing were:

- the case met the criteria of a national or international guideline for TB contact tracing (5/6 interviews);
- multidrug resistance (2/6 interviews);
- symptomatic index patients (5/6 interviews); and
- prolonged incubation period of TB gives time for intervention (5/6 interviews).

The median time delay between initiating contact tracing and the date of the event was 51 days (range: 25–77 days).

Comprehensive contact tracing (attempting to contact all passengers on board) was undertaken in 15 events. The crew was contacted in 18 events and contact categories were applied in six events, with information on contact tracing details. The WHO definition of 'contact category' for air passengers was the one most frequently used (passengers seated within two rows of the index case).

Flight details

The flight time for TB events was 2–14 hours. For some events, the flight time was given as 'at least eight hours', so the exact median flight time for TB events cannot be calculated.

We found one event with a (median) exposure time for the flight personal of only four hours during which transmission possibly occurred (medium evidence level). The majority of TB events (18/28, 64 %) occurred in flights longer than eight hours, regardless of actual transmission. Flight time for events where transmission occurred ranged from 4–14 hours. The majority (5/6 events) had flight times of over eight hours.

A ground delay was reported for only one event. Here, the flight time including ground delay was nine hours, and transmission had probably taken place (medium evidence level).

Information about the functionality of HEPA filter systems was acquired for nine events; the HEPA filter systems had been functional in eight events. In another event, a pilot infected with TB had been flying with colleagues in an aircraft type where the flight deck had no operative HEPA filters in place: no transmission occurred (high evidence level).

Detailed results for events are listed in Table 2 and Annex 3.

On-board infection transmission

Contacts were traced in 28 events. In six events, possible on-board transmission from sputum-positive index cases to at total of 18 contacts was reported. Of those, five were seated two rows behind the index case (rows 12, 13, 15, 23, 29), and for two of the five, close exposure to the index case/s during the flight was documented. In one event with a (median) flight time of four hours (range: 3–6 hours, accumulated flights) transmission occurred. The evidence level was rated as medium (less conclusive). In this particular event, 71 frequent fliers had been exposed to a sputum smear/culture-positive flight attendant with cavitary lesions. The median exposure time for passengers was four hours, and 4/71 passengers showed a TST conversion. More details can be found in Table 2 and Annex 3.

Transmission of TB according to our evidence criteria was found in 2/28 events with a high evidence level (seven contacts involved in two events). In another 3/28 events, transmission occurred with a medium evidence level (10 contacts involved in three events were infected on board with a medium — or less conclusive — evidence level). In one event, one passenger was found with a possible or but low likelihood of on-board transmission.

No transmission was detected in 16 events; of those, 10 were identified by the literature search in peer-reviewed articles, three through expert interviews, and another three were obtained through grey literature. For events obtained form the peer-reviewed literature, evidence levels for non-transmission were high in 1/10, medium in 2/10, low in 4/10, and unknown in 3/10.

In another 6/28 events from all sources (peer-reviewed literature, grey literature and telephone interviews), information about on-board transmission was completely lacking.

The following table summarises the features of events where TB was transmitted onboard.

Table 1: Features of events with highly likely (high evidence level) or probable (medium evidence level) transmission

Evidence for onboard transmission?	Nr. of passengers/ crew infected	Evidence level	Flight time (hours)	Ground delay?	HEPA functional?	Range of seating positions of infected passengers	Index patient's age	Index patient's symptoms during flight
Yes	3 passengers with TST conversions with no other RF	high	14	unknown	unknown	15, 23, 29 rows from index case	44	unknown
Yes	4 passengers with TST conversions with no other RF and 2 with single positive TST and no other RF	4 high, 2 medium	> 8	no	yes	0, 1, 12, 13 rows from index case and 1 crew member	32	cough, fever
Yes	2 crew members with TST conversion and no other RF, but contact on ground with colleague	medium	12 (median)	unknown	unknown	2 crew members	unknown	cough, shortness of breath

Evidence for onboard transmission?	Nr. of passengers/ crew infected	Evidence level	Flight time (hours)	Ground delay?	HEPA functional?	Range of seating positions of infected passengers	Index patient's age	Index patient's symptoms during flight
Yes	4 passengers with TST single positive and no other RF	medium	4 (median)	no	unknown	unknown	unknown	cough, shortness of breath
Yes	2 passengers with single positive TST and no other RF	medium	9	yes	yes	unknown	unknown	cough, fever, shortness of breath
Yes	1 passenger with TST single positive and unknown other RF	low	> 8	unknown	unknown	unknown	unknown	cough, haemoptysis

Index cases

In 20/28 events, the nationality of the index cases was known. Index cases originated from nine different countries, four of them from high-prevalence countries: Russia (three index cases), South Africa (two index cases), Thailand (two index cases) and Korea (three index cases). Other index cases originated from the USA (three index cases), Taiwan (three index cases), Denmark (one index case), Finland (one index case) and New Zealand (two index cases).

The median age of index cases was 34 years (range: 21–55 years).

We found a range of signs and symptoms shown by index cases such as cough, fever, and shortness of breath. The index cases had AFB positive sputum smears, were TB culture positive, and showed cavitary lesions on chest x-rays. Cavitary lesions, AFB positivity, and culture positivity were found in events in which index cases had infected fellow passengers as well as in events where there was no evidence of transmission.

Cough combined with shortness of breath was found in three events where index cases had infected fellow passengers (medium evidence level, see Box 1).

Contacts

All together, a minimum of 3677 contacts on board were identified in the peer-reviewed event articles. The actual number is likely to be much higher, since many articles do not mention the total number of contacts. Of the 3677 contacts on board, 2699 (73.4 %) were passengers and 374 (10.2 %) were crew. Only 1779/3677 contacts (48.4 %, identified in 18 events) could be traced successfully. Only in these cases it was possible to present evidence of transmission.

Of all events with available information on the status of infection of contacts, only 18/1779 contacts (1.0 %) were (potentially) infected while on board, possibly because we rated 11 of these 18 contacts with a medium (i.e. less conclusive) evidence level for on-board transmission.

All four events found in the grey literature involved index cases with MDR TB and occurred in 2007. In total, we identified 1085 contacts in the grey literature articles and another 93 contacts in our telephone interviews. Information on successfully traced contacts was not available due to organisational structures: organisations initiating the contact tracing did not always receive feedback from the institutions that actually carried out the contact tracing.

In the grey literature articles, flight time in three events clearly exceeded eight hours. There was no information on the functionality of HEPA filter systems on board or during ground delays. There was no clear evidence for on-board transmission in any of the four grey literature events. All together, 512 contacts were traced successfully, but the total number of traced contacts was not given. Therefore, we cannot provide evidence levels for the grey literature events.

Please see Table 2 for an overview of TB events. A detailed table of all events is available in Annex 3.

Table 2. Overview of events involving TB cases obtained from peer-reviewed literature, grey literature and expert interviews

Reference	Country	Year of event	Flight time including ground delay (hours)	HEPA func-tional	Ground delays?	Index patient	Index patient age	Index patient's symptoms during flight	On-board trans-mission?	Evidence level transmission / no transmission	Number of passengers / crew infected	Distance of contacts (seat rows)
Driver CR, Valway SE, Morgan WM, Onorato IM, Castro KG. Transmission of Mycobacterium tuberculosis associated with air travel. JAMA 1994; 272(13):1031-5	USA	May to Oct. 1992	12 (median)	unknown	unknown	female, flight attendant	unknown	cough, shortness of breath	yes	medium	2 other crew members (TST-conversion and no other RF, but possible exposure on ground by colleague)	unknown
Driver CR, Valway SE, Morgan WM, Onorato IM, Castro KG. Transmission of Mycobacterium tuberculosis associated with air travel. JAMA 1994; 272(13):1031-5	USA	May to Oct. 1992	4 (median) range 2-6 hrs	unknown	unknown	female, flight attendant	unknown	cough, shortness of breath	yes	medium	4 passengers (TST-conversion and no other RF)	unknown
Parmet AJ. Tuberculosis on the flight deck. Aviat Space Environ Med 1999; 70(8):817-8.	USA	1998	> 8 (8–60 exposure)	unknown	unknown	male, pilot	unknown	unknown	no	high	x	X
Whitlock G, Calder L, Perry H. A case of infectious tuberculosis on two long-haul aircraft flights: contact investigation. N Z Med J 2001; 114(1137):353-5.	New Zealand	1996	> 8	yes	unknown	female from New Zealand	21	cough, weight loss	no	medium	x	X
Whitlock G, Calder L, Perry H. A case of infectious tuberculosis on two long-haul aircraft flights: contact investigation. N Z Med J 2001; 114(1137):353-5.	New Zealand	1996	> 8	yes	unknown	female from New Zealand	21	cough, haemoptysis	no	medium	x	X
McFarland JW, Hickman C, Osterholm M, MacDonald KL. Exposure to Mycobacterium tuberculosis during air travel. Lancet 1993; 342(8863):112-3.	USA	1992	> 8	unknown	unknown	unknown	unknown	unknown	no	low	x	X
CDC. Exposure of passengers and flight crew to Mycobacterium tuberculosis on commercial aircraft, 1992–1995. MMWR Morb Mortal Wkly Rep 1995 Mar 3;44(8):137-40.	USA	1993	1	unknown	unknown	unknown	unknown	unknown	no	low	x	X
CDC. Exposure of passengers and flight crew to Mycobacterium tuberculosis on commercial aircraft, 1992–1995. MMWR Morb Mortal Wkly Rep 1995; 44(8):137-40.	USA	1994	unknown	unknown	unknown	US citizen	unknown	unknown	no	low	x	X
Miller MA, Valway S, Onorato IM. Tuberculosis risk after exposure on airplanes. Tuber Lung Dis 1996;77(5):414-9.	USA	1993	9	yes	yes	male, Russian		cough, fever, shortness of breath	yes	medium	2 passengers with single positive TST and no other RF	unknown
Miller MA, Valway S, Onorato IM. Tuberculosis risk after exposure on airplanes. Tuber Lung Dis 1996;77(5):414-9.	USA	1993	2	unknown	no	male, Russian	unknown	cough, fever, shortness of breath	no	unknown	x	X
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	> 8	yes	no	female, Korean	32	unknown	no	unknown	x	X
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	2	yes	no	female, Korean	32	unknown	no	unknown	x	X
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	2	yes	no	female, Korean	32	cough, fever	no	unknown	x	X

Reference	Country	Year of event	Flight time including ground delay (hours)	HEPA func-tional	Ground delays?	Index patient	Index patient age	Index patient's symptoms during flight	On-board trans-mission?	Evidence level transmission / no transmission	Number of passengers / crew infected	Distance of contacts (seat rows)
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	> 8	yes	no	female, Korean	32	cough, fever	yes	4 high, 2 medium	4 passengers with TST conversion with no other RF and 2 with single positive TST and no other RF	4: same row, 1 row, 12 rows, 13 rows 2: 1 row, 1 crew
Moore M, Fleming KS, Sands L. A passenger with pulmonary/ laryngeal tuberculosis: no evidence of transmission on two short flights. Aviat Space Environ Med 1996;67(11):1097-100.	USA	1994	each 1.25	unknown	no	male	unknown	cough, hoarseness	unknown	medium	Unknown	X
Vassiloyanakopoulos A, Spala G, Mavrou E, Hadjichristodoulou C. A case of tuberculosis on a long distance flight: the difficulties of the investigation. Euro Surveill 1999;4(9):96-7.	Greece	1998	> 8	unknown	no	young male, Thai	unknown	cough, haemoptysis	yes	medium	1 passenger with single positive TST and no other RF	X
Wang PD. Two-step tuberculin testing of passengers and crew on a commercial airplane. Am J Infect Control 2000;28(3):233-8.	Taiwan	1997	14	unknown	unknown	Female, Taiwanese	44	unknown	yes	high	3 passengers with TST conversions and no other RF	15, 23, 29 rows distance
Chemardin J, Paty M-C, Renard-Dubois S, Veziris N, Antoine D. CT of passengers exposed to an extensively drug-resistant tuberculosis case during an air flight from Beirut to Paris, October 2006. Eurosurveillance Weekly 2007;12(12).	France	2006	5	unknown	unknown	male, Russian	unknown	cough	no	low	x	X
Telephone interview	Denmark	2007	> 8	unknown	no	female, Danish	55	cough	no	x	x	X
Telephone interview	Estonia	2004	8	yes	unknown	Finnish	unknown	unknown	unknown	x	x	X
Telephone interview	France	2006	5	unknown	unknown	male, Russian	unknown	cough, loss of weight	no	x	x	X
Telephone interview	Germany	2007	8	unknown	unknown	female, South African	20	cough	unknown	x	x	X
Telephone interview	Ireland	2008	> 8	unknown	no	male, South African	31	cough, sweating	unknown	x	x	X
Telephone interview	Norway	2006	> 8	unknown	unknown	female, Thai	32	cough, loss of weight	no	x	x	X
Grey literature (ProMed)	USA	2007	> 8	unknown	unknown	male, USA	unknown	asymptomatic	no	x	x	X
Grey literature (ProMed)	Canada	2007	> 8	unknown	unknown	male, USA	unknown	asymptomatic	no	x	x	X
Grey literature (ProMed)	Taiwan/ China	2007	< 8	unknown	unknown	55-year-old man (and 57-year-old woman with standard TB) from Taiwan	55/57	unknown	unknown	x	x	X
Grey literature (ProMed)	Taiwan/ China	2007	< 8	unknown	unknown	55-year-old-man (and 57-year-old woman with standard TB) from Taiwan	55/57	unknown	unknown	x	x	x

Results from the guideline search

We collected information relevant for the contact tracing of TB cases from the following organisations: WHO, CDC, HPA UK, and the German Central Committee against Tuberculosis. The most recent and detailed guidelines for TB and air travel are the WHO guidelines for prevention and control [8]. WHO suggests that contact tracing should be limited to flights that took place in the past three months prior to the notification of the public health authorities. According to WHO, the minimal duration of exposure (on the basis of total flight duration) that mandates contact tracing is eight hours. Contact tracing is only recommended if a person was likely to have been infectious during the flight/s. For non-infectious persons, contact tracing is not recommended. Crew members are not normally considered close contacts of an index case. If an infectious or potentially infectious case is recognised before boarding, he or she should be denied boarding. If an infectious or potentially infectious case is noticed during the flight, the ill passenger should be given a surgical facemask to prevent dissemination of infectious droplets. If no mask is available or a mask cannot be tolerated, the passenger should be provided with an adequate amount of either paper tissues or towels and instructed to cover nose and mouth, at least while speaking, coughing or sneezing. The first public health authority to be informed should be the authority of the country where index case was diagnosed. Public health authorities should also be provided with the index case's recent air travel history.

The proposed follow-up procedure for possible exposure to TB from an infectious source during air travel includes tuberculin skin testing (TST), regardless of previous TB vaccination. TST should be performed as soon as possible after the flight. For baseline measurement, TST should be performed no later than three weeks after in-flight exposure. A positive TST within three weeks after exposure should be considered as exposure (or vaccination) prior to the flight, and no further TST is needed. A positive test result after three weeks might be due to vaccination, boosting or recent transmission. Persons with an initially negative TST that converts and becomes positive after a second test are considered to have been infected on board [8].

In its general 'Guidelines for investigation of contacts of persons with infectious TB', CDC recommends that contact tracing for index cases of pulmonary/pleural or laryngeal TB should be initiated if the sputum smear is AFB positive by microscopy. If AFB is not detected by microscopy, an investigation is still recommended if the chest radiograph indicates the presence of cavities in the lung. Even if these conditions are not present, contact tracing should be initiated, provided that the chest x-ray is consistent with pulmonary TB. Persons with AFB smear or culture-positive TB are assigned the highest tracing priority. When trying to determine the time of transmission (index case), CDC, in accordance with WHO guidelines, sets the infectious period to three months prior to TB diagnosis. CDC recommends that a minimal set of data concerning the index case should be available in order to perform adequate risk assessment (Table 4 in [25]).

In its clinical guideline no. 33 ('Clinical diagnosis and management of tuberculosis, and measures for its prevention and control'), The National Institute for Health and Clinical Excellence (UK) does not routinely recommend contact tracing following notification of an infectious airline passenger, but always recommends that disease control professionals are notified:

- if less than three months have elapsed, since the flight occurred and the flight was longer than eight hours; and
- if the index case is sputum smear positive and either is infected with MDR TB or coughed frequently during the flight.

If the index case is a crew member, contact tracing of passengers should not be routinely conducted for passengers, but contact tracing of other staff/crew members is considered appropriate [26].

The German Central Committee against Tuberculosis (DZK) recommends that contract tracing should be initiated if AFB are found in the index case's sputum or respiratory secretions. Furthermore, initiation of contact tracing is advisable if the culture or molecular tests (molecular amplification methods) of the index case's sputum or respiratory secretions are positive or if chest x-rays show cavernous lesions [27].

An overview of all mentioned guidelines is given in Table 3.

Table 3. Information relevant for contact tracing obtained from TB control guidelines.

Guideline	Contact tracing (CT) recommended if:	Mode of CT recommended	Time frame for CT recommended	Other measures recommended
WHO. Tuberculosis and air travel: Guidelines for prevention and control (3rd edition)	Index case with pulmonary or laryngeal TB either confirmed infectious (smear and culture positive) or potentially infectious (smear negative and culture positive) and risk assessment justifies CT*. * Presence of cavitations on chest x-ray or documented transmission to close contact or presence of symptoms (such as cough, haemoptysis) at the time of flight and flight time equalling at least eight hours, or result of risk assessment justifies CT.	CT for close contacts: +/- 2 seating rows around index case; crew not routinely considered as close contacts	Limited to flights that took place during the last three months before notification of the TB case to the public health authority.	Surgical facemask or paper tissues for index case during flight. Notification of public health authority of country where first diagnosis was made: information about index case.
CDC. Guidelines for the investigation of contacts of persons with infectious tuberculosis. Recommenda-tions from the National Tuberculosis Controllers Association and CDC.	Index cases of pulmonary/pleural or laryngeal TB if the sputum smear has AFB on microscopy. If AFB is not detected by microscopy in three sputum smears, an investigation is still recommended if the chest radiograph indicates the presence of cavities in the lung.	Not specified	Minimum of two face-to-face interviews no later than <=1 business day after reporting for infectious index cases, and no later than <= 3 business days for suspected cases.	Not specified
HPA: NICE. Tuberculosis: Clinical diagnosis and management of tuberculosis, and measures for its prevention and control. 2006. National Institute for Health and Clinical Excellence. Clinical Guideline 33.	Only if index case is sputum smear positive, and either is infected with MDR TB or index case coughed frequently during flight, and flight time was longer than eight hours.	Not specified	Less than three months have elapsed at point of notification since the flight.	Not specified
DZK. Empfehlungen für die Umgebungs-unter-suchungen bei Tuberkulose. 2007.	AFB from the index case's sputum or respiratory secretions have been found positive, or culture or molecular tests (molecular amplification methods) from the index case's sputum or respiratory secretions return positive results, or if chest x-ray shows cavernous lesions	Not specified	Not specified	Not specified

Expert opinion

Through our literature search, we found a high evidence level for on-board TB transmission in two passengers seated more than two seating rows away from the index case who reported a special exposure to the index case during the flight. When considering contact tracing, one needs to keep in mind that passengers seated more than two rows away from index cases can also be exposed. Therefore, in addition to the WHO recommendation to consider passengers seated in the same seating row or in +/- 2 rows distance from the index case (WHO's 'close contact' definition), passengers with a special exposure should also be considered for contact tracing. Special exposure includes being coughed or sneezed at by the index case or having close social interaction with the index case at any time during the flight.

A serious public health risk is also posed by passengers with infectious respiratory MDR/XDR TB or by infectious passengers that show symptoms or display a behaviour during the flight that increase transmissibility, e.g. frequent coughing or sneezing, or close social contact. These criteria — even if the flight time was less than eight hours — cause an enhanced public health risk and should be weighed carefully when considering the initiation of contact tracing.

Consequently, in cases of index passengers with confirmed infectious respiratory MDR or XDR TB, contact tracing should always be considered, regardless of flight time and seating details.

3.2 Influenza

Results from the survey

When asked about the need for contact tracing for air travel-related influenza events, 10/11 EU experts that responded to our survey considered contact tracing indispensable if there was a suspected or confirmed case (or cases) of infectious disease on board aircraft. Of the 10 colleagues responding, 8/10 opined that contact tracing was necessary for both seasonal *and* pandemic influenza. Two concluded that it was not necessary for seasonal influenza.

Results from literature search and event article analysis

In the peer-reviewed literature [10,28-30], we could identify five influenza-related events between 1977 and 1999. The events were reported from the USA (4) and Australia (1). The time delay for initiating contact tracing ranged between two and seven days. Reasons for contact tracing were not mentioned. The most frequent method of contact tracing for influenza events was active case finding through telephone interviews (3/5 events).

Flight details

Information on flight duration, including ground delays was available for 3/5 events. All flights lasted less than eight hours (3, 3 and 4 hours, respectively). In one event, a ground delay and a non-functional HEPA system were reported; transmission occurred in 38 passengers. In the remaining four events, data on the functionality of HEPA filter systems and ground delays were not given.

On-board disease transmission

On-board influenza transmission occurred in 4/5 events, resulting in 81 infected contact persons. Evidence for on-board transmission according to our definition was found to be high in one event [10] and medium in the three other events [28–30]. Infected contact persons were seated either in the same row or up to ten rows from the index case.

Index cases

All index cases in events where transmission occurred suffered from coughing and fever during the flight. 3/4 index cases also reported headaches, one index case reported chills. One index case from an event where transmission was inconclusive suffered from coughing and fever.

Age and sex of the index case was retrievable for only one event: 21 years, male. In 3/5 events, the nationality of the index case was mentioned; two index cases originated in the USA, another one in Australia.

Contacts

All together, 84 contact persons out of 181 successfully traced contacts (46.4 %) were infected.

An overview of influenza events can be found in Table 4.

Results from the guideline search

We found no specific guidelines discussing contact tracing for influenza cases on board airplanes. However, some guidelines gave generic advice on how to deal with ill passengers during a flight. The WHO guidelines on investigating human cases of avian influenza A (H5N1) provide some generic advice for contact tracing of suspected avian influenza cases in humans, but without referring to contact tracing in air travel-related events [31]. In its 'Interim guidance for airline flight crews and persons meeting passengers arriving from areas with avian influenza', CDC recommends that a surgical facemask should be worn by suspected influenza cases on board. Additionally, suspected influenza cases should be separated from other passengers (3–6 feet). If no facemask is available, a paper or gauze surgical mask should be used to reduce the number of droplets coughed into the air. Personnel should wear disposable gloves when coming into direct contact with blood or bodily fluids of any passenger [32].

In its general recommendations for reducing transmission of human influenza, ECDC recommends regular hand-washing, good respiratory hygiene, wearing masks in healthcare settings (by those with symptoms of acute febrile respiratory infections), early isolation (usually at home) of persons feeling unwell, feverish or showing other symptoms of influenza [33].

Expert opinion

Influenza is generally transmitted by droplets, has a basic reproductive number between 1.5 and 2.5 and a manifestation index of around 40 % [34–36]. Our literature search yielded evidence for on-board transmission in flights < 8 hours and for transmission to contacts seated up to 10 rows from index cases [10,28–30]. As far as the index case's symptoms are concerned, the intensity of symptoms generally coincides with the shedding curve [35]. Therefore, in the majority of events, contact tracing is advisable only if the index case is symptomatic during flight. Under certain circumstances, e.g. the emergence of a new subtype of human-to-human transmissible influenza, contact tracing may be considered even if the index case has been asymptomatic.

It is also essential to assess the specific strain attributes of the virus found in the index case and to evaluate the vulnerability and susceptibility of fellow passengers. In general, the very young and the very old have an increased risk of hospitalisation if becoming ill with influenza, and the very old have an increased risk of death if

falling ill [37]. These findings need to be taken into account if — due to lack of personnel or time — compromises have to be made during contact tracing.

In the case of influenza, it is particularly difficult to generalise and design a single contact tracing algorithm. Due to the short incubation period it is almost impossible to provide contacts with adequate PEP within 48 hours after the onset of symptoms. However, interrupting the chain of infection might be a strong enough reason to initiate contact tracing.

The decision to start contact tracing for an influenza event needs to be based on a thorough risk assessment. Criteria include the symptoms of the index case while on board, the global epidemiological situation (WHO pandemic level), susceptibility, vaccination status, and known vulnerable groups for disease or death, but also the specific purpose of contact tracing (interruption of infection chains/scientific research). In general, contact tracing for seasonal influenza cases is neither feasible nor recommendable, but may be indicated after individual risk assessment for some rare occasions such as outlying seasonal drift variants.

Immediate contact tracing is indicated in cases of human avian influenza with suspected potential for human-human transmission.

Also, during the early phases of an influenza pandemic, contact tracing can be indicated if only few imported cases have entered a country and there is still sufficient time for PEP. During the late stages of a pandemic, contact tracing is less useful. When non-pharmacological interventions such as school closures or ban of mass gatherings are launched, it is advisable to also stop contact tracing. Cauchemez et al. advise non-pharmacological interventions when population incidence reaches 0.1 % of the population [38].

Table 4. Overview of influenza events obtained from peer-reviewed literature

Reference	Country	Year of event	Flight time including ground delay (hours)	Ground delays?	HEPA filter functional?	Age of index patient	Index patient's symptoms	On-board trans-mission?	On-board trans-mission / non-transmission: evidence level	Number of passengers traced / infected	Infected contacts: distance from index case (seat rows)
Michael R. Moser et al. Am J Epidemiol. 110:1-6. 1979.	USA	1977	unknown	yes	no	21	cough, fever, chills	yes	high	38/52 (73.0 %) successfully traced passengers were infected.	unknown
Karl C. Klontz et al. Am J Epidemiol. 129:2. 1989.	USA	1986	3	unknown	unknown	unknown	cough, fever, headache	yes	medium	18/36 (50.0 %) successfully traced passengers were infected.	7 same row 8 one row 3 two rows
Karl C. Klontz et al. Am J Epidemiol. Vol. 129:2. 1989	USA	1986	3	unknown	unknown	unknown	cough, fever, headache	yes	medium	5/43 (11.6 %) successfully traced passengers were infected: 90 contacts in total.	1 same row 1 one row 2 three rows 1 four rows
Marsden AG. Med J Aust. 2003	Australia	1999	4	unknown	unknown	unknown	cough, fever, headache	yes	medium	20/20 (100 %) successfully traced passengers were infected; total number of contacts unknown.	4 same row 2 one row 5 two rows 3 three rows 1 four rows 1 five rows 2 six rows 1 eight rows 1 ten rows
Joseph F. Perz et al. Int J infect Dis. 2001	USA	1999	unknown	unknown	unknown	unknown	cough, fever	no	unknown	Only 3/30 (10.0 %) passengers were successfully traced; of those, none were infected; total number of contacts unknown.	unknown

3.3 SARS

Results from the survey

11 EU Member States responded to a questionnaire on criteria for initiating contact tracing for SARS events. All 11 respondents agreed that contact tracing was necessary if SARS was suspected.

Results from literature search and event article analysis

We identified nine events from seven peer-reviewed event articles concerning SARS [39–45]. All events dated from 2003, the year of the SARS epidemic. Events were reported from Canada, France, the USA and Germany.

The number of days after which contact tracing was initiated ranged between three and 90 days.

A comprehensive search, i.e. an attempt to contact all passengers of a flight where a SARS case was on board, was undertaken in 5/9 events.

Methods of active contact tracing included using passenger locator cards (2/9), passenger manifests (5/9), telephone contacting (4/9) and addressing passengers with a questionnaire (4/9). In one event, passive case finding (press release) was used.

Flight details

Flight times for the nine SARS events ranged between 2 and 13 hours. We found no information on ground delays or on the functionality of HEPA filter systems for any of the events.

On-board transmission

We obtained four events including 26 passengers who were infected during flight. Evidence for on-board transmission was high in 24/26 cases and medium and low in one case each.

Seat locations of infected contacts in relation to index cases was available for two events and ranged between the same row and seven rows away [40,41,43,44].

An overview of SARS events is given in Table 4.

Index cases

Age information was retrievable in 4/9 events. The age of index cases ranged between 48 and 72 years.

Information about the index cases' symptoms was obtained in 6/9 events. Only one index case was reported asymptomatic during the flight, and no fellow passengers were infected [44]. In two events, index cases who had most likely transmitted infection during the flight suffered from coughing and fever during the flight. In another event, an index case who had transmitted disease on board complained about difficulties breathing during the flight [41]. In two events, index cases complained about fever and coughing or fever in combination with general malaise. In these events, no indication for on-board transmission was found. However, evidence for non-transmission was inconclusive [44,45].

Contacts

At least 3436 contacts were identified in nine events where SARS index cases had travelled with airplanes in 2003. The total number of contacts successfully traced was available for six events: 2915 passengers were successfully traced. In summary, 24/2915 (0.8 %) of known (or identifiable) fellow passengers of SARS index cases were infected during flights.

Table 5. Overview of SARS events

Reference	Country	Year of event	Flight time including ground delay (hours)	Ground delays?	HEPA filter functional?	Age of index patient	Index patient's symptoms	On-board trans-mission?	On-board trans-mission / non-transmission: evidence level	Number of passengers traced / infected	Contacts: distance from index case (seat rows)
Vogt TM et al. (2006)Travel Med, Volume 13, Issue5,, 268-272	USA	2003	unknown	unknown	unknown	unknown	unknown	no	low	312/1766 (17.7%) successfully traced passengers; of those, none infected.	-
Wilder-Smith A et al. (2004) J Travel Med. Mar-Apr; 11(2):130	Singapore	2003	8	unknown	unknown	male	cough, fever	yes	medium	1 passenger infected; number of traced passengers unknown.	-
Desenclos JC, (2003) Emerg Infect Dis. Vol 10, No 2	France	2003	8	unknown	unknown	male	difficulty breathing	yes	high	2/401 (0.5%) total contacts infected; number of successfully traced passengers unknown.	-
Flint J et al. (2003) Can Commun Dis Rep. Jun 15; 29(12):105-110	Canada	2003	8	unknown	unknown	unknown	unknown	no	unknown	0/338 successfully traced passengers infected; total number of traced passengers unknown.	-
Lesens O. Presse Med 2003; 32: 1359-65	France	2003	8	unknown	unknown	male, 54	unknown	yes	low	1 passenger infected; total number of passengers traced/ successfully traced unknown.	1 one row

Reference	Country	Year of event	Flight time including ground delay (hours)	Ground delays?	HEPA filter functional?	Age of index patient	Index patient's symptoms	On-board trans-mission?	On-board trans-mission/ non-transmission: evidence level	Number of passengers traced/ infected	Contacts: distance from index case (seat rows)
Sonja J. Olsen et al. N Engl J Med. 349: 2416-22.	Thailand	2003	2	unknown	unknown	male, 54	asymptomatic	no	low	74/315 (23.5%) successfully traced passengers; of those, none infected.	-
Sonja J. Olsen et al. N Engl J Med. 349: 2416-22	Thailand	2003	3	unknown	unknown	male, 72	cough, fever	yes	high	22/120 (18.3%) total contacts infected; number of successfully traced passengers unknown.	1 same row, 3 one row, 5 two rows, 2 three rows, 2 four rows, 3 five rows, 2 seven rows
Sonja J. Olsen et al. N Engl J Med. 349: 2416-22	Thailand	2003	2	unknown	unknown	unknown	cough, fever	no	medium	166/246 (67.5%) successfully traced passengers; of those, none infected.	-
Breugelmans et al (2004) Emerg Inf Dis. 10:8, 1502-03	Germany	2003	2–13 (7 flights)	unknown	unknown	male, Chinese, 48	fever, general malaise	no	low	36/250 (14.4%) successfully traced passengers; of those, none infected.	-

Results from the guideline search

We consulted guidelines from CDC, WHO, Robert Koch Institute, the Canadian Commonwealth Department of Health, the US Aerospace Medical Association Task Force (ASMA), the International Air Travel Association (IATA) and the Australian New South Wales Department of Health [46–56]. None of them gave specific advice for contact tracing in SARS events related to air travel.

WHO recommends that suspected SARS cases should be separated from other passengers during the flight. They should be provided with a surgical facemask and a designated toilet should be provided for the use of the sick person only. WHO defines a 'contact' of a suspected SARS case as:

- a passenger seated in the same row as the suspected SARS case;
- a passenger two rows in front or behind the suspected SARS case;
- a person providing care for the suspected SARS case;
- a person having intimate contact with the suspected SARS case;
- a person having contact with respiratory secretions of the suspected SARS case;
- a person living in the same household with the suspected SARS case; and
- all crew members.

If a crew member happens to be a suspected SARS case, all passengers should be regarded as contacts. Contacts should provide identification and contact addresses (valid for at least another 14 days after the flight) to the health authorities responsible for contact investigations. Additionally, contacts should be given information about SARS and advised to seek medical attention if they develop any symptoms compatible with SARS within 10 days of the flight. If it becomes apparent that a suspected case is a probable case of SARS, health authorities in the contact's country of residence should be informed and encouraged to carry out active contact surveillance, including daily body temperature checks for 10 days after the flight. As a precautionary measure, WHO recommends that all crew and passengers not rated as 'contacts' should also leave their contact details (valid for at least another 14 days after the flight) with the investigating health authorities. This group of persons should be also be provided with information about SARS and be advised to seek medical attention if they develop any symptoms compatible with SARS within 10 days of the flight. Also, the pilot should radio ahead to the destination airport in order to alert health authorities about the arrival of a suspected case of SARS [53].

The guidance provided by the following publications proved to be in accordance with the WHO recommendations: the Canadian Commonwealth Department of Health's recommendations, the Australian Department of Health's 'Infection control guidelines', the New South Wales Department of Health's 'Infection control guidelines for Severe Acute Respiratory Syndrome (SARS)', the US Aerospace Medical Association (ASMA) Medical Guidelines Task Force's 'Suspected communicable disease — general guidelines for cabin crew', and the International Air Travel Association's (IATA) 'Guidelines for suspected communicable diseases' [47;49;50:51;55].

IATA and other agencies recommend that crew members wear facemasks [55] if the index case does not tolerate a facemask.

The US CDC recommends that suspected SARS patients should be separated from other passengers. Suspected SARS patients should also have access to individual toilet facilities and a surgical facemask. Crew members should ensure that their hand hygiene is appropriate. After the arrival of the airplane, the ill passenger should be

separated from exposed and asymptomatic passengers, placed in an isolation facility, and assessed medically. All other passengers should be assessed for illness, types of exposure to the index case and other potential SARS exposures. Passengers should also be informed about SARS and advised to seek medical attention if they develop any symptoms compatible with SARS within 10 days of the flight [56].

In its recommendations for prolonged SARS surveillance, the German Robert Koch Institute (RKI) defines three contact categories for SARS: Category 1 includes close and intimate contacts (including contacts with body fluids) such as medical caretakers, people living in the same household, or persons staying in the same closed environment where the distance is two metres or less. Next-seat passengers in airplanes clearly belong to Category 1. In accordance with WHO, RKI recommends the following measures for Category 1 contacts: taking detailed contact information, providing information about signs and symptoms of SARS, ensuring home isolation of contacts for 10 days after having contact with the index case, and monitoring of Category 1 contacts for 10 days after the flight. Contacts in Category 2 are contacts as defined in Category 1 but with adequate infection protection measures in place at the time of contact. Contacts staying in the same closed environment at a distance of more than two metres from the index case are also categorised as Category 2. RKI recommends that Category 2 contacts should receive information about signs and symptoms of SARS and should be asked to provide detailed contact information. In addition, their body temperature should be monitored daily for 10 days after having contact with the index case. Immediate consultation of local public health services or other healthcare providers is recommended. [52].

Table 6 provides an overview of guidelines concerning SARS.

Table 6. Information retrieved from SARS control guidelines relevant to contact tracing (CT)

Guideline	CT recommended if...	Recommended CT mode	Time frame for CT recommended	Other measures recommended
WHO recommended measures for persons undertaking international travel from areas affected by severe acute respiratory syndrome (SARS). Wkly Epidemiol Rec. 2003 Apr 4;78(14):97-9.	N/A	N/A	N/A	• Provide index case with surgical facemask • Provide individual toilet to index case • Contacts should provide investigating health authorities with identification and contact addresses valid for at least another 14 days after the flight. • If crew member is a SARS case, all passengers should be regarded as contacts. • Inform contacts about SARS; radio ahead to airport of destination about suspected SARS case on board.
CDC: Guidance about SARS for Airline Flight Crews, Cargo and Cleaning Personnel, and Personnel Interacting with Arriving Passengers (2004).	N/A	N/A	N/A	See WHO recommendations. – AND – After the arrival of the airplane, the ill passenger should be separated from exposed and asymptomatic passengers, placed in an isolation facility and assessed medically. All other passengers should be assessed for illness and types of exposure to the index case and other potential SARS exposure. They should also be informed about SARS and advised to seek medical attention if they develop any symptoms compatible with SARS within 10 days of the flight.
RKI: Fortgesetzte SARS-Surveillance: Empfehlungen zum Umgang mit Kontaktpersonen bei erneutem Auftreten von Schwerem Akuten Respiratorischen Syndrom (SARS) in der Nach-Ausbruchsphase.	N/A	N/A	N/A	RKI defines Contact Categories 1 and 2 in relation to the risk of exposure/infection. All on-board contacts are considered Category 1 if they were within a two-metre distance from the index case or had contact with index case's body fluids or intimate contact. For contacts in Category 1, home isolation for 10 days after having contact with the index case, and health monitoring for 10 days after having contact with the index case is recommended. On-board contacts fall under Category 2 if they stayed in the same closed environment as the index case, at a distance of more than two metres from the index case. RKI recommends that Category 2 contacts should be asked to provide detailed contact information and receive information about signs and symptoms of SARS. In addition, their body temperature should be monitored daily for 10 days after contact with the index case. Immediate consultation of local public health services or other healthcare providers is recommended.
Public Health Agency of Canada: SARS and air travel: Interim guidelines for prevention and control. (2003)	N/A	N/A	N/A	See WHO recommendations.
NSW infection control guidelines for SARS (2003)	N/A	N/A	N/A	See WHO recommendations.
US Aerospace Medical Association (ASMA) Medical Guidelines Task Force: Emerging infectious disease including SARS; guideline for commercial air travel and medical transport.	N/A	N/A	N/A	See WHO recommendations.
IATA Suspected communicable disease: General guidelines for cabin crew (2006).	N/A	N/A	N/A	See WHO recommendations. – AND – If the facemask is not tolerated by the passenger, crew members should wear facemasks to protect themselves.

Expert opinion

There are no reported cases of transmission before the onset of symptoms [57].

Based on WHO data, transmission is most likely from severely ill patients or from those experiencing rapid clinical deterioration, usually during the second week of illness [58].

In general, there is little information regarding the exact conditions of SARS transmission on board of airplanes. We retrieved some evidence for on-board transmission in flights < 8 hours and for transmission to contacts seated up to seven seating rows from index cases. It remains unclear whether these findings should be considered sufficient criteria for initiating contact tracing for flights < 8 hours and if contact tracing can be limited to 1–7 seating rows around the index case. When taking into account the public health risk of SARS, a comprehensive contact tracing of all passengers and crew should be carefully considered in all SARS events.

Developing a contact tracing algorithm that fits all situations is next to impossible. But there are some basic concepts that apply to all situations, e.g. breaking the chain of infection makes more sense in the early phase of re-emergence. When making a decision to contact trace in a SARS event, a separate risk assessment has to be conducted each time. Public health experts need to consider a variety of aspects, such as the symptoms of the index case while on board, the global epidemiological situation for SARS (interpandemic/pandemic), and the objectives of contact tracing (breaking the chain of infection, scientific research).

3.4 Meningococcal disease

Results from the survey

11 EU Member States responded to a questionnaire on criteria for initiating contact tracing for meningococcal-related events. 8/11 agreed that contact tracing was necessary.

Results from literature search and event article analysis

We identified nine events: four through peer-reviewed event articles, two through grey literature event articles, and three through telephone interviews [59–64]. Peer-reviewed event articles originated from Australia, Germany, Israel and the USA. The number of days after which a contact tracing was initiated ranged between one and five days. The exact reasons for contact tracing were not obtainable.

A comprehensive search (i.e. an attempt to contact all passengers of flights where there was a case on board) was undertaken in 4/9 events. Crews were contacted in 4/9 events. Traced contacts were close contacts (4/9), next-seat passengers (2/9) or business contacts travelling on board (1/9). Methods of active contact tracing were passenger locator cards (2/9), passenger manifests (5/9), telephone contacting (4/9) and addressing passengers with a questionnaire (4/9). In one event, passive case finding was conducted by a press release.

Flight details

The flight duration for events ranged between 2 and 15 hours. Information on ground delays was not available in 9/9 events. Information on the functionality of HEPA systems was given for only one event (not functioning, no information for on-board transmission available in this event).

Index cases

The median age of index cases was 38 years. Information on index cases' symptoms were obtainable for 8/9 events; index cases showed a range of symptoms including headache (2/9), vomiting (1/9), photophobia (1/9), cough (3/9), fever (3/9), petechiae (1/9), influenza-like illness (1/9), rash and general malaise (1/9). 2/9 were asymptomatic during the flight.

On-board transmission

We found evidence for on-board transmission in 1/9 events. The evidence for on-board transmission in this event was high since the molecular structure of the strains found in the index person and the contact person was a perfect match. The two passengers had not met before the flight and there was no common exposure. In another five events, no transmission was found, yet evidence for non-transmission was less conclusive. In three events, information on transmission was not mentioned at all. Table 7 gives an overview of meningococcal events.

Contacts

All together, 17 contacts were identified in nine events. Of these, only one was found to be infected on board.

Results from the guideline search

There are several guidelines directly addressing the issue of passenger air travel related to *Neisseria meningitides* [65–69]. The CDC and the Connecticut Department of Public Health recommend evaluating the need for chemoprophylaxis for household members travelling with the index case or passengers who have had direct contact with respiratory secretions/were seated next to the index case during prolonged flights ≥ 8 hours. The Public Health Agency of Canada mentions that chemoprophylaxis for fellow passengers is not recommended in the

UK unless the index case has been identified as a close contact. (In its guidance for public health management of meningococcal disease, the UK Health Protection Agency does not recommend that next-seat passengers of index cases should be treated with chemoprophylaxis. The same opinion is held by the 'Working group on bacterial meningitis and related conditions' of the Irish Department of Health and Children [67–69].) It is unclear whether the Canadian authorities agree with this recommendation. Nevertheless, Canadian authorities recommend that contacts of meningococcal cases should be contact traced if these cases were travelling while still infectious (seven days before the onset of symptoms; up to 24 hours after the onset of effective treatment), if the flight took place within the last ten days, and the total time spent on the aircraft was at least eight hours [67].

Expert opinion

The incubation period of meningococcal disease is three to four days and ranges between 2 and 10 days. It can last longer because invasive diseases show colonisation patterns of variable duration [70]. The rate of secondary cases among close contacts is highest immediately after the onset of symptoms in the index case [71].

Persons at risk are those directly exposed to the index case's oral secretions: kissing and mouth-to-mouth resuscitation, but also medical staff managing endotracheal intubation or handling endotracheal tubes). Further risk factors for becoming ill are asplenia, terminal complement deficiency (C3, C5–C9), and HIV infection [71]. Risk groups prone to an increased risk of infection should be given priority when contact tracing. For close contacts, chemoprophylaxis is ideally administered within the first 24 hours, and no later than 14 days after exposure [71].

Among all surveyed events, there was one event where transmission possibly occurred during an 11-hour flight during which two passengers contracted serogroup B meningococcal disease (onset of symptoms two and five days after landing, respectively). The two passengers were seated 12 rows apart; according to reports, one passenger walked repeatedly around the aircraft, while the other one was seated in an aisle seat [62]. Surveillance data have shown that only < 3 % of cases are due to secondary transmission, implying that most transmissions occur from asymptomatic carriers [71,72].

It is not known whether the dry air in aircraft might facilitate the formation of droplet nuclei or what the exact effects of the dry cabin environment are on large droplet transmission. For all types of transmission, prolonged close contact is essential. The vertical pattern of air circulation in airplanes with little horizontal air flow, combined with the filtration of recirculated air with HEPA filters, probably requires contact or close proximity for transmission to occur on board an aircraft [5,73].

The information obtained and summarised above indicates a low risk of transmission on board of aircraft. Nevertheless, due to the severity of meningococcal disease, contact tracing can be considered for persons sitting next to the suspected or laboratory-confirmed index case, and for persons who were directly exposed to oral secretions of the index case, so that post-exposure prophylaxis can be administered.

Provided that the vaccination status for contacts is known, information on the serogroups of index cases is helpful. Nevertheless, waiting for the results of serogrouping is not advisable as serogroup B (non-vaccinable) is the most common serogroup in Europe. Administering PEP to contacts should have the first priority. The need for scientific studies should add an additional incentive to improve contact tracing in meningococcal events.

Table 7. Overview of meningococcal events found in event articles and telephone interviews

Reference	Country	Year of event	Flight time including ground delay (hours)	Ground delays?	HEPA filters functional?	Index patient's age	Index patient's symptoms	On-board trans-mission?	On-board transmission/ non-transmission: evidence level	Number of passengers traced/ infected	Infected contacts: seat rows distance from index case
Bar-Oz et al (2003). Letter in: Emerg Inf Dis 9: 757-758	Israel	2000	11	unknown	unknown	20	malaise, numbness of feet, rash	unknown	-	unknown; close contacts of index case provided with PEP immediately	unknown
CDC, MMWR Weekly, June 15, 2001, 50 (23); 485-9.	USA	2001	8	unknown	unknown	62	unknown	no	medium	1/2 contacts successfully traced; not infected. Information on second contact not available	unknown

Reference	Country	Year of event	Flight time including ground delay (hours)	Ground delays?	HEPA filters functional?	Index patient's age	Index patient's symptoms	On-board trans-mission?	On-board transmission/ non-transmission: evidence level	Number of passengers traced/ infected	Infected contacts: seat rows distance from index case
Grey literature. RKI: Epid. Bull. 15/2001	Germany	2001	3	unknown	unknown	57	No symptoms during flight; two days later: fever, vomiting and progress to Waterhouse-Friderichsen syndrome.	unknown	-	unknown; two passengers seated next to the index case traced successfully, PEP administered.	unknown
O'Connor BA et al. Commun Dis Intell. 2005; 29(3): 312-4	Australia	2003	15	unknown	unknown	68	Index patient asymptomatic. Three days after flight, patient shows fever, diarrhoea , vomiting and petechiae; both index patient and infected contact recover after antibiotic treatment.	yes	high: genotyping suggested epidemiological link; serogroup B	1/9 identified contacts infected	1; twelve rows
Riley LK. Aviat Space Med Vol 77, No.7. July 2006	USA	2005	11	unknown	unknown	unknown	headache, vomiting, photophobia	no	unknown	-	unknown
Telephone interview	Germany	2005	4	unknown	no	38	cough, fever, petechiae	no	unknown	-	unknown
Grey literature RKI. Epidemiol. Bulletin 24/2005	Germany	2005	< 8	unknown	unknown	unknown	cough	unknown	-	CT unsuccessful	unknown
Telephone interview	Greece	2008	2	unknown	unknown	27	fever	no	unknown	0/4 identified contacts infected	unknown
Telephone interview	Germany	2008	2	unknown	unknown	29	influenza-like illness	no	unknown	unknown	unknown

3.5 Measles

Results from literature search and event article analysis

We identified six events in six peer-reviewed event articles reporting cases of measles that occurred on board airplanes. One additional event was acquired through cross-referencing [74]. All covered events took place between 1981 and 2005. Contact tracing for measles events was initiated by the USA (4), Brazil (1) and Israel (1). A comprehensive search was conducted for four events. Information was not available for two events. Active case finding was undertaken in 5/6 events. Sources for active case finding were passenger manifests (3/6), passenger locator cards (3/6), customs declarations (2/6) and other methods such as on-board announcements, questionnaires, and letters to hotel guests.

Flight details

For the two events with on-board transmission, the flight duration was recorded as eight hours or more. No information was retrievable about the functionality of HEPA filter systems. In one event, a ground delay of one hour was reported; on-board transmission occurred.

Index cases

The age of index cases ranged between 4 and 36 years. Information on the index cases' symptoms was available in only two events. In 1/4 cases, the index case — a 36 years old male with unknown symptoms — infected two passengers seated three and eight rows, respectively, from the index case's position. In another event, a child of unknown age infected two fellow passengers. In one of the events with on-board measles transmission, a ground delay was reported. There was no information available on the function of HEPA filter systems in all four events where on-board transmission of measles was reported. Post-exposure prophylaxis was administered in all six events where measles transmission was found or suspected. An overview of measles events is given in Table 8.

On-board transmission

We found evidence for on-board measles transmission in 5/6 events. Evidence obtained was high in one event, medium in three events, and unknown in another event. Seating information for the contact was available only for one event that was rated as 'high evidence for on-board transmission'; two passengers were infected in rows 2 and 8, as counted from the index case.

Contacts

In a total of six measles events, 6/122 contacts were infected on board.

Results from the guideline search

No specific guidelines for contact tracing for measles and air travel were found through the guidelines search. We found generic recommendation algorithms for the management of measles case contacts that we used as a basis for the expert discussion [75]. HPA advises to administer PEP (passive immunisation with intramuscular HNIG) as soon as possible after exposure if the index case is suspected of measles, based on epidemiology and clinical features [76].

Table 8. Overview of measles events obtained from event articles and telephone interviews

Reference	Country	Year of event	Flight time (hours)	Ground delays?	HEPA filter functional?	Index patient's age	Index case's symptoms	On-board trans-mission?	On-board trans-mission: evidence level	Number of passengers infected	Distance of contacts (seat rows)
CDC. Interstate importation of measles following transmission in an airport — California, Washington, 1982. MMWR Morb Mortal Wkly Rep. 1983 Apr 29;32(16):210, 215-0, 216.	USA	1981	unknown	unknown	unknown	27	index case symptomatic, (not specified)	yes	medium	1	unknown
Amler RW, Bloch AB, Orenstein WA, Bart KJ, Turner PM Jr, Hinman AR. Imported measles in the United States. (1982) JAMA 248(17).	USA	1982	unknown	unknown	unknown	(child)	yes, prodromal stage symptoms	yes	unknown	2	unknown
Slater PE, Anis E, Bashary A. An outbreak of measles associated with a New York/Tel Aviv flight. Travel Med Int 1995;13:92-5.	Israel	1994	10	1	unknown	4	no	yes	medium	unknown	unknown
Amornkul PN, Takahashi H, Bogard AK, Nakata M, Harpaz R, Effler PV. Low risk of measles transmission after exposure on an international airline flight. J Infect Dis 2004 May 1;189 Suppl 1:S81-S85.	USA	2000	7	unknown	unknown	17	cough, fever, headache, rash, sore throat, conjunctivitis	unknown	-	-	-
CDC. Postexposure prophylaxis, isolation, and quarantine to control an import-associated measles outbreak. Iowa, 2004. MMWR Morb Mortal Wkly Rep 2004 Oct 22;53(41):969-71.	USA	2004	8	unknown	unknown	unknown	unknown	yes	medium	1	unknown
de Barros FR, Segatto TC, Luna E: Measles transmission during commercial air travel in Brazil. (Letter in: Journal of Clinical Virology 36 (2006) 235–236).	Brazil	2005	unknown	unknown	unknown	36	unknown	yes	high	2/118	3–8

Expert opinion

Cases are infectious one to two days before the onset of rash [70], and probably several days before the onset of symptoms [77].

Measles are most contagiousness during the late prodomal period, when cough and coryza are peaking [78].The incubation period lasts 6 to 19 days, the median incubation period is 13 days [77].

The shedding occurs between two days before and three days after the onset of symptoms [77]. Therefore, contact tracing should be considered if the patient travelled two days prior to the onset of symptoms until four days after the onset of symptoms.

Contact tracing for measles events in the EU cannot be generally recommended since measles are vaccine-preventable and the majority of air passengers can be considered as non-susceptible. It is particularly important to

consider the epidemiological situation of measles in the index case's country of origin and in the destination country, especially in regard to IHR 2005 relevancy.

Unvaccinated pregnant women are particularly vulnerable: measles during pregnancy are associated with spontaneous abortion and premature delivery as the clinical course of measles is likely to be more severe during pregnancy [78]. When considering contact tracing, this group deserves special attention. Also, any immunocompromised passengers and infants < 1 year are at a higher risk of severe clinical courses and should be traced early and provided with post-exposure prophylaxis [77].

All flights during which measles were transmitted were at least eight hours long. Since measles are highly infectious, we consider the flight duration of little relevance when initiating contact tracing. We obtained evidence that transmission of measles occurred in passengers seated up to eight rows from the index case. When the decision for contact tracing is made, eight rows is the minimal distance that should be considered for contact tracing. However, due to the high transmissibility of measles it would be more sensible to contact trace all passengers and crew members — provided that the epidemiological situation and susceptibility for measles in the countries of origin and destination were carefully considered.

If the decision for contact tracing is made, we recommend that contact tracing is initiated if the flight occurred within the last two weeks prior to the index case's diagnosis in order to be able to implement containment measures or even administer PEP or IG.

There was no information retrievable indicating that HEPA filters on board influence transmission. Therefore, our recommendations cannot take the functionality of HEPA filters into consideration.

3.6 Rubella

Results from literature search and event article analysis

We did not find any peer-reviewed event articles, grey literature event articles or experts that could provide information on rubella events related to passenger air travel.

Results from the guideline search

No air-travel-related guidelines for contact tracing for rubella events were retrieved from the guidelines search. We found a generic recommendation algorithm for managing rubella case contacts which we used as a basis for the expert discussion [75].

Expert opinion

The incubation period for rubella is 15 to 20 days [70]. The exact period of infectiousness for rubella is not known. Maximum contagiousness occurs during the prodomal period in adults [70] and during the eruption of the rash [79]. Shedding occurs between 13 days before and 6 days after the onset of symptoms [70]. We recommend that patients that are contagious two weeks before and one week after the onset of symptoms should be considered for contact tracing. The diagnosis has to be laboratory confirmed, since clinical diagnosis is unreliable.

A general recommendation for the contact tracing of rubella events in the EU cannot be made as rubella is vaccine-preventable and the majority of air passengers can be considered non-susceptible. It is particularly important to consider both the epidemiological situation of rubella in the index case's country of origin and in the destination country when assessing the susceptibility of affected passengers. Between 1998–2002, several countries had an incidence of reported cases of rubella below 1 per 100 000 and endemic rubella cases were virtually non-existent, as, for example, in the USA [80,81].

In case of a positive decision for contact tracing after assessing susceptibility, informing susceptible pregnant women of their potential exposure on board should be considered. Infection within the first 11 weeks of gestation may lead to a pattern of birth defects called congenital rubella syndrome in up to 90 % of fetuses [80]. If infection occurs after the first trimester, 16-18 % of babies of mothers infected between 13-20 weeks develop rubella induced defects; after 20 weeks, less than 2 % develop deafness and retinopathy [82].

If the decision for contact tracing is made, we recommend that contact tracing is initiated if the flight occurred within the last two weeks. Containment measures through PEP vaccination should be considered as early as possible after exposure.

Through our literature review, we retrieved no events that involved rubella. Since rubella is one of the more contagious illnesses, we suggest that the decision for or against contact tracing should not be based on flight time. Persons seated within two rows of the index case should be considered for contact tracing. In addition, all cabin crew members in the index case's seating section should be considered for contact tracing. For extended contact

tracing, any person sitting within +/- 2 rows of the index case should be traced, as well as persons who experienced direct exposure.

Our recommendations cannot take into consideration the functionality of HEPA filter systems.

3.7 Diphtheria

Results from literature search and event article analysis

We did not find any peer-reviewed event articles, grey literature event articles or any experts that could provide information on passenger air travel and diphtheria.

Results from the guideline search

The Public Health Agency of Canada defines close contacts of diphtheria index cases as household members, friends, relatives and caretakers who regularly visit, sexual contacts (including kissing), persons sharing the room at school or work, and healthcare staff exposed to an infected person's oropharyngeal secretions. Regardless of their vaccination status, those contacts should be kept under daily surveillance for seven days beginning on the day of the last contact with the index case. Contacts whose occupations involve food handling (especially milk) or close contact to non-immunised persons should be excluded from their work until bacterial examination proves them not to be carriers [83].

In their guidance for consultants in communicable disease control, Bonnet and Beg mention that persons sleeping in the same household as the index case, kissing or sexual contacts of the index case, healthcare workers who have given mouth-to-mouth resuscitation to an index case or who have dressed the wounds of a cutaneous case are at the greatest risk of getting infected [84].

Expert opinion

If the disease is untreated, a patient stays infectious for two to three weeks. It is unclear if the infectious period starts with the onset of symptoms or earlier, since there is an asymptomatic carrier status. With antibiotic treatment the patient is rendered non-infectious within 24 hours [85]. Infectiousness is higher in symptomatic patients than in asymptomatic carriers [86]. Although the incubation period is only two to five days [87] (rarely eight days [86]), infectiousness lasts up to three weeks. We suggest that no more than 14 days should have passed when considering contact tracing, which allows for the implementation of containment measures and necessary preventive measures. In the WHO Region Europe suspected (possible), probable or confirmed cases of diphtheria are notifiable to the local health authorities [85].

Since diphtheria is associated with high lethality (5–10 %), we suggest that flight duration should not be a criterion when contact tracing is considered.

As we are lacking evidence for transmissibility on board, and in analogy to our TB guidelines, we recommend contact tracing for 1) persons seated within two rows of the index case, 2) members of the cabin crew in the index case's seating section, and 3) any person with direct exposure to the index case. In addition, we recommend contact tracing any person exposed to the index case's oral secretions or exudates from infected skin lesions. Since diphtheria is transmissible through fomites, contact tracing is recommended for all persons standing or sitting close to the index case, being frequently coughed or sneezed at, or having received objects from the index case.

When assessing the susceptibility of passengers, it is essential to consider the epidemiological situation for diphtheria in the index case's country of origin and in the destination country of the flight.

As there was no information retrievable that documents how on-board HEPA filter systems influence transmission, the role of HEPA filters in on-board diphtheria transmission remains inconclusive. The decision to conduct contact tracing should therefore be taken without any consideration of HEPA filter systems.

3.8 Ebola

Results from literature search and event article analysis

We did not find any event articles in the peer-reviewed literature related to Ebola virus. Experts interviewed reported no events related to Ebola virus. We retrieved one event article from the grey literature that reported the 1996 case of an ill index case from Gabon with rhabdomyolysis, erratic body temperature of up to 42 °C, and signs of hepatitis. The patient was flown to Johannesburg for hospital treatment [88]. During the time of flight,

the diagnosis (Ebola haemorrhagic fever, later laboratory confirmed) was not known. No infections occurred during that flight, and little information exists about the hygienic precautions on board.

Results from the guideline search

We identified one specific guideline addressing Ebola fever in the context of air travel [89]. CDC recommends the following precautions for everyone who handled a contaminated package, or cleaned a contaminated aircraft: self-monitoring of health for 21 days following the exposure. Persons developing a sudden fever, chills, muscle aches, rash, or other symptoms consistent with Ebola virus infection should seek immediate medical attention.

More generic guidelines on infection control for Ebola fever recommend the isolation of suspected or proven Ebola cases, protective equipment for persons involved in contact tracing when index cases are symptomatic, and the isolation of healthcare workers suspected of infection. Persons with percutaneous or mucocutaneous exposure to blood, body fluids, secretions or excretions from a patient with suspected haemorrhagic fever should immediately wash the affected skin surfaces with soap and water [90]. The authors of a review article about viral haemorrhagic fevers (VHF) recommend that contacts should be differentiated by risk exposure [91]:

Category Ia: Contacts with a high risk

- Persons who had skin injuries, direct contact with blood or other body fluids, or the patient's tissue (e.g. through needle prick injuries, during an invasive intervention, resuscitation, or autopsy).

Category Ib: Contacts with an increased risk

- Persons who had contact with blood or other body fluids, or the patient's tissue on intact skin or through aerosol contact (e.g. nursing and medical staff, laboratory staff, cleaning staff, possibly staff of external laboratories).
- Persons who had contact with the blood, excretions, tissue or the carcass of an animal which was infected with VHF.

Category II: Contacts with a moderate risk

- Persons who nursed a patient or processed examination samples of the patient, e.g. household members living in a relationship or sharing a flat, nursing friends and/or neighbours, possibly physicians consulted prior to hospital admission, ambulance staff, nursing hospital staff (including physicians, cleaning staff, etc.).
- Persons who had direct contact with the corpse of a patient who died from VHF or with persons suspected of having had the disease, prior to the closing of the coffin.
- Persons who had contact with a VHF-infected animal.
- Persons who were seated in the immediate neighbourhood of an index patient showing symptoms during a longer flight.
- Persons who had direct contact with the clothes, linens or other objects that could have been contaminated with the patient's blood, urine or body fluids.

Category III: Contacts with a low risk

- Any kind of contact with the index patient (e.g. staying in the same room, use of the same means of public transportation, general social contact).
- Medical staff, provided that adequate full-protective overalls and breathing masks were worn.

Based on these recommendations, most airplane contacts pose a low to moderate risk of exposure.

Expert opinion

No evidence was available on the potential of transmission of the Ebola virus during flights. Thus, the recommendations for risk assessment during flights should be based on general Ebola virus recommendations and consider the transmissibility of Ebola. The incubation period for Ebola is between 2 and 21 days [92]. The transmissibility of the Ebola virus in outbreak situations ranges between 16 % and 61 % of all cases [93,94]. Lethality is between 77 % and 81 % [95-97]. Some authors have noted an absence of illness among persons who were exposed to cases in confined spaces, but had no physical contact with the patient/s, and conclude that there is no risk of airborne transmission [98]. Although most airplane passengers — due to the virus's high pathogenicity and mortality — have a low to moderate risk of exposure, we still recommend immediate and comprehensive contact tracing (i.e. all passengers and crew contacts) when index cases are laboratory confirmed.

Due to the high pathogenicity of Ebola and an expected high susceptibility in airplane passengers, contact tracing should be considered when a potentially infectious, laboratory-confirmed index case of Ebola fever was on board a

flight within the last 26 days (longest incubation period 21 days plus five days due to possible non-specific symptoms during the first five days). Contact tracing should always be initiated if an index case has been symptomatic on board or was flying within four days before the onset of symptoms. Contact tracing should be considered for the entire cabin and crew.

Since there is no evidence that the Ebola virus is transmitted by air, the decision to conduct contact tracing should be taken without any consideration of HEPA filter systems.

3.9 Marburg virus

Results from literature search and event article analysis

We did not find any event articles in the peer-reviewed literature related to Marburg virus. Experts interviewed reported no events related to Marburg virus.

Results from the guideline search

We identified one specific guideline addressing Marburg fever in the context of passenger air travel [99]. In its 'Interim guidance about Marburg virus infection for airline flight crews, cargo and cleaning personnel, and personnel interacting with arriving passengers', CDC recommends to:

- keep the sick person separated from close contact with others as much as possible;
- provide the sick passenger with a surgical mask (if the passenger can tolerate wearing one) to reduce the number of droplets expelled into the air by talking, sneezing, or coughing (tissues can be given to those who cannot tolerate a mask); and
- make all personnel wear disposable gloves for direct contact with blood or other body fluids (see IATA's Guidelines for Suspected Communicable Diseases).

CDC recommends that everyone who handled a contaminated package or cleaned a contaminated aircraft should self-monitor their health for ten days following the exposure. If a passenger develops a sudden fever, chills, muscle aches, rash, or other symptoms consistent with Marburg virus infection, one should seek immediate medical attention. More generic guidelines on infection control on Marburg virus infection recommend that persons involved in contact tracing of suspected or proven Marburg cases should wear protective equipment when index cases are symptomatic. Healthcare workers suspected to be infected should be isolated. Persons with percutaneous or mucocutaneous exposure to blood, body fluids, secretions or excretions from a patient with suspected haemorrhagic fever are recommended to immediately wash the affected skin surfaces with soap and water [90].

Expert opinion

Incubation period for Marburg fever ranges between 2 and 14 days [92]. In 1980, a Kenyan Marburg virus patient was airlifted to Nairobi, and one secondary case was most likely infected during resuscitating the index case who suffered from severe haemoptysis. However, the secondary case seems to have been infected on ground; the air ambulance staff was not infected [100]. In an outbreak of Marburg haemorrhagic fever in Germany, 25 index cases infected five secondary cases; transmission in the affected medical staff occurred most likely through needlestick injury or similar accidents [101]. Bausch et al. examined risk behaviours for Marburg virus infection. Living under the same roof, being in the same room or even touching an index case's skin was not related to an increased risk, but touching of cadavers or coming in contact with body fluids was associated with an increased infection risk [102]. Passengers seated within +/- 2 rows should be considered for contact tracing as should be anybody on board with a known exposure to the index case's body fluids.

Contact tracing should always be considered when potentially infectious, laboratory-confirmed index cases of Marburg fever were on a flight within the last 19 days (longest incubation period 14 days, plus five days due to possible non-specific symptoms within the first five days). Although there is no evidence that index cases are infectious before the onset of symptoms, all index cases falling ill up to three days after a flight should be included. Contact tracing should be considered for the entire cabin and crew due to the high pathogenicity of Marburg fever and the high susceptibility in the general population.

3.10 Lassa

Results from literature search and event article analysis

We identified seven events related to Lassa fever, three of which came from the peer-reviewed literature [103–105]. We held three telephone interviews involving the contact tracing of an index case with Lassa fever. In

addition, we retrieved one event from grey literature [106]. The incidents took place between 2000 and 2006; France, Germany and the USA were the reporting countries that initiated contact tracing. The time for initiating CT ranged between 5 and 10 days. For two other events the time delay was unknown.

In all surveyed cases, contact tracing was initiated because the index cases were symptomatic on board, the pathogen was transmissible from human to human, and the incubation period still allowed for preventive measures to be taken. Contact tracing was done by actively contacting cases with the help of passenger manifests provided by the airlines. Customs declarations and passenger locator cards were not used in the three events involving Lassa fever.

Contact tracing was initiated in all seven events where Lassa fever was involved. A comprehensive search was initiated in two events, and in two events passengers could be traced because their relative seat location in relation to the index case's seat was known. Contact categories according to risk exposure were applied in two events.

Flight details

The flight duration was two hours in one event, > 8 hours in another two events, and unknown in the two remaining events. Information on the functionality of the HEPA filter systems was retrievable from only one event (functional).There was no ground delay reported for any of the five events.

Index cases

The age of index cases ranged from 23 to 68 years, 4/5 index cases were symptomatic on board, symptoms reported were fever, cough, headache, vomiting and haemorrhage.

Contacts

Overall, 179/293 (61.1 %) contacts were successfully traced in seven events.

Contact categories (according to risk exposure) were applied in two events: close contacts were considered to be at a higher risk of exposure.

On-board transmission

179/293 contacts were successfully traced, none were infected. Evidence for non-transmission was high for 55/179 (30.7 %) and medium for 124/179 (69.3 %) successfully traced contacts. Table 9 gives an overview of results for Lassa fever.

Results from the guideline search

We identified no specific guidelines addressing Lassa fever in the context of passenger air travel. More generic guidelines on infection control for Lassa fever recommend that persons involved in contact tracing of suspected or proven Lassa cases should wear protective equipment when index cases are symptomatic. Healthcare workers suspected to be infected should be isolated.

Table 9: Overview of Lassa fever events

ID / Type of event	Country	Year of event	Flight time including ground delay (hours)	Ground delays?	HEPA filter functional?	Index patient age	Index patient's symptoms / lab status during flight	On-board trans-mission?	On-board transmission / non-transmission: evidence level	Number of passengers infected	Distance of contacts (seat rows)
Cooper et al. BMJ Vol (1982); 285: 1003-05	UK	1981	> 8	unknown	unknown	18	Asymptomatic during flight, fever five days before the flight: fever, abdominal pain, vomiting and headache eight days after flight.	unknown	High: 159/173 (91.9) ground contacts successfully traced: no transmission.	-	-
Haas W, Breuer Th. Imported Lassa Fever in Germany: Surveillance and Management of Contact Persons. CID 2003:36 (15 May)	Germany	2000	> 8	unknown	unknown	unknown	fever, cough	no	High: 51/56 (91 %) of categorised contacts underwent serological testing, none of them were infected.	-	-

ID/Type of event	Country	Year of event	Flight time including ground delay (hours)	Ground delays?	HEPA filter functional?	Index patient age	Index patient's symptoms/lab status during flight	On-board trans-mission?	On-board transmission/ non-transmission: evidence level	Number of passengers infected	Distance of contacts (seat rows)
Telephone interview	Germany	2000	3	unknown	yes	23	cough, fever, haemorrhage, headache	no	High: 34/34 (100.0 %) contacts successfully traced.	-	-
Crowcroft et al Journal of Infection (2004); 48, 221-228	UK	2000	> 8, air ambulance	unknown	unknown	unknown	fever	no	Medium: 78/125 (62 %) contacts, including five air ambulance staff, successfully traced.	-	-
CDC: Imported Lassa fever – New Jersey, 2004. MMWR Morb Mortal Wkly Rep 2004; 53: 894-7.	USA	2004	> 8	unknown	unknown	unknown	fever, chills, sore throat, diarrhoea, back pain	no	High: 5/5 passengers classified as high risk contacts (family members) and 16/19 passengers classified as low risk were not ill within one incubation period.	-	0–3 rows
Telephone interview	France	2006	10	yes	unknown	68	fever, headache haemorrhage, rash	no	Medium: 10/18 (55.6 %) contacts successfully traced.	-	-
Telephone interview	Germany	2006	10	yes	unknown	68	fever, headache haemorrhage, rash	no	Medium: 36/92 (39.1 %) contacts successfully traced.	-	-

Expert opinion

The incubation period for Lassa fever ranges between 6 and 21 days. The virus is detectable in urine between three and nine weeks after infection [107]. Up to 80 % of infected cases have only mild or no observable symptoms [107].

Our review identified a total of 179/293 (61.1 %) contacts exposed to Lassa patients during air travel; of those, none were infected, indicating that the risk of human-to-human transmission of Lassa virus during air travel is low.

Since the majority of passengers are expected to be highly susceptible to Lassa fever, contact tracing should be considered if potentially infectious, laboratory-confirmed index cases of Lassa fever were on a flight within the last 26 days (longest incubation period 21 days, plus five days as first symptoms may occur late). Although there is no evidence that index cases are infectious before the onset of symptoms, index cases falling ill within three days after a flight should be included.

It can be helpful to categorise contacts into high-risk contacts such as family members, persons coming into contact with urine, or persons having unprotected exposure of skin or mucous membranes to blood or other bodily secretions of index cases.

Although our literature review indicates that Lassa fever transmission on board is unlikely, contact tracing for passengers seated within +/- 2 seating rows around the index case may have to be considered, given the morbidity in a susceptible population. In addition, contact persons with 'special exposure' during a flight should be traced.

When assessing the risk, the different phases of a disease must be considered as well. In addition to the degree of exposure, the acute phase of the disease at the time of exposure may also influence transmission [104].

When dealing with asymptomatic index cases, one has to keep in mind that even asymptomatic cases may pose a minor risk of transmission since viral shedding can be detected in urine up to nine weeks after infection. Taking into account that the risk of transmission even from symptomatic cases is low, contact tracing should not be conducted routinely, but it can still be initiated after assessment on a case-by-case basis.

3.11 Smallpox

Results from literature search and event article analysis

We identified one event related to air travel from the peer-reviewed literature [108] and two more events though cross-referencing. In 1970, a symptomatic index case that was thought to be suffering from dysentery had flown

from Afghanistan to Denmark. After smallpox had been diagnosed, a total of 550 contacts were isolated between day 8 and day 17 after the suspected contact. The patient eventually died [108], but no secondary cases occurred. In two other events dating back to the 1950s, passengers infected with smallpox had been on board of airplanes; transmission did not take place [109–110].

Results from the guideline search

We did not find any specific guidelines addressing smallpox in the context of passenger air travel.

Expert opinion

The incubation period of smallpox is usually 12–14 days (range 7–17) during which there is no evidence of viral shedding. During this period, the person looks and feels healthy and cannot infect others. The transmission of smallpox is most efficient during close contact with an infected person. Some experts have estimated today's rate of transmission to be more in the order of ten new infections per infected person [111]. The estimated highest secondary transmission rate is between three and six days after onset of fever [112].

If the aim of contact tracing is to inform fellow passengers and crew of possible exposure to an infectious laboratory-confirmed smallpox case on board, the flight had to occur during the infectious period.

If the aim of contact tracing is to confirm or discard the possibility that the aircraft was the location of a deliberate release, in which passengers were exposed to smallpox virus, the flight had had to occur during the incubation period.

Comprehensive contact tracing should be initiated: all passengers and crew members should be traced. These recommendations only apply to the current epidemiological situation (smallpox is declared eradicated). If this situation changes these recommendations have to be revised.

3.12 Anthrax

Results from literature search and event article analysis

We did not obtain any peer-reviewed event articles, grey literature event articles, or expert interviews on the issue of anthrax related to passenger air travel.

Results from the guideline search

We did not retrieve specific guidelines on anthrax related to passenger air travel.

Expert opinion

Anthrax is not transmitted by air from person to person. Cutaneous anthrax is difficult to transmit through direct contact with infected tissues [113].

There are two scenarios where contract tracing should be considered:

1. A person infected with anthrax was on board a flight: since human-human transmission does not occur, contact tracing does not have to be considered.

2. If officials conclude that anthrax spores were deliberately released (after having excluded other means of release/exposure), contact tracing should be considered in order to locate the source of exposure and prevent further infection (spores may contaminate objects on board, including the passengers' clothes and personal belongings).

Deliberate release should be considered 1) if a single confirmed case of cutaneous anthrax occurs in an individual who does not have routine contact with animals or animal hides; 2) if a single confirmed case of inhalation anthrax is identified, or 3) if two or more suspected cases of anthrax are linked in time and place to the flight in question [109]. Other causes and routes of on-board transmission, e.g. through animal hides or other animal products brought into the cabin (not necessarily related to bioterrorism), may also lead to the infection of passengers with no history of animal exposure and should therefore be assessed when considering contact tracing.

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Annex 1: Questionnaire used for event article analysis and expert telephone interviews

1. Key information for event

1.1 Country of interviewee or where publication originates from. _____

1.2 Year the event began [YYYY]. _____

1.3 Disease/pathogen found. _____ /unknown

1.4 Contact tracing performed? □ yes □ no □ unknown

If no, why was contact tracing not performed (please specify)?

_____

If yes, contact tracing started how many days after the event? _____ days/unknown

1.5 Contact tracing initiated by □ your country □ other country (please specify)? _____

1.6 How many seat rows before/after the index patient did you consider for CT? +/- ____ rows/unknown

Or did you do a comprehensive search (entire passenger list searched)? □ yes □ no □ unknown

1.7 Did you contact cabin crew members after the event? □ yes □ no □ unknown

1.8 Did you apply any type of category to contact trace
(such as 'category 1= close contact of index patient by family member', 'category 2= air cabin crew', etc.).
Please specify: _____

2. Flight details

2.1 How long was the duration of the flight? _____ hours. □ unknown

2.2 Flight destination from_____ to_____. □ unknown

2.3 Were there any major ground delays (hours)? □ yes □ no □ unknown

If yes, please specify □ < 1 hour □ > 1 hour □ unknown

2.4 Was the on-board HEPA* filter system fully functional? □ yes □ no □ unknown

*High-efficiency particulate air

3. Reasons for launching contact tracing (CT) on occasion of this event

3.1 Pathogen transmissible human-to-human? □ yes □ no □ unknown

3.2 Threat of emerging pathogen circulation? □ yes □ no □ unknown

3.3 Resistant pathogen? □ yes □ no □ unknown

3.4 Index patient symptomatic? □ yes □ no □ unknown

3.5 Incubation period of pathogen allowing for action? □ yes □ no □ unknown

3.6 Duration of flight increased transmission possibility? □ yes □ no □ unknown

3.7 Bioterrorist potential of pathogen? □ yes □ no □ unknown

3.8 We followed national guidelines for contact tracing (CT). □ yes □ no □ unknown

3.9 We followed other guidelines for CT. □ yes □ no □ unknown

3.10 Other (please specify): _____

4. Method of CT

4.1 □ Active case finding launched.

□ Telephone contacting

□ Passenger manifest used

□ Passenger locator card used

□ Customs declaration used

□ Questionnaire

□ Other methods (please specify) _____

4.2 □ Passive case finding launched

□ Press release launched

□ Other methods (please specify) _____

4.3 □ Method unknown

5. Index patient

5.1 Age [years] _____

5.2 Sex □ male □ female □ unknown

5.3 Nationality _____

Symptoms of index patient

5.4 Index patient had symptoms: □ yes □ no □ unknown

Cough □ yes □ no □ unknown

Diarrhoea □ yes □ no □ unknown

Fever □ yes □ no □ unknown

Haemorrhage □ yes □ no □ unknown

Headache □ yes □ no □ unknown

Rash □ yes □ no □ unknown

Vomiting □ yes □ no □ unknown

Other (please specify) _____

5.5 How would you finally grade the level of infectiousness of the index case during that flight? □ low □ medium □ high

5.6 Contact information

	Total	Passengers		Crew
	(number/unknown)	Residents (number/unknown)	Non-residents (number/unknown)	(number/unknown)
All contacts identified (traced or not traced).				
All contacts successfully* traced.				
All contacts susceptible to disease (lacking immunity).				
All contacts successfully traced who are confirmed infected.				

*Case definition 'successfully traced': any passenger who was contacted through any case finding method and resulted in confirmation of infection/illness or not.

At what distance from the index patient did each of the contacts sit?

	Proximity to index patient (no. of seat rows/unknown)
Contacts who are confirmed infected (asymptomatic only)	
1	
2	
3	
Contacts who are confirmed infected *and* symptomatic	
1	
2	
3	

6. Final outcome

6.1 Did transmission take place on board the aircraft? □ yes □ no □ unknown

6.2 Evidence level for disease transmission: □ low □ medium □ high

7. Actions taken

7.1 Structured telephone interview with contacts? □ yes □ no □ unknown

7.2 Post-exposure prophylaxis (PEP) recommended for all contact persons? □ yes □ no □ unknown

If yes, how many contact persons actually received PEP? _____contacts/unknown

7.3 Other (please specify): _____

Annex 2: Variables list used for dataset

Platzierung in DB	Feldtyp / Frontend	Variablenname	Ausprägungen	Codierung der Ausprägung	Kann / muss
	Text [TTNNNN]	Event ID Ref.man.			kann
1	Ordinal [Drop-down]	Event source	Peer-reviewed literature. Grey literature. Telephone interview. ProMed. Other. Unknown.	1 2 3 4 5 9	
2	Ordinal [Drop-down]	Country of source for event (telephone interviewee or authors)	Austria Australia Belgium Bulgaria Canada China Czech Republic Cyprus Denmark Germany Estonia Finland France Greece Hungary Ireland Italy India Japan Latvia Lithuania Luxembourg Malta Netherlands Poland Portugal Rumania South Africa Sweden Slovakia Slovenia Spain UK USA Other Unknown	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 99	muss
3	Year [YYYY]	1.1 Year event began	Year [YYYY]		kann
4	Ordinal [Drop-down]	1.2 Disease/pathogen Found	TB including MDR SARS Measles Influenza incl. new subtype Ebola virus Smallpox Yersinia pestis Diphtheria Cholera Adenovirus Neisseria meningitidis Marburg Virus Norovirus Mumps Rubella Chickenpox Polio Haemophilus influenzae Staphylococcal food Poisoning Salmonellosis Crimean-Congo Haemorrhagic fever Lassa fever Rift Valley Fever Anthrax Other Unknown	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 99	muss
5	Ordinal [Drop-down]	1.3. Contact tracing performed?	Yes No Unknown	1 2 9	muss
6	Text	Frage 1.3.1 Contact tracing not performed — why?	Freitext		kann

Platzierung in DB	Feldtyp / Frontend	Variablenname	Ausprägungen	Codierung der Ausprägung	Kann / muss
7	Numerisch [NN]	1.3.2. If yes: contact tracing performed how many days after onset of event?	Numerisch [NN/99=unknown]	[NN/99=unknown]	muss
8	Ordinal [Drop-down]	1.4. Contact tracing initiated by which country?	Austria Australia Belgium Bulgaria Canada China Czech Republic Cyprus Denmark Germany Estonia Finland France Greece Hungary Ireland Italy India Japan Latvia Lithuania Luxembourg Malta Netherlands Poland Portugal Rumania South Africa Sweden Slovakia Slovenia Spain UK USA Other Unknown	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 99	muss
9	Freitext	1.4. Other country	Freitext		
10	List	1.5. Contacts traced: Distance from index patient in seating rows	Same row 1 row 2 rows 3 rows 4 rows 5 rows 6 rows 7 rows 8 rows 9 rows 10 rows (etc., up to 50) Unknown	0 1 2 3 4 5 6 7 8 9 10 usw. bis 50… 99	kann
11	Ordinal [Drop-down]	1.6. Crew contacted?	Yes No Unknown	1 2 9	muss
12	Freitext	1.7. Contact categories applied?	Freitext		kann
13	Numerisch [NNN]	2.1 Flight duration (hours)	[NN/99=unknown]	[NN/99=unknown]	muss
14	Feitext	2.2 Flight destination (from/to)	Freitext		kann
15	Ordinal [Drop-down]	2.3. Ground delays?	Yes No Unknown	1 2 9	muss
16	Numerisch [NNN]	2.3.1. Duration of ground delay	<1h >1h unknown	1 2 9	muss
17	Ordinal [Drop-down]	2.4. Hepa system on board functional?	Functional Non-functional Unknown	1 2 9	muss
18	Ordinal [Drop-down]	3.1. Reason contact tracing: human-human	Yes No Unknown	1 2 9	kann
19	Ordinal [Drop-down]	3.2 Reason contact tracing: Threat emerging pathogen	Yes No Unknown	1 2 9	kann
20	Ordinal [Drop-down]	3.3 Reason contact tracing: Resistant pathogen	Yes No Unknown	1 2 9	kann

Platzierung in DB	Feldtyp / Frontend	Variablenname	Ausprägungen	Codierung der Ausprägung	Kann / muss
21	Ordinal [Drop-down]	3.4 Reason contact tracing: Index patient symptomatic	Yes No Unknown	1 2 9	kann
22	Ordinal [Drop-down]	3.5 Reason contact tracing: Incubation period of pathogen allows action	Yes No Unknown	1 2 9	kann
23	Ordinal [Drop-down]	3.6. Reason contact tracing: Duration of flight increases transmission possibility	Yes No Unknown	1 2 9	kann
24	Ordinal [Drop-down]	3.7. Reason contact tracing Bioterrorist potential	Yes No Unknown	1 2 9	kann
25	Ordinal [Drop-down]	3.8. Reason contact tracing Followed national guideline	Yes No Unknown	1 2 9	kann
26	Ordinal [Drop-down]	3.9. Reason contact tracing Followed other guideline	Yes No Unknown	1 2 9	kann
27	Feitext	3.10. Specification of other than national guideline	Freitext		kann
28	Ordinal [Drop-down]	4.1. Method of contact tracing	Active case finding Press release Telephone contacting Passenger locator card Other	1 2 3 4 9	kann
29	Freitext	4.2. Other method of contact tracing	Freitext		kann
30	Numerisch [NNN]	5.1. Age of index patient	[NN/99=unknown]	[NN/99=unknown]	muss
31	Ordinal [Drop-down]	5.2. Sex of index patient	Male Female Unknown	1 2 9	kann
32	Ordinal [Drop-down]	5.3. Nationality of index patient	Resident of EU country Resident of non-EU country Unknown	1 2 9	kann
33	Ordinal [Drop-down]	5.4 Index patient symptomatic	Yes No Unknown	1 2 9	muss
34	Ordinal [Drop-down]	5.4.1. Index patient's symptoms Cough		1 2 9	muss
35	Ordinal [Drop-down]	5.4.2. Index patient's symptoms Diarrhoea		1 2 9	muss
36	Ordinal [Drop-down]	5.4.3. Index patient's symptoms Fever		1 2 9	muss
37	Ordinal [Drop-down]	5.4.4. Index patient's symptoms Haemorrhage		1 2 9	muss
38	Ordinal [Drop-down]	5.4.5. Index patient's symptoms Headache		1 2 9	muss
39	Ordinal [Drop-down]	5.4.6. Index patient's symptoms Rash		1 2 9	muss
40	Ordinal [Drop-down]	5.4.7. Index patient's symptoms Vomiting		1 2 9	muss
41	Freitext	5.4.8. Index patient's symptoms Other	Freitext	Freitext	kann
42	Ordinal [Drop-down]	5.5 Final assessment of index patient's infectiousness in this event	Low Medium High Unknown	1 2 3 9	muss
43	Numerisch [NNN]	6 All contacts identified (traced or non-traced)	[NNN/999=unknown]	[NNN/999=unknown]	kann
44	Numerisch [NNN]	6 Crew of 43	[NNN/999=unknown]	[NNN/999=unknown]	kann
45	Numerisch [NNN]	6 Passengers (EU) of 43	[NNN/999=unknown]	[NNN/999=unknown]	kann
46	Numerisch [NNN]	6 Passengers (Non-EU) of 43	[NNN/999=unknown]	[NNN/999=unknown]	kann
47	Numerisch [NNN]	6 All contacts successfully traced	[NNN/999=unknown]	[NNN/999=unknown]	kann

Platzierung in DB	Feldtyp / Frontend	Variablenname	Ausprägungen	Codierung der Ausprägung	Kann / muss
48	Numerisch [NNN]	6 Crew of 47	[NNN/999=unknown]	[NNN/999=unknown]	kann
49	Numerisch [NNN]	6 Passengers (EU) of 47	[NNN/999=unknown]	[NNN/999=unknown]	kann
50	Numerisch [NNN]	6 Passengers (Non-EU) of 47	[NNN/999=unknown]	[NNN/999=unknown]	kann
51	Numerisch [NNN]	6 All contacts successfully traced who are confirmed infected	[NNN/999=unknown]	[NNN/999=unknown]	kann
49	Numerisch [NNN]	6 Crew (of) 51	[NNN/999=unknown]	[NNN/999=unknown]	kann
50	Numerisch [NNN]	6 Passengers (EU) of 51	[NNN/999=unknown]	[NNN/999=unknown]	kann
51	Numerisch [NNN]	6 Passengers (Non-EU) of 51	[NNN/999=unknown]	[NNN/999=unknown]	kann
52	List	6 Contacts who are confirmed infected: Distance from index patient in seating rows	Same row 1 row 2 rows 3 rows 4 rows 5 rows 6 rows 7 rows 8 rows 9 rows 10 rows (usw. bis 50…) Unknown	0 1 2 3 4 5 6 7 8 9 10 usw. bis 50… 99	kann
53	List	6 Contacts who are confirmed infected and symptomatic: Distance from index patient in seating rows	Same row 1 row 2 rows 3 rows 4 rows 5 rows 6 rows 7 rows 8 rows 9 rows 10 rows (usw. bis 50…) Unknown	0 1 2 3 4 5 6 7 8 9 10 usw. bis 50… 99	kann
54	Ordinal [Drop-down]	7.1. Outcome/actions taken: structured telephone interview with contacts	Yes No Unknown	1 2 9	kann
55	Ordinal [Drop-down]	7.2. Outcome/actions taken: Post-exposure prophylaxis recommended for contact persons?	Yes No Unknown	1 2 9	kann
56	Numerisch [NNN]	7.2.1. Post-exposure prophylaxis provided for how many persons?	Numerisch [NNN/99=unknown]	[NNN/99=unknown]	kann
57	Freitext	7.3. Other measures taken (please specify)	Freitext	Freitext	kann

Annex 3: Detailed event list for TB events

Reference	Country	Year of event	Flight destination	Flight time including ground delay (hours)	HEPA filters functional?	Ground delays?	Index patient	Index patient age	Index patient's symptoms during flight	Symptoms at time of diagnosis/ lab status	Infectiousness of index patient (on ground)	Time period for contact tracing	Who was traced?	Definition of contacts	Actions taken	On-board transmission?	Evidence level (transmission /no transmission)	Number of passengers/ crew infected	Distance of contacts (range of seat rows)
Driver CR, Valway SE, Morgan WM, Onorato IM, Castro KG. Transmission of *Mycobacterium tuberculosis* associated with air travel. JAMA 1994; 272(13):1031-5	USA	May to October 1992	several flights	12 (median)	unknown	unknown	female, flight attendant	unknown	cough, shortness of breath	November 1992: cavitary lesions with bilateral infiltrates, AFB+, culture positive, active pulmonary TB	4/9 close contacts TST positive, 4 other TST conversions	estimated infectious period: 6 months, (May–Oct 1992) based on presence of respiratory symptoms (cough)	274 crew member contacts (266 successfully traced)	9 household contacts, crew members working with index patient between May and August, frequent fliers	Informed by certified letter, skin test, self-administered standardised questionnaire, skin test for all contacts; 5 TU purified protein derivative tuberculin by Mantoux testing; results read 48–72 hours later; no baseline skin tests, control group required; for clinical management: positive if 5 mm of induration of contacts and at least 10 mm of induration for comparison; for analysis positive if 5 mm induration for both; significantly higher TST-positive test rates in the later half of infectious period (August–October), both for 5 mm and 10 mm induration.	yes	medium	2 other crew members with TST-conversion and no other RF, but possible exposure by colleague on ground	unknown
Driver CR, Valway SE, Morgan WM, Onorato IM, Castro KG. Transmission of *Mycobacterium tuberculosis* associated with air travel. JAMA 1994; 272(13):1031-5	USA	May to October 1992	several flights	4 (median)	unknown	unknown	female, flight attendant	unknown	cough, shortness of breath	November 1992: cavitary lesions with bilateral infiltrates, AFB+, culture positive, active pulmonary TB		estimated infectious period: 6 mo, (May-Oct 92) based on presence of respiratory symptoms (cough)	71 frequent fliers (62 successfully traced)	9 household contacts, crew members working with her between May and August, frequent fliers	Informed by certified letter, skin test, self-administered standardised questionnaire, skin test for all contacts; 5 TU purified protein derivative tuberculin by Mantoux testing; results read 48–72 hours later; no baseline skin tests, control group required; for clinical management: positive if 5 mm of induration of contacts and at least 10 mm of induration for comparison; for analysis positive if 5 mm induration for both; significantly higher TST-positive test rates in the later half of infectious period (August–October), both for 5 mm and 10 mm induration.	yes	medium	4 passengers with single positive TST and no other RF	unknown
Parmet AJ. Tuberculosis on the flight deck. Aviat Space Environ Med 1999; 70(8):817-8.	USA	1998	several flights within 6 months	> 8 (8–60 exposure)	Not installed on the used aircraft (DC 9)	unknown	male, pilot	unknown	unknown	active TB	actively infectious	6 months	48 other pilots/co-pilots	pilots, since no exchange between cabin and cockpit	All contacts were skin tested (IPPD) or chest x-rayed, if previously positive.	no	high	x	x
Whitlock G, Calder L, Perry H. A case of infectious tuberculosis on two long-haul aircraft flights: contact investigation. N Z Med J 2001; 114(1137):353-5.	New Zealand	1996	Auckland to Honolulu	> 8	functional	unknown	female from New Zealand	21	cough, weight loss	sputum smear strongly positive (100+ acid-fast bacilli per high-powered field), pulmonary cavitation, apical pneumothorax, extensive pulmonary TB, sputum culture positive		5 weeks (series of flights took place over the course of 5 weeks)	67 contacts	all passengers in her sections and crew	TST, x-ray, one kid 7 years with nearly converted TST (0 to 7 mm) test, isoniazid chemoprophylaxis, follow up, with x-ray six month later.	no	medium	x	x

Reference	Country	Year of event	Flight destina-tion	Flight time including ground delay (hours)	HEPA filters functional?	Ground delays?	Index patient	Index patient age	Index patient's symptoms during flight	Symptoms at time of diagnosis/ lab status	Infectious-ness of index patient (on ground)	Time period for contact tracing	Who was traced?	Definition of contacts	Actions taken	On-board trans-mission?	Evidence level (trans-mission /no trans-mission)	Number of passengers/ crew infected	Distance of contacts (range of seat rows)
Whitlock G, Calder L, Perry H. A case of infectious tuberculosis on two long-haul aircraft flights: contact investigation. N Z Med J 2001; 114(1137):353-5.	New Zealand	1996	Honolulu to Auckland	> 8	functional	unknown	female from New Zealand	21	cough, haemoptysis	sputum smear strongly positive (100+ acid-fast bacilli per high-powered field), pulmonary cavitation, apical pneumothorax, extensive pulmonary TB, sputum culture positive	regarded as highly infectious	5 weeks (series of flights took place over the course of 5 weeks)	171 contacts	all passengers in her section and crew	TST, x-ray, one kid 7 years with nearly converted TST (0 to 7 mm) test, isoniazid chemoprophylaxis, follow up, with x-ray 6 month later.	no	medium	x	
McFarland JW, Hickman C, Osterholm M, MacDonald KL. Exposure to Mycobacterium tuberculosis during air travel. Lancet 1993; 342(8863):112-3.	USA	1992	London to Minneapolis	> 8	unknown	unknown	unknown	unknown	unknown	AFB+++, cavitary lesions	highly infectious		all passengers and cabin crew (342)		Letter, TST up to 12 weeks after flight (positive if > 5 mm).	no	low	x	x
CDC. Exposure of passengers and flight crew to Mycobacterium tuberculosis on commercial aircraft, 1992-1995. MMWR Morb Mortal Wkly Rep 1995 Mar 3;44(8):137-40.	USA	1993	Mexico City to San Francisco	1	unknown	unknown	unknown	unknown	unknown	pulmonary TB	unknown		Attempts were made to contact all 92 passengers , 22 completed TST testing.	entire plane, not cabin crew	TST	no	low	x	x
CDC. Exposure of passengers and flight crew to Mycobacterium tuberculosis on commercial aircraft, 1992-1995. MMWR Morb Mortal Wkly Rep 1995; 44(8):137-40.	USA	1994	4 flights	unknown	unknown	unknown	US citizen	unknown	unknown	pulmonary TB and underlying immune disorder	unknown		661 passengers (345 US citizens)	all passengers that were US citizens	TST	no	low	x	x
Miller MA, Valway S, Onorato IM. Tuberculosis risk after exposure on airplanes. Tuber Lung Dis 1996;77(5):414-9.	USA	1993	Frankfurt to New York	9	functional	yes	male, Russian		cough, fever, shortness of breath	4 days after flight: bilateral infiltrates and cavities, AFB+, culture positive	high	4 days prior to admission (only domestic flight, and flight into the US)	219 passengers (153 US citizens and 16 crew members successfully traced)	no definitions made	Certified letter notification, advised to have TST as soon as possible (to be repeated after 12 weeks, if initial was negative), telephone calls, visits by health officials, self-administered questionnaire, for positive cases, chest x-ray (positive > 10 mm, analysis also for > 5 mm)	yes	medium	2 passengers with single positive TST and no other RF	unknown
Miller MA, Valway S, Onorato IM. Tuberculosis risk after exposure on airplanes. Tuber Lung Dis 1996;77(5):414-9.	USA	1993	New York to Cleveland	2	unknown	no	male, Russian	unknown	cough, fever, shortness of breath	4 days after flight: bilateral infiltrates and cavities, AFB+, culture positive	high	4 days prior to admission (only domestic flight, and flight into the US)	unknown	no definitions made	Certified letter notification, advised to have TST as soon as possible (to be repeated after 12 weeks, if initial was negative), telephone calls, visits by health officials, self-administered questionnaire, for positive cases, chest x-ray (positive > 10 mm, analysis also for > 5 mm)	no	unknown	x	x

Reference	Country	Year of event	Flight destina-tion	Flight time including ground delay (hours)	HEPA filters functional?	Ground delays?	Index patient	Index patient age	Index patient's symptoms during flight	Symptoms at time of diagnosis/ lab status	Infectious-ness of index patient (on ground)	Time period for contact tracing	Who was traced?	Definition of contacts	Actions taken	On-board trans-mission?	Evidence level (trans-mission /no trans-mission)	Number of passengers/ crew infected	Distance of contacts (range of seat rows)
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	Honolulu to Chicago	> 8	functional	no	female, Korean	32	unknown	extensive pulmonary disease, AFB+++, culture positive, had received medication for 1 month, died of pulmonary haemorrhage and respiratory failure 5 days after hospitalisation	unknown	about 6–7 weeks, during the time when flight occurred	298 contacts traced (all passengers and crew)	entire planes, no categorisation and household contacts	Certified letter notification, advised to have TST as soon as possible (to be repeated after 12 weeks if initial test was negative), self-administered questionnaire TST, for positive cases, chest x-ray (positive > 10 mm, analysis also for > 5 mm); small infected child in the advanced stages of the disease; management: administer no preventive therapy and watch carefully for the appearance of signs and symptoms of tuberculosis, or consider six months of preventive therapy with rifambutin, to which the isolate was fully susceptible	no	unknown	x	x
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	Chicago to Baltimore	2	functional	no	female, Korean	32	unknown	extensive pulmonary disease, AFB+++, culture positive, had received medication for 1 month, died of pulmonary haemorrhage and respiratory failure 5 days after hospitalisation	unknown	about 6–7 weeks, during the time when flight occurred	104 contacts traced (all passengers and crew)	entire planes, no categorisation and household contacts	Certified letter notification, advised to have TST as soon as possible (to be repeated after 12 weeks, if initial was negative), self-administered questionnaire TST, for positive cases, chest x-ray (positive > 10 mm, analysis also for > 5 mm); small kid infected in the later part of the disease: management: administer no preventive therapy and watch carefully for the appearance of signs and symptoms of tuberculosis, or consider six months of preventive therapy with rifambutin, to which the isolate was fully susceptible	no	unknown	x	x
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	Baltimore to Chicago	2	functional	no	female, Korean	32	cough, fever	extensive pulmonary disease, AFB+++, culture positive, had received medication for 1 month, died of pulmonary haemorrhage and respiratory failure 5 days after hospitalisation	high	about 6–7 weeks, during the time when flight occurred	109 contacts traced (all passengers and crew)	entire planes, no categorisation and household contacts	Certified letter notification, advised to have TST as soon as possible (to be repeated after 12 weeks, if initial was negative), self-administered questionnaire TST, for positive cases, chest x-ray (positive > 10 mm, analysis also for > 5 mm); small kid infected in the later part of the disease: management: administer no preventive therapy and watch carefully for the appearance of signs and symptoms of tuberculosis, or consider six months of preventive therapy with rifambutin, to which the isolate was fully susceptible	no	unknown	x	x

Reference	Country	Year of event	Flight destina-tion	Flight time including ground delay (hours)	HEPA filters functional?	Ground delays?	Index patient	Index patient age	Index patient's symptoms during flight	Symptoms at time of diagnosis/ lab status	Infectious-ness of index patient (on ground)	Time period for contact tracing	Who was traced?	Definition of contacts	Actions taken	On-board trans-mission?	Evidence level (trans-mission /no trans-mission)	Number of passengers/ crew infected	Distance of contacts (range of seat rows)
Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med 1996;334(15):933-8.	USA	1994	Chicago to Honolulu	> 8	functional	no	female, Korean	32	cough, fever	extensive pulmonary disease, AFB+++, culture positive, had received medication for 1 month, died of pulmonary haemorrhage and respiratory failure 5 days after hospitalisation	high	about 6–7 weeks, during the time when flight occurred	249 contacts traced(all passengers and crew)	entire planes, no categorisation and household contacts	Certified letter notification, advised to have TST as soon as possible (to be repeated after 12 weeks, if initial was negative), self-administered questionnaire TST, for positive cases, chest x-ray (positive > 10 mm, analysis also for > 5 mm); small kid infected in the later part of the disease: management: administer no preventive therapy and watch carefully for the appearance of signs and symptoms of tuberculosis, or consider six months of preventive therapy with rifambutin, to which the isolate was fully susceptible	yes	4 high, 2 medium	4 passengers with TST conversion and no other RF and 2 passengers with single positive TST no other risk factors	4: same row, 1 row, 12 rows, 13 rows 2: 1 row, 1 crew
Moore M, Fleming KS, Sands L. A passenger with pulmonary/laryngeal tuberculosis: no evidence of transmission on two short flights. Aviat Space Environ Med 1996;67(11):1097-100.	USA	1994	2 short domestic flights	each 1.25	unknown	no	male	unknown	cough, hoarseness	AFB+, culture positive, cavitary lesions, pulmonary and laryngeal TB	highly infectious (2 siblings TST positive 4/5 close contacts positive)	about 2 months before diagnosis	227 contacts friends and siblings on camping trip (siblings positive, 4 converters)	no definitions made	Certified letter notification, advised to have TST as soon as possible (to be repeated after 12 weeks, if initial was negative), telephone calls, self-administered questionnaire TST, for positive cases, chest x-ray (positive > 5 mm), interview with physician and patients of positive test	unknown	medium	unknown	x
Vassiloyanakopoulos A, Spala G, Mavrou E, Hadjichristodoulou C. A case of tuberculosis on a long distance flight: the difficulties of the investigation. Euro Surveill 1999;4(9):96-7.	Greece	1998	Bangkok to Athens	> 8	unknown	no	young male, Thai	unknown	cough, haemoptysis	AFB+, culture positive, resistant to isoniazid		2 weeks after notification to cover flight	144 passengers in section and crew		Telephone, letter, advised baseline test, questionnaire, retesting after 12 weeks, if test negative, chest x-ray if positive	yes	medium	1 TST positive	x
Wang PD. Two-step tuberculin testing of passengers and crew on a commercial airplane. Am J Infect Control 2000;28(3):233-8.	Taiwan	1997	Los Angeles to Taibei	14	unknown	unknown	female, Taiwanese	44	unknown	AFB+, extensive pulmonary disease with cavitary lesions	high	the first TSTs were performed within 4 weeks after flight	308 passengers and crew	entire plane incl. crew, no categorisation	Letter, telephone, TST, self-administered questionnaire, chest x-ray for contacts with conversion	yes	high	3 passengers with TST conversions and no other risk factors (and 6 with TST conversions and other risk factors)	15, 23, 29 rows distance
Chemardin J, Paty M-C, Renard-Dubois S, Veziris N, Antoine D. CT of passengers exposed to an extensively drug-resistant tuberculosis case during an air flight from Beirut to Paris, October 2006. Eurosurveillance Weekly 2007;12(12).	France	2006	Beirut to Paris	5	unknown	unknown	male, Russian	unknown	cough	severe cough, cavernous lesions, AFB+++, XDR-TB, died 10 days after flight	highly infectious (wife and child pulmonary TB, other child positive TST)	13 days	11 passengers (close contacts within 2 rows distance, cabin crew [according to WHO], wife and children)	WHO criteria	Information about TB provided and follow-up including chest X-ray (at 0, 6, and 12 months) recommended. Treatment was considered not relevant for LITB, screening medical follow-up was recommended mainly based on chest x-ray (0, 6, 12 months), information for TB provided	no	low	x	x
Telephone interview with Peter Andersen	Denmark	2007	Bangkok to Copenhagen	> 8	unknown	no	female, Danish	55	cough	x	high					no	x	x	x
Telephone interview with Jelena Rjabinina	Estonia	2004	Thailand to Helsinki	8	yes	unknown	Finnish	unknown	unknown	x	medium		3 passengers from Estonia (close contacts +/- 2rows)			unknown	x	x	x
Telephone interview with Jaques Chemardin	France	2006	Beirut to Paris	5	unknown	unknown	male, Russian	unknown	cough, loss of weight		very high infectious		risk assessment: just 5 hours, but highly infectious and XDR-TB			no	x	x	x

Reference	Country	Year of event	Flight destina-tion	Flight time including ground delay (hours)	HEPA filters functional?	Ground delays?	Index patient	Index patient age	Index patient's symptoms during flight	Symptoms at time of diagnosis/ lab status	Infectious-ness of index patient (on ground)	Time period for contact tracing	Who was traced?	Definition of contacts	Actions taken	On-board trans-mission?	Evidence level (trans-mission /no trans-mission)	Number of passengers/ crew infected	Distance of contacts (range of seat rows)
Telephone interview with Bonita Brodhun	Germany	2007	Johannesburg to Munich	8	unknown	unknown	female, South African	20	cough		medium		5 rows (+/- 2rows = 30 passengers)			unknown	x	x	x
Telephone interview with Joan O'Donnell	Ireland	2008	several flights	> 8	unknown	no	male, South African	31	cough, sweats	smear positive pulmonary TB			passengers within +/-2 rows			unknown	x	x	x
Telephone interview with Brita Winje	Norway	2006	Oslo to Bangkok via Amsterdam	> 8	unknown	unknown	female, Thai	32	cough, loss of weight	positive sputum smear	high		passengers within +/-2 rows			no	x	x	x
ProMed event	USA	12.05.2007	Atlanta to Paris	> 8	unknown	unknown	male, USA	unknown		no cough or other symptoms, chest x-ray positive, stained smears of sputum negative (MDR-TB)	very low risk of transmitting the disease (did not even infect his wife)		433 passengers, 18 crew members, 250 US passengers were tested (99 % of the US passengers; 25 close contacts) (CDC)			no	x	x	x
ProMed event	Canada	24.05.2007	Prague to Montreal	> 8	unknown	unknown	male, USA	unknown		no cough or other symptoms, chest x-ray positive, stained smears of sputum negative (MDR-TB)	very low risk of transmitting the disease (did not even infect his wife)		191 passengers, 9 crew members, 29 close contacts were traced (23 Canadian residents)			no	x	x	x
ProMed event	Taiwan/ China	25.07.2007	Taiwan via Hong Kong to Nanjing	< 8	unknown	unknown	55-year-old man, (and 57-year-old woman with standard TB) from Taiwan	55/57		Woman: infectious (sputum positive)			1st flight 270 passengers, 2nd flight 120 passengers China: testing of close contacts and flight crew, quarantine for index patients. Taiwan: no CT necessary			unknown	x	x	x
ProMed event	Taiwan/ China	25.07.2007	Taiwan via Hong Kong to Nanjing	< 8	unknown	unknown	55-year-old man, (and 57-year-old woman with standard TB) from Taiwan	55/57		Woman: infectious (sputum positive)			1st flight 270 passengers, 2nd flight 120 passengers China: testing of close contacts and flight crew, quarantine for index patients. Taiwan: no CT necessary			unknown	x	x	x