**eAppendix 1** - **Search strategies**

**Embase (embase.com)**

#1 'aerospace medicine'/exp OR 'aircraft'/exp OR 'flight'/exp OR 'airplane crew'/exp OR 'airplane pilot'/exp OR 'aviation'/exp OR 'aero transport':ab,ti OR aircraft\*:ab,ti OR aeroplane\*:ab,ti OR airline\*:ab,ti OR airplane\*:ab,ti OR flight\*:ab,ti OR aircrew:ab,ti OR airflight\*:ab,ti OR aviation:ab,ti OR airport\*:ti,ab OR aeroport\*:ti,ab OR 'air port':ti,ab OR steward:ti,ab OR stewardess:ti,ab OR inflight:ti,ab OR 'in-flight':ti,ab OR 'cabin crew':ti,ab OR cabin:ti,ab OR cabins:ti,ab OR 'air-travel':ab,ti OR ((travel\* OR transport\* OR journey\* OR trip OR trips) NEAR/4 air):ab,ti OR ‘air-transport’:ti,ab OR ((plane OR planes) AND (air OR travel\* OR transport\* OR journey\* OR trip OR trips)):ti,ab OR ((passenger\* OR crew OR traveller\* OR personnel OR staff) NEAR/4 (flying OR air OR fly)):ab,ti

#2 'influenza'/exp OR influenza:ab,ti OR flu:ab,ti OR influenzae:ab,ti OR grippe:ab,ti OR influenzas:ab,ti

#3 #1 AND #2

#4 ("time of flight"[tiab] AND spectrometry[tiab])

#5 #3 NOT #4

Limits: not limits

Results 354

**Medline (Pubmed)**

#1 "Aerospace Medicine"[Mesh] OR "Aircraft"[Mesh] OR "Aviation"[Mesh] OR "Airports"[Mesh] OR aircraft\*[tiab] OR aeroplane\*[tiab] OR airline\*[tiab] OR flight\*[tiab] OR aircrew[tiab] OR airflight\*[tiab] OR airplane\*[tiab] OR aviation[tiab] OR airport\*[tiab] OR aeroport\*[tiab] OR "aero transport"[tiab] OR "air port"[tiab] OR steward[tiab] OR stewardess[tiab] OR inflight[tiab] OR "in-flight"[tiab] OR "cabin crew"[tiab] OR cabin[tiab] OR cabins[tiab] OR ((travel\*[tiab] OR "Travel"[Mesh] OR transport\*[tiab] OR journey\*[tiab] OR trip[tiab] OR trips[tiab]) AND air[tiab]) OR ((plane[tiab] OR planes[tiab]) AND (air[tiab] OR travel\*[tiab] OR "Travel"[Mesh] OR transport\*[tiab] OR journey\*[tiab] OR trip[tiab] OR trips[tiab])) OR ((passenger\*[tiab] OR crew[tiab] OR traveller\*[tiab] OR personnel[tiab] OR staff[tiab]) AND (flying[tiab] OR fly[tiab] OR air[tiab]))

#2 "Influenza, Human"[Mesh] OR influenza[tiab] OR flu[tiab] OR influenzae[tiab] OR grippe[tiab] OR influenzas[tiab] OR "Influenzavirus A"[Mesh] OR "Influenzavirus B"[Mesh] OR "Influenzavirus C"[Mesh]

#3 #1 AND #2

#4 ("time of flight"[tiab] AND spectrometry [tiab])

#5 #3 NOT #4

Limits: no limits

Results 280

Date of searches 19/07/2013 with constant update until July 2015

**eAppendix 2.** Characteristics of the studies investigating transmission of influenza aboard airplane

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***Study (year)*** | **Flight details** |  | **Index case(s)** | **Contact tracing** | **Secondary cases** |
| **Influenza strain** | **Origin – stopover – destination1** | **Flight duration** | **Number** | **Symptoms during flight with onset in relation to flight** | **Seating****index** | **Strategy** | **Passengers successfully followed up/passengers** | **Attack rate: Number cases/number of contacted px excluding index cases** | **Seating in relation to closest index case** |
| Shankar (2014)\*24A(H1N1) pdm09 | nonstop: (MX)-Birmingham (UK)Boeing 767-3002009 (21 April) | 9:50 | 1 px: | fever cough, headache, myalgia, and chills)  | rear cabin | 2 rows\*2 | 39/39 (100%) incl. travel companion | 1/38; (2·6%) excl. index, and travel companion | 2 rows (1) |
| retrospective review of the national database | 4/238 (1·7%)(278px aboard excl. 38 px within 2 rows, travel companion, index) | 4/238; (1·7%) excl. 38 px within 2 rows, travel companion, index4/96; (4·2%) rear section | 4 rows (2) 5 rows (1) 8 rows (1) |
| Young (2013)\* 23A(H1N1) pdm09 | nonstop: Cancun (MX) – Birmingham (UK) Boeing 767-3002009 (21 April) | 9:50 | 6 px | ILI (fever, and cough or sore throat) | seating in all sections: 5A, 8E, 8F, 19E, 35G, 38D | cohort studyall invited for serological testingRetrospective review of the national database | 239/278 (86%) clinical data available | 10 ILI/232 (4·3%)excl. 6 infectious, 1 immune | rear section: 8/10 cases, 1 front, 1 unknown;0 row (3)1 row (1)2 rows (1)3 rows (1)4 rows (1)5 rows (1)8 rows (1) |
| Zhang (2013) 34 A(H1N1) pdm09 | 1st flight with stop-over: New York (US) - Vancouver (CA) all px remained seated for 1:15 – Hong Kong (CN)2009 (27 May) | 20:20(leg A 5:50, leg B 13:15) | 1 px | no fever or respiratory symptoms | economy class (two cabin aircraft) | all px, and crew | 82/274 (30%) (260px, 14crew) 19/91 (21%) px that disembarked in HK | 9/82; (11%) index not identified1/19; (5·3%) px that disembarked in HK8/63; (13%) transfer flight 2 | dispersed in economy rear cabin (6)0 row (3)2 rows (4)5 rows (1)2/8 rows (1), changed seats |
| 2nd flight: Hong Kong (CN) – Fuzhou (CN) 2009 (28 May) | 1:40 | 1 px | no fever or respiratory symptoms | economy class (single cabin aircraft) | all px, and crew | 140/144 (97%) (136px, 8crew) 63/63 (100%) px transferred from flight 1 to flight 273/73 (100%) px boarded in HK to flight 2 | no additional (all 8 were on flight 1) 0/73; (0%) boarded in HK to flight 2 | dispersed 0 row (3)2 rows (4)4 rows (1) |
| Neatherlin (2013) 32A(H1N1) pdm09 | 1st flight; leg A1: San Diego (US) - El Paso (US); leg A2: El Paso (US) - Dallas (US) A1&A2: Boeing 7372009 (3 April)  | leg A1 1:45leg A2 1:35 | 1 px | fever, cough, fatigue, headache, vomiting, no sneezing nor coughing reported during flight  | row 2, other seats unassigned | cohortcontacts defined as 2rows\* | 159/265 (60%) (A1: 127px; A2: 138px) 211px+14crew identified, 155px+13crew contacted, 146px+13crew interviewedexcl. index, and sibling | 8 ARI/159 (5·0%)among them 4 ILI (2·5%)3 ARI/46 “near front” (7%)excl. index, and sibling | 3/8 cases “near front”, close contact |
| 2nd flight: leg B1: Cancun (MX) – Houston (US) leg B2: Houston (US) – Witchita (US)B1: Boeing 737; B2: Embraer RJ 1452009 (19 April)  | leg B1 2:25leg B2 1:40 | 1  | diarrhoea, chills, fever, cough, sore throat | row 21 | cohortcontacts defined as 2rows\* | 133/167 (80%)(B1: 129px; B2: 46px)158px+9crew identified128px+9crew contacted124px+9crew interviewedexcl. index, and 7 travel companions | 7 ARI/133 (5·3%)among them 3 ILI (2·3%)excl. index, and 7 travel companions | 3/7 probable cases within 2 rows at flight B13 probable cases >2rows, but 2 household contacts5 rows (1) |
| Català (2012) 28A(H1N1) pdm09 | nonstop: Mexico city (MX) – Barcelona (ES) 2009 (23 April) | 11:00 | 3 ILI on departure (2 with fever), 3 were developing symptoms during flight, (students of a group) | 60% mild symptoms (cough, headache) | 33A, 34F, 23F (changed seats to sit next to each other) | all students;retrospective identification using the national database none of flight crew | 3/94 (3%) other px | 0/94; (0%) | unclear, students changed seats to sit next to each other |
| 71/71 (100%) students | 4/65; (6%) excl. index |
| Foxwell (2011) 29A(H1N1) pdm09 | 1st flight: Los Angeles (US) – Sydney (AU) Airbus A380-8002009 (24 May) | 14:00 | 8 ILI before the flight (4 confirmed, 1 negative, 3 not tested)2 ILI developed during flight (2 confirmed) | ILI | economy | only economy class pxretrospective identification using the national database  | flight 1188/445 (42%) responded to survey | flight 1: 24 ILI /178 (13·5%)(2 PCR confirmed, 15 neg, 7 not tested)excl. px with ILI during flight | 20/24 ILI px in aisle seats within 2 rows (9) |
| 2nd flight: Singapore (SG) – Sydney (AU) Boeing 747-4002009 (23 May) | unknown(assumed 8h) | 3 ILI 1 before flight (not tested), 2 during flight (1 negative, 1 not tested) | ILI | economy, 33D, 62D | only economy class pxretrospective identification using the national database  | flight 2131/293 (45%) | flight 2: 6 ILI/128 (4·7%)(1 PCR confirmed, 1 negative, 4 not tested)excl. px with ILI before, and during flight, | within 2 rows (4)8 rows (1)9 rows (1) |
| Ooi (2010) 33A(H1N1) pdm09 | stopover: New York (US) – Europe-Singapore (SG) 2009 | unknown(assumed 21h, 8h + 13 h, without stop-over time) | unclear: 1 px onset of symptoms before flight  | fever, malaise, cough, or rhinorrhoea | crew (1)  | 2 rows\*, then comprehensive | 26/596 (4%) (19px, 7crew) | 5/26 (19·2%)excl. index | economy >=row 50 (4)business class (1)within 2 rows\* (2)  |
| Kim (2010) 31A(H1N1) pdm09 | nonstop: Los Angeles (US) – Seoul (KR)Boeing 747-4002009 (25 April) | 13:00 | 1 px | cough, and fever  | 29J; economy  | comprehensive for non-transit (214)  | 199/338 (59%)  | 1/199 (0·5%) excl. index | 6 rows (different sections) |
| Baker (2010) 26A(H1N1) pdm09 | nonstop: Los Angeles (US) – Auckland (NZ) Boeing 747-4002009 (25 April) | 13:00 | 9 px of student group of 24 persons), 2 other px suspected | cough and other flu like symptoms |  | rear section only (126) | 121/126 (96%) of px in rear section | rear section: 2/107; (1·9%) 2 rows\*: 2/57; (3·5%) excl. immune px, suspected cases, and index | all within 2 rows\* |
| Han (2009) 30A(H1N1) pdm09 | 1st flight: Hong Kong (HK) - Chengdu (CN)Boeing 7572009 | 2:35 | 1 px | chills |  | comprehensive | 91/91 (100%) excl tour group  | 0/91 (0%)excl. tour group | not applicable  |
| 2nd flight: Chengdu (CN) - Juizhaigou (CN)Boeing 7572009 | 0:45 | 1 px | chills, cough  |  | comprehensive | 87/87 (100%) excl tour group  | 0/87; (0%)excl. tour group | not applicable |
| 3rd flight: Juizhaigou (CN) - Chengdu (CN) Boeing 7572009 | 0:45 | 2 px | cough | 7A; 7B | comprehensive | 87/87 (100%) excl tour group | 1/87; (1%)excl. tour group | within 2 rows (1)  |
| comprehensive | 30/30 (100%) tour group | 9/29; (31%)excl. index | >2 rows (5)within 2 rows (2) |
| Bin (2009) 27A(H1N1) pdm09 | nonstop: Beijing (CN) – Chendu (CN)2009 | estimated 2:30  | 1 px | fever  | no information provided | comprehensive  | 141/141 (100%) | 0/140; (0%)excl. index | not applicable |
| Marsden (2003) 10unknown | nonstop: Unknown (AU) – Mine in North-Western Australia (AU) BAe 146 (75 seats)1999 (Sept) | 3:20 | 1 | ILI, coughing, and sneezing |  | comprehensive | 75/75 (100%) | 20/74; (27%) (15 ILI, 5 ARI)excl. index | 0 rows (4)1 row (1)2 rows (4)3 rows (3)4 rows (1)5 rows (1)8 rows (1) |
| Klontz (1989) 11A/Taiwan/1/86 (H1N1) | 2 nonstop flights: Puerto Rico Air base (PR) – Key West (US) 2 DC-9 Aircrafts 1986 | 2:30 each | 8 px (flight1)3 px (flight 2) | cough, fever, headache |  | comprehensive | 90/90 (100%)flight 144/44 (100%) flight 246/46 (100%) | 23/77; (29·.9%) flight 118/34; (53%) flight 25/43; (12%) excl. index, and 2 immune/recovered  | flight 1within 2 rows\*flight 2all in the rear 0 rows (1)1 row (1)3 rows (2)4 rows (1) |
| Moser (1979) 9A/Alaska/1-8/77 (H3N2) | Anchorage (US) – Homer(US) Boeing 737 stopover, engine failure >4.5hTurboprop to Kodiak (US) - Anchorage (US) – Kodiac (US) 1977 (14 March) | unknown | 1 px | fever, chills, and severe cough 15min after boarding | forward freight compartment with 56 seats | comprehensive | 59/60 (98%)29 persons on flight Anchorage-Homer. Homer 6 left, 31 boarded; 34 persons directly to Kodiak, other 20 via Anchorage to Kodiak | 38/53; (72%) 0/6; (0%) px disembarked in Homer | free movement aboard during delay 30 persons including index remained on board, 23 left, and returned for varying periods of time to the terminal  |

\*Appears to be the same flight– but slightly different numbers/denominator

1. countries are abbreviated according to ISO 3166 (2 digits)
2. 2rows\*– persons seated in the same row as or in the 2 rows in front of or behind the row in which the index sat

Nd not described - no information provided

Px: Passenger

+7 7 days after onset of symptoms

**eAppendix 3**. Criteria for quality assessment, interventions and summary of the limitations

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study**  | **Case classification**  | **Quality of contact tracing**  | **Alternative exposure** | **Intervention** | **Mayor limitations** |
| **(year)** | **Index case definition** | **Secondary case definition**  | **Timeliness** | **Case identification/ascertainment** | **Completeness of follow up**  | **Before flight** | **During flight**  |  |  |
| Shankar (2014) 24 | Symptomatic during flight, PCR positive | ILI ˂= day +7(fever, measured or subjective and two or more of the symptoms: cough, sore throat, rhinorrhoea, myalgia, headache, vomiting and diarrhoea)ANDtested positive for A(H1N1) pdm09 | Day +8 to +20 (median 13 days)  | 2rows2complete Retrospective identification Asymptomatic /mild cases not reporting for testing might have been missed  | 2rows\*All traced (100%)Retrospective identification: unclear (4/238, 2%) | Common exposure in Mexico possible (for the 6 cases onset of symptoms was on day +1 to +5) | Only one of the detected case reported symptoms during flight, however other asymptomatic index cases cannot be excluded  | Nd | CT was limited to close contacts (2rows2)Not all rear cabin px were tested or interviewedConfirmation was based on PCR testing of a single nasopharyngeal swab samples (possible underestimation of transmission risk) |
| Young (2013) 23 | ILI (CDC) and onset –day -1 with recovery of the symptoms not earlier than day -1 | Px with ILI symptoms (day 0 to +6) | 2rows\* day +8 to +20 Cohortday +49 to+106 | Of the 10 secondary cases 4/4 tested PCR positive Of the 6 index cases 1/4 tested PCR positiveOf the 222 non cases 10/94 with positive serology | Cohort 86% information determine case status 96/239; 40% serology testing 30/239 PCR testing | Exposure in Mexico possible e.g. holiday resort, tour busses (30-120 min) to airport, departure lounge | Asked for toilet use and movement (RR not calculated) | Investigated 2rows\* for need of antiviral medication | Misclassification of cases possible (due to clinical case definition)Single samples with titres >+ 1:32 by HI were considered seropositive, suggestive of recent infection |
| Zhang (2013) 34 | No symptoms during flight | Suspected caseAcute febrile respiratory illness (ILI = fever >= 37.5ºC and cough or sore throat) with onset during day -6 to +7Confirmed case PCR positive | Nd | Specimen of suspected case px were tested by PCR during the 7 days of quarantine | *Flight 1:* 82/274 (30%)*Flight 2:* 140/144; (97%) | Exposure period included final 12 hours in NY (at airport)  | No association with lavatory use or frequency of moving around detected | (Home-) quarantine, 7 day follow up | Unidentified index case (s)No laboratory information of non-casesLack of seating and illness information for 68% of the px on flight 1  |
| Neatherlin (2013) 32  | Virologically confirmed infection, travelled within 7 days of symptom onset | *Probable cases* individuals (contacts and non-contacts) who developed ARI 1-7 days after the flightConfirmed cases probable case with positive serology | Average 29 days after flight (day 18-47)Average 14 days after flight (day 9-29) | Most cases were not laboratory confirmed Serology only for 43/290 persons Earliest sample on day +18, used threshold titers instead of sero-conversion  | *Flight 1:* 159/265; 60%,*Flight 2:* 133/167; 80% Crew included | Identified px with onset of ARI/ILI before and during flight  | Asymptomatic but laboratory positive travel companion(s) | Nd | MisclassificationSmall percentage lab confirmedRecall bias (symptoms/onset and seating)More / undetected index cases on the flights |
| Català(2012) 28 | Confirmed A(H1N1) infection  | Confirmed A(H1N1) infection | Student group 3 days after flight Other px: review of influenza surveillance databases 4 weeks after flight | Lab testing (PCR) for all ILI (fever, cough and myalgia) who travelled to Mexico or had contact to someone who travelled to Mexico | Overall 74/165 (45%) Student group (100%)Unclear for other px (3/94, 3%) | Exposure in Mexico during 7 day travel in group  | Unclear seating | Antiviral therapy and 7 day home isolation for ILI with travel history  | Asymptomatic /mild cases not reporting for testing might have been missed Overall and secondary AR may be underestimated; use of antiretroviral prophylaxis  |
| Foxwell (2011) 29 | Flight 1confirmed H1N1 infection within 24h after flight arrival from USFlight2: identification of H1N1 confirmation from country without endemicity | Sensitive definition of ILI >= 1 symptom (cough, runny nose, sore throat or fever within 7-14 days before the flight or during the flight or <= 7 days after exclusion of known causes | Survey distributed 3 month after flight | Survey and triangulation method / cross-checking with national surveillance data | Flight 1 188/445; 42%Flight 2 131/293; 45% | Nd | Nd | Unclear description of application of antiviral therapy and day home quarantine | Asymptomatic /mild cases not reporting for testing might have been missed Response bias / contact with PH authorities after flight Potential for ILI after flight from another source |
| Ooi (2010) 33 | Nd | Nd | Unclear when CT was initiated  | Lab testing ndPhylogenetic analysis of 4 strains | 4% followed-up  | Unclear previous exposures | Nd | Oseltamivir to close contacts (2 row\*) and 7 day quarantine | Exposure before flight possible (onset of symptoms +3) |
| Kim (2010) 31 | Clinical symptoms and laboratory confirmation | Nd | + 2days for px (2 rows); for others unclear | Only symptomatic px were tested | 59% of all px, 8/20 px seated within 2 meters of the index interviewed | Index case with characteristic features; alternative exposures surveyed | Index case with characteristic features; alternative exposures surveyed (e.g. lavatories)  | Oseltamivir to close contacts (2 row\*) and home isolation | 60% px seated within 2 meters of the index case were interviewed. Px not reporting illness were not tested.  |
| Baker (2010) 26 | ILI any two of fever, or feverishness, cough, sore throat, or rhinorrhoea Confirmed case:nasopharyngeal swab + and/or serology + | Suspected secondary caseILI onset within 3.2 days of arrival and laboratory for pandemic not done or incompleteConfirmed secondary case:ILI onset within 3.2 days of arrivalAnd swab or serology influenza positive | 52% contacted within 72h after flight | Only symptomatic px were tested;Swabs were taken from 26/97 px. (among them 14 px with symptoms) | 96%px in rear section, assumed 32% of all px (121/379)  | Alternative exposure were considered to be unlikely, due to the incubation period/flight duration | No other exposures during flight investigated  | Oseltamivir treatment and isolation or quarantine for 72h  | Underreporting of symptoms in asymptomatic/ mild case might lead to reduced case ascertainment (not all lab tested)Low AR despite several index cases. Possibly underestimating the risk |
| Han (2009) 30 | Suspected case: >=1 symptoms as fever, cough, sore throat, chills or headache in a px of flight 1 or flight 2 or in a member of the tour group. Confirmed case: suspected case with positive PCR for H1N1. | A confirmed case with onset of symptoms 24 hours after the onset of the primary cases symptoms | CT completed within 7 days (4-5 days after onset of symptoms of index cases) | Only symptomatic px were tested; swabs were taken of the members of the tour group and all symptomatic px aboard of any of the three flights | Complete (100%)  | Alternative exposures among tour group members travelling 3 days on a bus tour with shared meals in between flights | No other exposures during flight investigated  | Isolation of symptomatic or confirmed cases(tour group) | Only one case outside tour group detected Unclear how the non-tour group members were followed up Other cases exposure during bus trip (tour) |
| Bin (2009) 27 | Confirmed laboratory H1N1 virus infection | Confirmed laboratory H1N1 virus infection in a close contact (persons who had lived with a person with probable or confirmed infection or who had direct contact with respiratory or body fluids of such persons).  | CT started after diagnosis day +1 | All suspected cases were tested (pharyngeal swabs)Controlled for asymptomatic infections | Complete (100%) | Virus was not known to be present in Beijing at this time. Alternative exposures were not investigated. | No other exposure during flight investigated | Isolation of all px for 7 days | Unclear whether case was infectious during this rather short flight (mild, unclear symptoms) False negative (due to lower sensitivity of pharyngeal swabs)  |
| Marsden (2003) 10 | ILI without serological confirmation | ILI and upper respiratory infections diagnosed after flight  | CT within 6 days after flight  | No laboratory confirmation  | Complete (100%); for clinical outcome | Exposure possible in airport lounge  | After flight – workers possibly exposed during flight worked together in the mine/social mingling One secondary case walked the length of the aircraft during flight  | Nd | No definite diagnosis as no laboratory testing performed  |
| Klontz (1989) 11 | Active duty naval person, who reported experiencing a respiratory illness characterized by both fever and cough, and either sore throat or myalgia. | Active duty naval person, who reported experiencing a respiratory illness characterized by both fever and cough, and either sore throat or myalgia. | CT performed 8-9 days after flight | Unclear; review of medical records for ILI, Seven symptomatic patients were tested (unclear relation to flight)  | Complete (100%) | Previous exposure, epidemics ongoing before flight in the squadron with shared barracks | No other exposure during flight investigated | No intervention | Common exposure before and after flightCase definition based on clinical symptoms |
| Moser (1979) 9 | Temperature>37.7°C or complained of feverAND two of: cough, chills, myalgia or arthralgia, difficulty walking, chest pain, severe malaise or headache OR no fever and any 3 symptoms.  | Temperature>37.7°C or complained of feverAND two of: cough, chills, myalgia or arthralgia, difficulty walking, chest pain, severe malaise or headache OR no fever and any 3 symptoms.  | Unclear > 60 hours after flight  | Index 8-fold rise, negative throat swabVirus isolation 31/38 cases had specimen collected 2-3 days after onset of symptoms (8/31 were positive)Serology 20/22 showed 4-fold rise  | One person not reached for interview (98%) | No alternative exposure detected Investigated ILI background level in Kodiac (school absenteeism) and in contacts before the flight  | Possible exposures aboard surveyed  | No intervention  | Secondary case definition based on clinical symptoms |