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Healthcare-associated infections in European long-term care facilities: how big is the challenge?

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Europe is aging. The percentage of the population in the European Union (EU) aged 65 years and over increased from 9.6% in 1960 to 16.0% in 2010, and is projected to increase to 29.3% (152.6 million) in 2060 [1,2]. The population aged 80 years and over is projected to increase from 16.8 million (4.1%) in 2010 to 43.3 million (11.5%) in 2060, almost as many as the expected percentage of children (0–14 years, 15%) in 2060 [2,3]. At the same time, healthcare systems are striving for cost optimisation, which results, among other things, in shorter hospital stays and early discharge. These two factors combined have led to a rapid rise in the demand for nursing homes and other social and healthcare services for the elderly such as long-term care facilities (LTCFs), residential homes and home care. The Organisation for Economic Co-operation and Development (OECD) estimated that across OECD countries (these include 22 countries of the EU and European Economic Area (EEA)), about 12% of the population aged 65 years and older received some form of long-term care service in 2009 , either at home (64.5% of the services) or in institutions (35.5%) [3]. Based on these figures, the European Centre for Disease Prevention and Control (ECDC) estimates the number of residents in LTCFs in the EU at approximately 3.7 million in 2010, a number that will certainly increase in the coming decades.

Because of age-related dysfunctions of the immune system and physiological changes, the elderly are more sensitive to infection and therefore predisposed to the most frequent infections occurring in nursing homes: urinary tract infections, pneumonia, skin and soft tissue infections and gastro-intestinal infections, in particular those for which previous antibiotic use is a risk factor, such as *Clostridium difficile* infection [4]. Healthcare-associated infections in LTCFs are also associated with severe consequences including debilitation, hospital admission and sometimes death [5]. Because of the ageing population, the frequent transfer of patients from LTCFs to hospitals and back to LTCFs, the increasing prevalence of multidrug-resistant microorganisms such as meticillin-resistant Staphylococcus aureus (MRSA), extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and vancomycin-resistant Enterococcus spp. (VRE), and the low availability of infection control resources in these facilities [6,7], prevention and control of healthcare-associated infections in European LTCFs is becoming an increasing challenge.

The number of patients acquiring a healthcare-associated infection in acute care hospitals in the EU has previously been estimated at 4.1 million each year [6], but there is no similar estimate for LTCFS. Facing the lack of EU-wide data on healthcare-associated infections in LTCFs, ECDC provided funding for the Healthcare Associated infections in Long-Term care facilities (HALT) project from December 2008 to May 2011.

The project's aims were to support prevention of healthcare-associated-infections and antimicrobial resistance in European LTCFs and to provide a tool for the assessment of the prevalence of healthcare-associated infections, antimicrobial use as well as performance indicators for infection prevention and control practices and antimicrobial stewardship in LTCFs. A methodology for repeated point prevalence surveys tailored to the LTCF/nursing home setting was developed by HALT and implemented in a Europe-wide network of LTCFs.

The HALT project estimated that there were at least 62,000 LTCFs in the EU in 2010, with a capacity of approximately 3.1 million beds, 58% of which were located in general nursing homes (residents needing 24-hour medical or highly skilled nursing supervision), 32% in residential homes (residents needing 24-hour supervision of daily activities) and 10% in mixed facilities. Even though these figures are probably an underestimate because of the difficulty to collect precise data in several countries, in particular on privately owned LTCFs, the estimated number of long-term care beds was of the same order of magnitude as the above-mentioned estimate of residents in European LTCFs.

After a pilot survey in 2009 [8], a first EU-wide point prevalence survey was performed from May to September 2010, including a total of 64,007 residents surveyed in 722 LTCFs in 25 countries (Austria, Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic,

Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Slovenia, Spain, Sweden and the United Kingdom) [9,10]. Participating LTCFs were nursing homes (75%), mixed facilities (15%) and residential homes (7%).

Signs and symptoms of an infection were reported for 2,495 (4.0%) of the 61,932 eligible residents, but following the application of the case definitions to the collected signs and symptoms, these were only confirmed as a healthcare-associated infections in 1 488 (2.4%) residents. The most frequently reported types of healthcare-associated infection were respiratory tract infections (33.6%), urinary tract infections (22.3%), skin and soft tissue infections (21.4%), conjunctivitis (8%) and gastro-intestinal infections (4.6%). Among the eligible residents, 4.3% received at least one antimicrobial agent. The five most prescribed antimicrobials were amoxicillin-clavulanic acid (12.7%), nitrofurantoin (10.4%), trimethoprim (9.9%), amoxicillin (7.3%) and ciprofloxacin (6.9%). Almost half (48.9%) of all antimicrobial agents in participating LTCFs were prescribed for a urinary tract indication. Uroprophylaxis represented 27.7% of all prescribed antimicrobial agents in participating LTCFs.

Based on the results of this point prevalence survey, and assuming an occupancy rate of 95% [11], the number of LTCF residents with signs and symptoms of an infection on any given day in the EU is estimated at 117,800 or 140,600, depending on the denominator used. With an average duration of an infection episode of 10 days, the total number of infections in LTCFs in EU/EEA countries could be estimated at 4.3 million each year based on signs and symptoms, of which 2.6 million would be confirmed as healthcare-associated infections according to the case definition. Using a different method based on an average annual incidence rate of 4.4 (range: 2.2–6.0) healthcare-associated infections per 1,000 resident-days from recent studies in developed countries [12-16], the number of infections in LTCFs could be estimated at 4.7 million each year, similar to the above-mentioned prevalence-based estimate. Because residents stay in LTCFs for long periods of time, from two to 60 months on average according to the country [11], and may have more than one infection per year, the number of individual residents acquiring these infections is likely to be substantially lower.

This week's and last week's issue of Eurosurveillance report on two point prevalence surveys performed using the HALT methodology, in Frankfurt am Main [17] and in the Netherlands [18]. While the latter survey was part of the European HALT survey (May to September 2010), the former was performed independently and during a different time period (January to March 2010). Both surveys reported a relatively low prevalence of healthcare-associated infections (4.3% and 2.8%, respectively). The possible reasons for the large differences compared with the results of previously published surveys are discussed by the authors, as well as some of the methodological issues which are currently addressed in the follow-up European project funded by ECDC (HALT-2), including case definitions of healthcare-associated infections in LTCFs. This improved European surveillance methodology will be implemented in 2013 in a second survey of healthcare-associated infections and antimicrobial use in European LTCFs [8], as a next step of ECDC's efforts to support EU Member States in assessing the effect of implemented prevention and control measures and to raise the awareness about infection control and antimicrobial stewardship in European LTCFs.

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Healthcare-associated infections in long-term care facilities (HALT) in Frankfurt am Main, Germany, January to March 2011

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Healthcare-associated infections (HAIs) are a potentially serious threat to elderly people living in long-term care facilities. Therefore, the European HALT (Healthcare-associated infections in long-term care facilities) project was launched in 2008. HAIs and the use of antibiotics were studied in all 40 nursing homes (100% response) in the city of Frankfurt am Main, Germany, from January to March 2011, using the HALT protocol. Of the 3,732 residents in the homes, 4.3% (n=161) had either signs or symptoms of infections and/or were on oral antibiotics. The most common infections were urinary tract infections (n=45; 1.2%), followed by infections of the respiratory tract (n=41; 1.1%) and skin except mycosis (n=25; 0.7%). The overall prevalence of oral antibiotic use was 2.4% (n=90). The most frequently prescribed oral antibiotics were quinolones (n=31), cephalosporins (n=19), penicillins (n=11) and co-trimoxazole (n=11). The prevalence of HAIs was about the same as that in a European pilot study carried out in November 2009 (5%), but was higher than in several national surveys carried out between May and September 2010 (1.6–3.6%).

Introduction

Healthcare-associated infections (HAIs) are among the most important threats to health in Europe, especially those caused by multidrug-resistant bacteria [1]. Hygiene and appropriate use of antibiotics is necessary for prevention of such infections, not only in hospitals but also in long-term care facilities (LTCFs) for elderly people. However, surveillance of HAIs is mandatory in hospitals only, not in LTCFs. In various studies, the prevalence rates of these infections in LCTFs ranged from 2.8% to 32.7% [2-8] and incidence rates from 1.8 to 13.5 infections per 1,000 resident days [6,9-14]. Thus prevention of infection in LTCFs is necessary [15].

A European project called HALT (Healthcare-associated infections in long-term care facilities) was launched by the European Centre for Disease Prevention and Control (ECDC) in 2008 [16-18]. National HALT programmes were established and in 2009, a pilot point prevalence study on HAIs and antibiotic use was performed in 117 nursing homes in 13 European countries [16]. In summer 2010, a point prevalence survey on HAIs and antibiotic use in European LTCFs was carried out, coordinated by ECDC, with 722 nursing homes across 25 European countries taking part [17].The aims of the HALT project are to measure and describe HAI, antibiotic use, antimicrobial resistance and current infection control/prevention practices in LTCFs all over Europe in order to establish baseline rates and identify priorities for improvement [16]. Participating LTCFs were asked to survey HAIs and antibiotic use on one day, using standardised questionnaires. To date, data from the pilot study are available [16], as well as from national surveys in Ireland, Scotland, Germany and the Netherlands in 2010 [19-22].

From January to March 2011, the HALT project was conducted in nursing homes of the city of Frankfurt am Main (hereafter referred to as Frankfurt), Germany. As all the nursing homes participated, we report here on data from this 100% response.

Methods

From 4 January to 9 March 2011, all nursing homes in Frankfurt were visited by an external surveyor, who was a member of the local public health service. Data on the organisation of the homes as well as point prevalence of infections and antibiotic use were obtained according to the HALT protocol [16]. Two HALT questionnaires were used to obtain data about the institution and residents.

Institutional questionnaire

This questionnaire collected detailed information about the home, including bed capacity, staffing, number of single rooms, medical care, infection control and antibiotic stewardship practices. Data were obtained on the number of residents present at 8 a.m. of the day of the study (eligible residents, hereafter referred to as 'all residents') as well as the number of residents aged over 85 years, male residents, recent surgery, antibiotic therapy, residents with urinary or vascular catheters, pressure sores and other wounds.

Resident questionnaire

This questionnaire was completed for all residents who were on antibiotic therapy and/or who had signs and/or symptoms of infections on the day of the survey giving data on resident demographics, recent hospital stay or surgery, presence of indwelling medical devices, incontinence, disorientation and impaired mobility. We also collected information on diabetes, which had been included in the questionnaire used for the German HALT project [20]. Details of antimicrobial therapy including type of antimicrobial agents, administration route, indication (therapeutic or prophylactic) and prescriber details were collected. We asked for information on HAIs, according to the McGeer criteria [23], which were adapted by the HALT project, i.e. physician diagnosis of infection was included as a criterion in all categories of infection in order to avoid underestimation of the infection rate due to lack of on-site diagnostic testing [16]. The following infections were included: respiratory tract infection (common cold syndromes/pharyngitis, influenza-like-illness, pneumonia); urinary tract infection; eye, ear, nose and mouth infection; skin infection (cellulitis, soft tissue infection, wound infection), skin mycosis; herpes simplex and herpes zoster infection, scabies); gastrointestinal tract infections; systemic infections (primary bloodstream infection; unexplained febrile episode).

Results

Home characteristics, hygiene and organisation

All 40 nursing homes in Frankfurt took part in this survey. The total number of beds was 4,308. The percentage of single rooms per total bed capacity was 60.9% (n=2,624), one home provided single rooms only, and one provided no single rooms at all. The eligible population, i.e. residents present in the home on the day of the survey, numbered 3,732 (determined from the total number of beds minus the non-occupied beds (n=445), minus residents absent because of hospitalisation (n=118) or other reasons (n=13)). The mean capacity of the homes was 108 beds (range: 23–208). All the homes provided round-the-clock professional nursing care: in 23 out of 31 homes only, at least one of the staff had special training in infection control; in the other nine homes, this information was not documented. In all the homes, standard operating procedures for hygiene and nursing had been established to ensure appropriate hygiene and prevention of infection. All homes also had written protocols for hand hygiene, management of indwelling catheters, management of meticillin-resistant Staphylococcus aureus (MRSA) infection, enteral catheters (i.e. percutaneous endoscopic gastrostomy tubes). However, an infection surveillance system was established in only one home.

In all homes, medical care was provided by private general practitioners, with up to 20 physicians in one home. In only one home, an additional so-called home physician was available, with daily presence in the home. According to the German medical system, all these physicians treated only their own patients. Medical coordination of infection prevention, infection surveillance, medical activity and antibiotic stewardship was missing in all the homes.

Table 1

Characteristics of residents in 40 nursing homes in Frankfurt am Main, Germany, HALT project, January–March 2011 (n=3,732)

Characteristic	Total number	%	Range (%)
Aged >85 years	1,912	51.2	25.0–93.0
Male	1,063	28.5	4.6–47.4
Had urinary catheter	377	10.1	2.0–21.4
Had vascular catheter	10	0.3	0.0–1.8
Had pressure sores	158	4.2	0.0–8.8
Had other wounds	197	5.3	0.0–15.5
Were disoriented	2,215	59.4	32.9–96.8
Had impaired mobility	1,903	51.0	19.1–68.6
Had surgery in the past 30 days	50	1.3	0.0–4.6
Were incontinent	3,015	80.8	42.6–100.0
Had percutaneous endoscopic gastrostomy tube	246	6.6	0.0–21.7
Had diabetes	387	10.4	0.0–17.6

HALT: Healthcare-associated infections in long-term care facilities.

Residents' characteristics, including risk factors for healthcare-associated infections

In Table 1, the characteristics of residents at time of the study are shown.

Healthcare-associated infections and antibiotic use

Of the 3,732 residents, 161 had an infection according to the adapted McGeer criteria. Table 2 summarises the infections reported: the most common sites of infection were urinary tract (n=45), upper and lower respiratory tract (n=41), skin (n=25) and skin mycosis (n=20), the eye (n=14) and gastrointestinal tract (n=11).

Point prevalence of all infections was 4.3%, comprising 1.2% urinary tract infections, 1.1% respiratory tract infections, 0.7% skin infections except mycosis, 0.5% skin mycosis, 0.4% eye infections, 0.3% gastrointestinal tract infections and 0.1% mouth infection (periodontitis). We included three residents diagnosed by physicians as having HIV infection, although the HIV infections were not nosocomial, as they were treated prophylactically with oral antibiotics (Table 2). Other infections mentioned in the McGeer criteria such as bacteraemia and scabies did not occur.

Table 3 shows the odds ratios for HAIs by residents' characteristics. Residents with an indwelling urinary

Table 2

Prevalence of healthcare-associated infections in 3,732 residents of 40 nursing homes in Frankfurt am Main, Germany, HALT project, January–March 2011

Type of infection	Infected residents n=161	All residents n=3,732	
	Number of residents with the infection (%)	Percentage of infected residents per total number of residents	Range of percentage infection in the homes
Urinary tract	45 (28.0)	1.2	0.0–8.7
Respiratory tract	41 (25.5)	1.1	0.0–4.3
Skin infection, except mycosis	25 (15.5)	0.7	0.0–7.8
Skin mycosis	20 (12.4)	0.5	0.0–4.3
Eye	14 (8.7)	0.4	0.0–12.5
Gastrointestinal tract	11 (6.8)	0.3	0.0–2.4
Mouth (periodontitis)	2 (1.2)	0.1	0.0–1.2
Other[a]	3 (1.9)	0.1	0.0–1.5
Total	**161 (100.0)**	**4.3**	–

HALT: Healthcare-associated infections in long-term care facilities.

[a] Three residents diagnosed by physicians as having HIV infection were included although the HIV infections were not nosocomial, as the residents were treated prophylactically with oral antibiotics.

catheter, pressure sores, other wounds or diabetes had significantly higher odds for having an HAI . Having a urinary catheter, pressure sores as well as a vascular catheter or diabetes were each found to increase significantly the odds of urinary tract infection. The odds of skin infection were significantly increased by the presence of pressure sores, other wounds or diabetes. However, sex, age, incontinence and dementia (disoriented residents) were not significantly related to a higher risk of having any HAI or of having urinary tract, respiratory tract or skin infections except mycosis. Hence, sex, age, incontinence and dementia proved not to be risk factors for infection.

Of the 161 residents with an HAI, 90 (55.9%) were being treated with oral antibiotics, one (0.6%) resident was treated intravenously and 27 (16.8%) with topical antibiotics; for the remaining 43 (26.7%), no antibiotics had been prescribed (Table 4). Oral antibiotics were prescribed mainly for urinary tract infections (n=39) or respiratory tract infections (n=28), less often for skin infections except mycosis (n=15) and gastrointestinal tract infections (n=4). Topical antibiotics were prescribed to 27 residents, to 18 residents for treatment of skin infections and skin mycosis and to 9 residents for eye infection. About 90% of the oral antibiotics were for therapeutic use, while 10% were used prophylactically.

Table 3

Odds ratios for healthcare-associated infections by residents' characteristics (161 residents of 40 nursing homes), Frankfurt am Main, Germany, HALT project, January–March 2011

Type of infection	Odds ratio (95% CI)			
	All infections n=161	Urinary tract infections n=45	Respiratory tract infections n=41	Skin infections, except mycosis n=25
Male	0.823 (0.572–1.186)	1.259 (0.675–2.350)	0.514 (0.227–1.163)	0.976 (0.407–2.344)
Aged >85 years	1.096 (0.798–1.504)	0.995 (0.553–1.792)	1.659 (0.876–3.142)	0.746 (0.338–1.649)
Had urinary catheter	**3.058** (2.096–4.460)	**8.187** (4.512–14.855)	0.962 (0.341–2.713)	1.703 (0.581–4.986)
Had pressure sores	**2.463** (1.411–4.299)	**2.887** (1.124–7.419)	0.563 (0.077–4.120)	**5.807** (2.151–15.680)
Had other wounds	**2.385** (1.428–3.983)	0.405 (0.055–2.954)	0.446 (0.061–3.260)	**12.549** (5.563–28.310)
Disoriented	0.700 (0.510–0.960)	1.028 (0.564–1.873)	0.588 (0.317–1.090)	0.536 (0.243–1.183)
Incontinent	1.040 (0.694–1.560)	2.457 (0.877–6.883)	0.734 (0.358–1.505)	0.951 (0.356–2.542)
Had surgery in the past 30 days	2.511 (0.983–6.415)	3.526 (0.830–14.974)	NA	3.111 (0.413–23.452)
Had vascular catheter	2.474 (0.311–19.644)	**9.288** (1.152–74.889)	NA	NA
Had diabetes	**2.642** (1.795–3.890)	**2.849** (1.432–5.670)	1.489 (0.564–3.622)	**2.757** (1.094–6.945)

HALT: Healthcare-associated infections in long-term care facilities; NA: not applicable.
Numbers in bold figures are statistically significant odds ratios.

Table 4

Antibiotics prescribed for healthcare-associated infections in 40 nursing homes in Frankfurt am Main, Germany, HALT project, January–March 2011 (n=161)

Type of infection	Infected residents			
	Number infected	Number given oral antibiotics	Number given topical antibiotics	Number given no antibiotics
Urinary tract	45	39	0	5
Respiratory tract	41	28	0	13
Skin, except mycosis	25	15	3	7
Skin mycosis	20	1	15	4
Eye	14	0	9	5
Gastrointestinal tract	11	4	0	7
Other[a]	3	3	0	0
Mouth (periodontitis)	2	0	0	2
Total	**161[b]**	**90**	**27**	**43**

HALT: Healthcare-associated infections in long-term care facilities.

[a] Three residents diagnosed by physicians as having HIV infection were included although the HIV infections were not nosocomial, as the residents were treated prophylactically with oral antibiotics.

[b] Includes one resident treated intravenously with antibiotics.

The majority of the antibiotics were prescribed in the nursing homes (81% (73/90) of the oral and all of the 27 topical antibiotic prescriptions), whereas 17 (19%) of the oral antibiotics had been prescribed in hospital. Most antibiotics were prescribed by a general practitioner (59 (66%) of the oral and 26 (96%) of the topical antibiotics), 21 (23%) of the oral and 1 (4%) of the topical antibiotics had been prescribed by a specialist (i.e. urologist and ophthalmologist) and 10 (11%) of the oral antibiotics by an emergency specialist.

The most frequently prescribed oral antibiotics were quinolones (n=31), other beta-lactam antibacterials (n=19), 17 of which were second-generation cephalosporins and two of which third-generation cephalosporins, penicillins (n=11) and co-trimoxazole (combination of a sulfonamide and trimethoprim) (n=11). A total of 19 of the 45 residents with urinary tract infections, 6 of the 25 residents with skin infections except mycosis and 6 of the 41 residents with respiratory tract infections received quinolone therapy. Antivirals were given to two residents with skin infection (no mycosis) and to another with skin mycosis. Penicillins or cephalosporins were given to 14 of the residents with respiratory tract infections, to eight of those with urinary tract infections and to six of those with skin infections except mycosis. Seven urinary tract infections were treated with co-trimoxazole and four with nitrofurantoin (Table 5).

Oral antibiotics were given for 39 urinary tract infections; however, tests had been documented for only 17 of the 39 before therapy (in 14 cases, a urine stick test had been used and in three, microbiological tests had been carried out).

Discussion

Due to demographic changes, more and more elderly people will depend on qualified nursing in the coming years – at home or in LTCFs: in Germany, for example, the population depending on nursing is estimated to increase between 2007 and 2030 from 2.65 million to 3.37 million [24]. Structures of LTCFs differ greatly throughout Europe, including having different nursing and medical facilities for the residents.

In Frankfurt, all homes were privately run, mostly on a non-profit basis. All residents had their own private physician, so there was no common antibiotic stewardship in the facilities.

The data of our study, conducted from January to Mach 2011, can be compared with the results of the European pilot study in November 2009 [16] as well as the prevalence studies in Ireland, June 2010 [19], Germany, May to September 2010 [20], Scotland, July 2010 [21], and the Netherlands, May to June 2010 [22] (Table 6). The residents in our study were older, more often incontinent than in all other studies cited. More of them also had an indwelling urinary catheter than the residents of the Irish and Scottish cohorts, whereas prevalence of a urinary catheter was roughly the same as in the pilot study and the German and Dutch cohorts. The Frankfurt residents exhibited fewer pressure sores and other wounds compared with the pilot study and the Irish cohort, whereas the rate was nearly the same in the German study. The rate of impaired mobility was comparable to that in the pilot study and the Irish survey, was lower than in the Dutch study, but was higher than in the Scottish and German national surveys.

Table 5

Oral antibiotics prescribed for healthcare-associated infections in 40 nursing homes in Frankfurt am Main, Germany, HALT project, January–March 2011 (n=90)

Type of infection	Infected residents			
	All infections	Respiratory tract infections	Urinary tract infections	Skin infections, except mycosis
J01A Tetracyclines	4	3	0	1
J01C Beta-lactam antibacterials, penicillins	11	7	1	3
J01D Other beta-lactam antibacterials	19	7	7	3
J01E Sulfonamides and trimethoprim	11	2	7	0
J01F Macrolides, lincosamides and streptogramins[a]	4	3	0	0
J01M Quinolone antibacterials	31	6	19	6
J01X Other antibacterials[b]	6	0	4	0
J05 Antivirals for systemic use[c]	3	0	0	2
No data	1	0	1	0
Total	**90**	**28**	**39**	**15**

HALT; Healthcare-associated infections in long-term care facilities.

[a] Only macrolides (n=2) and lincosamides (n=2) were used.

[b] Nitrofurantoin was used.

[c] Given to two residents with skin infection (no mycosis) and to a third with skin mycosis.

The infection prevalence was 4.3% and thus roughly the same as the prevalence in the pilot study, but higher than in the national studies published. This might be influenced by the season: our study, like the pilot study, had been carried out in autumn/winter (between November and March), whereas the other cited national surveys were carried out between May and September. In all studies, infections of the respiratory tract, urinary tract and skin infection were the most abundant. The 1.2% prevalence of urinary tract infections in our study is less than that in the Irish and the Scottish studies although indwelling urinary catheters were used much more often in the Frankfurt homes than in Irish and Scottish LTCFs. However, the prevalence of urinary tract infections in our study was higher than in the German and Dutch studies.

The prevalence of all HAIs was less than in the pilot study, but higher than in the other four studies. Comparability of the data may be limited, as in three other studies (in Ireland, Germany and Scotland), the data were collected by staff from each nursing home, whereas in our study and that from the Netherlands, all homes were visited by the same external surveyor, documenting the data in the same standardised way. Moreover, in our study, all homes agreed to participate in the study (100% response rate), so any bias related to the voluntary participation of homes that are especially interested in the subject need not to be taken into account.

Although the Frankfurt study was done to from January to March, the prevalence of respiratory infections was low, compared with the pilot study (November 2009), but higher than the German, Irish and Scottish ones, which were carried out between June and September 2010, and no influenza was reported. However, 3% of the residents were in hospital on the day of investigation and some of them might have been hospitalised because of infections, pneumonia, etc.

Although antibiotics were prescribed by external private physicians in the Frankfurt LTCFs and there were no standard guidelines for antibiotic therapy in the homes, the use of oral antibiotics was low (2.4%) in our study compared with the pilot study (5.2%), the Irish study (10.2%), the Dutch study (3.5%) and the Scottish study (7.3%). It was roughly comparable to the German study (1.15%), though somewhat higher. Antibiotic prescription for prophylactic reasons was 10% and thus in line with the German national survey (6.4%), but much lower than in Ireland and Scotland, where 42% and 48% of the cases received antibiotics for prophylaxis. The German guidelines of the Paul Ehrlich Society for antibiotic therapy [25] of ambulatory infections seem to have been followed in the Frankfurt nursing homes, although compliance to these guidelines is not obligatory. In these guidelines, regarding infections of the lower respiratory tract in persons at risk (i.e. residents of LTCFs), the first choice for therapy is beta-lactam antibacterials, with quinolones and third-generation cephalosporins as second choice. With regard to urinary tract infections, acute cystitis should be treated with trimethoprim and sulfonamides, with third-generation cephalosporins as a second alternative. The first-choice antibiotic for pyelonephritis are quinolones, alternatives are trimethoprim and sulfonamides, with third-generation cephalosporins and penicillins with an extended beta-lactamase spectrum [25-27].

Table 6

Characteristics of residents and healthcare-associated infections in the Frankfurt HALT study 2011, compared with previous HALT projects

Characteristic	Frankfurt, Germany	European pilot study (13 countries)	Ireland	Germany	Scotland	The Netherlands
	Jan–March 2011	Nov 2009	Jun 2010	May–Sep 2010	Jul 2010	May–Jun 2010
	% (range)[a]	%[a]	%[a]	%[a]	%[a]	%[a]
Number of homes	40	117	69	73	83	10
Number of residents	3,732	14,491	4,170	6,496	4,870	1,429
Residents						
Aged >85 years	51.2 (25.0–93.0)	44.3	34.3	47.6	40.8	40
Male	28.5 (4.6–47.4)	25.8	NR	26.6	25.7	32
Incontinent	80.8 (42.6–100.0)	67.5	63.0	74.5	61.3	61
Disoriented	59.4 (32.9–96.8)	55.1	50.6	56.7	57.6	59
Had Impaired mobility	51.0 (19.1–68.6)	51.1	52.4	44.8	34.8	57
Had urinary catheter	10.1 (2.0–21.4)	9.1	5.6	10.2	7.4	12
Had vascular catheter	0.3 (0.0–1.8)	1.5	0.3	0.2	0.0	0
Had pressure sores	4.2 (0.0–8.8)	6.7	2.9	3.8	2.9	7
Had other wounds	5.3 (0.0–15.5)	8.0	9.4	5.1	4.1	NR
Had surgery in the past 30 days	1.3 (0.0–4.6)	2.0	1.1	1.8	0.0	3
Infection type						
Urinary tract infection	1.2 (0.0–8.7)	1.50	1.5	0.6	1.4	0.7
Respiratory tract infection	1.1 (0.0–4.3)	2.10	1	0.3	0.5	NR
Skin infection except mycosis	0.7 (0.0–7.8)	0.68	0.7	0.4	0.4	NR
Skin mycosis	0.5 (0.0–4.3)	NR		NR	0.0	NR
Eye	0.4 (0.0–12.5)	0.19	0.1	0.03	0.2	NR
Mouth	0.1 (0.0–1.2)	0.03	0.1		0.1	NR
Gastrointestinal tract	0.3 (0.0–2.4)	0.23	0.2	0.09	0.0	NR
Other	0.1[b] (0.0–1.5)	0.08	NR	NR	0.0	NR
Prevalence of all infections	**4.3**	**4.98**	**3.6**	**1.6**	**2.6**	**2.8**
Antibiotic therapy						
Number of residents undergoing oral antibiotic therapy	90	762	426	75	357	50
Prevalence of oral antibiotic therapy	2.4	5.4	10.2	1.15	7.3	3.5

HALT; Healthcare-associated infections in long-term care facilities; NR: data not reported.

[a] Unless otherwise indicated.

[b] Three residents diagnosed by physicians as having HIV infection were included although the HIV infections were not nosocomial, as the residents were treated prophylactically with oral antibiotics.

Source: European pilot study [16] and studies from Ireland [19], Germany [20], Scotland [21] and the Netherlands [22].

In only six (3%) of the 161 infections identified in our study were the results of microbiological tests available, i.e. in 155 infections neither the bacteria nor antibiogram was available. This level is in line with data from the German survey, but far lower than in the Scottish survey.

All the Frankfurt homes have been supplied with the aggregated data as well as those relating to their particular home. The data have been discussed with the homes and the physicians in order to achieve further improvements in antibiotic therapy and restrictions for the use of invasive medical devices, which are well-known risk factors for HAIs [28,29].

Our data can serve as baseline data for forthcoming surveillance studies in Frankfurt, thus giving an opportunity for observation of trends in the Frankfurt nursing homes. Furthermore, the Frankfurt data and national German data could be used as reference for future HALT projects in Germany, which would preferably be coordinated by the local or regional public health services in addition to the hygiene control visits they are obliged to conduct according to the German Protection against Infection Act.

Because of the standardised and harmonised methodology, it is possible to compare the data from various HALT surveys in other European countries. Such

comparisons, including a discussion of differences seen, i.e. in antibiotic stewardship, can help to prevent infections and the further increase in the prevalence of multidrug-resistant organisms.

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Evidence for airborne infectious disease transmission in public ground transport – a literature review

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While guidelines on contact tracing (CT) after exposure to certain infectious pathogens during air travel exist, no guidance documents are available on CT in response to potential exposure on public ground transport. We reviewed scientific and non-scientific literature on transmission of airborne pathogens in public ground transport and on factors potentially influencing transmission. We identified 32 relevant publications (15 scientific and 17 non-scientific). Most of the selected studies dealt with transmission of tuberculosis. However, the relation between travel duration, proximity to the index case and environmental factors, such as ventilation, on disease transmission in public ground transport is poorly understood. Considering the difficulty and probably limited effectiveness of CT in ground transport, our results suggest that only exceptional circumstances would justify CT. This contrasts with the high level of attention CT in air travel seems to receive in international regulations and recommendations. We question whether the indication for CT should be revisited after a risk–benefit assessment that takes into account exposure in both ground and air transport.

Introduction

Passengers using public transport may be at risk of infectious disease when they are exposed to infected passengers. Although guidelines on contact tracing (CT) after exposure to selected airborne infectious diseases during air travel exist, no guidance documents are available on CT in response to potential exposure on public ground transport. Comparing the share of performance of air and ground travel respectively, the share of performance in public ground transport, such as buses/coaches, trams, metros and railways, of total transport performance of passengers in Europe in 2007 was nearly twice as high (15.7%) as the share of air transport performance (8.8%) [1,2].

CT is defined as the identification of persons who may have been exposed to an infectious disease by an infected person and ensuring that they are aware of their exposure [3,4]. Although a recent literature review concentrated on published studies on tuberculosis (TB) transmission and recommendations for CT related to use of public transport [5], our review was carried out to analyse available publications on the evidence for transmission of any airborne infectious disease and on factors potentially influencing the risk of transmission in public ground conveyances. In addition to searching the scientific literature, we also performed a search of non-scientific literature.

Methods

Search strategy

Scientific literature

In May and June 2009, a review of scientific literature was carried out using Scopus, the largest abstract and citation database of peer-reviewed literature and high-quality web sources [6,7]. It provides 100% MEDLINE coverage and contains more than 19,500 titles from 5,000 publishers [8]. We searched the database for mentions of airborne transmission of infectious diseases in public ground conveyances. We decided to perform the broadest possible search to include publications that might touch upon airborne disease transmission and CT without necessarily being the paper's main subject. Through the 'all fields' search, the following keywords were used: 'railway', 'train', 'bus', 'school bus', 'coach', 'tram', 'tramway', 'metro', 'subway', 'underground' and 'tube'. We combined each means of public ground transport keyword with each of the following keywords (through 'AND'): 'infection', 'infectious disease', 'transmission', 'contact tracing', 'contact investigation', 'passenger tracing', 'tuberculosis', 'mycobacterium tuberculosis', 'TB', 'meningitis', 'meningococcal disease', 'avian influenza', 'viral hemorrhagic fever', 'SARS', 'bubonic plague', 'rubella', 'Lassa fever', 'measles', 'diphtheria' and 'smallpox'. In early December 2010, we updated the search using the identical keywords through the 'all fields' search.

In a first step, search hits were screened by three reviewers: articles were selected if they contained information on airborne infectious disease transmission in public ground transport. English titles of all the selected publications were reviewed. If the title information was insufficient, the abstract was looked at to decide if the publication potentially met the selection criterion. The full text of each paper was obtained

when the selection criteria were met or when further information was needed to decide whether to include an article or not. When a reviewer was uncertain about making a decision at any of these steps, the other team members were consulted and a joint decision was taken. The selected articles were then reviewed for events of airborne infectious disease transmission in public ground transport.

The following data were retrieved from each study: publication details (year, author(s), location), means of transport, diagnostic tests, number of infected persons, number of tested contacts, transmission rate and number of cases with active disease. The publications were evaluated on factors potentially influencing transmission of infectious disease such as cumulative exposure related to repeated trips (e.g. on a school bus or commuter bus), duration of travel and environmental factors (ventilation and air conditioning systems, seating position, distance to contact person). Bibliographies of potentially relevant publications were checked for additional studies.

Non-scientific literature

In February 2009, we performed a structured search for non-scientific literature through the search engines Google News, Google Scholar, GENIOS and World News. The search was limited to English and German publications.

The search with GENIOS allowed a maximum of two keywords, the search of the World News archive was limited to the previous six months (September 2008–February 2009), the World News advanced search was only searchable day by day, whereas the search with Google News archive and Google Scholar was limited to the previous five years (February 2004–February 2009). Due to the differing time frame for searches provided by the engines we decided not to update the search.

The keywords 'bus', 'railway' and 'metro' were combined with 'infectious disease'. The first 200 hits from each keyword combination with each search engine were screened to assess potential relevance to transmission of infectious disease and CT in public ground transport. We reviewed title, abstracts or both of all retrieved publications. Potentially relevant articles were selected: inclusion criteria were events or cases of potential airborne infectious disease transmission. The full text of each selected publication was obtained and evaluated.

We adopted the following definitions: an infection with *Mycobacterium tuberculosis* was evidenced by a positive tuberculin skin test (TST) reaction and/or a positive interferon-gamma release assay (IGRA) without any sign of clinically or radiologically manifest disease. Active tuberculosis was defined by bacteriologically, histologically or radiologically confirmed active disease. Measles was diagnosed through testing of serum specimens for measles-specific IgM and IgG antibodies using an enzyme immunoassay: persons who were IgM positive were defined to have a recent measles infection. A classical measles case was defined as a person who meets the clinical case definition and/or meets the serological criteria [9]. Mild or asymptomatic measles was defined as a recent measles infection indicated by the presence of measles IgM, but who did not meet the clinical case definition [10-12]. Meningococcal disease was evidenced through culture of blood and cerebrospinal fluid (CSF) or polymerase chain reaction (PCR) of CSF.

Results

Scientific literature

Our 'all fields' search identified a total of 21,764 hits. After screening abstracts and/or titles, 72 potentially relevant publications were identified for full-text evaluation. Finally, 15 publications were selected. All selected publications describe CT. Of the selected publications, all but one reported disease transmission in buses; the other described a combined trip by bus and train, but CT focussed solely on the passengers who travelled by train [13]. In total, 14 events, dating from 1961 to 2008, were included in our study (the same event was described by two publications). No relevant publication was found reporting on airborne infectious disease transmission in a tram or metro/underground/subway. Of the 14 events related to airborne infectious disease transmission followed by CT in ground transport, 11 events were on TB, two on meningococcal disease and one on measles. Three reported on singular exposure during single trips and 11 on events related to cumulative exposure during repeated trips.

Single-trip exposure

Event 1, TB in train trip

A combined single bus and multiple train trips taken in January 1996 by a 22 year-old male index case with bilateral cavitation, cough and haemoptysis in the United States was reported, but CT was only undertaken for passengers who travelled by train [13]. The train journeys lasted 29.1 hours (12.3 hours from Chicago to Pittsburgh, and 16.8 hours from Washington, DC, to Florida). The median duration of travel by co-passengers was 12.3 hours (range: 1–34.7 hours). The train operator provided a list of passengers and crew-members; the telephone number was the only available contact information. Passengers and crew members were notified via telephone (to obtain addresses) and by recorded delivery. A total of 76.8% of passengers (368/479) could be located and 50.1% of persons (240/479) were evaluated: 15 of 240 persons (6.3%) seroconverted; of the 15, two developed active disease. The possibility of more extensive transmission could not be excluded.

Event 2, TB in bus trip

In a single bus trip in Spain from Malaga to the Sierra Nevada in March 1998 [14], the index case was an 18

Table 1

Review results: contact tracing after exposure to cases with tuberculosis or measles during single trips

Event number	Infectious disease	Means of transport	Duration of travel	Tests	Number of infected contacts/ number of tested contacts (trans-mission rate)/ number of cases with active disease	Other potential factors influencing trans-mission (e.g. ventilation system, distance to index case)	Location	Reference
1	Tuberculosis	Train[a]	12.3 hours + 16.8 hours	– TST – sputum culture	15/240 (6.25%)/ active disease: 2	Each train car had a separate ventilation system. Windows could not be opened. Air circulation through a typical air-conditioning filter was at 10–15 air exchanges per hour.	USA	Moore et al. 1999 [13]
2	Tuberculosis	Bus	6 hours	– TST – X-ray – sputum culture	21/53 (39.6%)/ active disease: 5	No external ventilation, windows closed.	Spain	Extremera Montero et al. 2001 [14]
3	Measles	Bus	3 days	Serum (measles-specific IgM antibodies by using an enzyme immunoassay)	10/44 (23%)	College trip with two buses. At stops, persons from both buses could interact.	USA	Helfand et al. 1998 [15]

TST: tuberculin skin test; USA: United States of America.

[a] In addition to the train trip, also a bus trip (additional travel time with the bus: 5.5 hours). No contact investigation of co-passengers in the bus trip performed.

year-old male student with active TB, but without cavitations. Including the bus driver, 53 persons travelled on the bus. Two of three teachers became infected. Of the 49 students, 41 were traced: 19 seroconverted. Of these 19, five developed active disease. In total, there were 21 secondary cases. Through multivariate analysis, bus exposure was identified as an independent risk factor for TST reactivity (attributable risk: 15.9%).

Event 3, measles in bus trip

A study in the United States investigated the frequency of mild or asymptomatic measles infections of persons exposed to a student with measles during a three-day bus trip in May 1996 involving two buses [15]. On the first day of the trip, one student became ill with clinical signs of classic measles, which was subsequently confirmed by serological studies. The exposed persons travelled on the two buses and could interact with persons on the other bus at other times, such as during meals, visits to museums and at rest stops. Most persons travelled on the same bus throughout the trip. The results demonstrated that mild or asymptomatic measles infections can occur in previously immune populations. A total of 94 persons participated in the trip: for the investigation, 45 persons agreed to participate in the study. None of the participants developed classic measles symptoms. However, 10 persons were IgM positive for measles, probably arising from exposure to the index case.

The outcome from the CT following exposure to TB or measles during a single trip are summarised in Table 1.

Repeated trip exposure

Event 4, TB in bus trip

As part of an investigation of a school- and community-based TB outbreak in late 1992 in northern Italy, independent risk factors for TST were analysed by multivariate analysis for students travelling in the same bus as the index patient [16]. The index patient was an 18 year-old student with active disease (cavitations). Out of 212 contact persons tested, 70 (33.0%) seroconverted. The adjusted odds ratio (OR) for classroom contact was at 4.4 (95% CI: 3.4–5.7) and for living in the same town was 4.8 (95% CI: 3.8–6.0). The OR was highest for travelling on the bus with the index patient: 5.4 (95% CI: 4.3–6.7). The attack rates for the bus passengers in relation to the duration of travel are shown in Table 2.

Event 5, TB in bus trip

CT was carried out after transmission of TB on a school bus in 1998 in the United States [18]. The nine year-old index case with bilateral cavitation travelled on the school bus for 90 minutes each morning; the co-passengers were exposed between 35 and 75 minutes daily. Out of 32 school bus contacts, 10 seroconverted; among those, two students developed active disease.

Table 2

Review results: daily travel time of students in two school buses in relation to attack rate (seroconversion) in tuberculosis transmission

Event number	Number of infected contacts/ number of tested contacts (transmission rate)	Travel time in minutes[a]	Percentage attack rate (seroconversion)	Reference
4	70/212 (33%)	10–20 min	15.4	Ariano et al. 1994 [16]
		25–35 min	14.9	
		40 min	55.0	
10	85/266 (32%)	<10 min	21.6	Rogers et al. 1962 [17]
		10–19 min	33.7	
		20–29 min	27.0	
		30–39 min	27.3	
		40–49 min	50.0	
		≥50 min	62.5	

[a] Travel time per trip (in most cases trip twice daily).

Event 6, TB in bus trip

A brief report described transmission of TB on a school bus in April 2007 in the United Kingdom; however, the daily duration of the bus trip was not mentioned [19]. The cumulative mean duration of exposure of students to the index case, a smear-positive 46 year-old bus driver, exceeded 24 hours. Transmission from the bus driver was extensive: 18 of the 33 students had a positive IGRA; among those, four children developed active TB.

Event 7, TB in bus trip

In the United States in 2001, of 33 passengers in a school bus exposed to the index case, 18 seroconverted. The index case was a 15 year-old student with cavitation. One of the seroconverted contacts developed active disease [20]. There was daily exposure of the contacts to the index case, but the duration of exposure was not discussed.

Event 8, TB in bus trip

In the United States in 1985, of 29 students exposed to the index case, a 13 year-old student with cavitation, 17 seroconverted; however, there was exposure in the school choir, school bus and the school itself [21]. Of the 17 students who seroconverted, eight had no other direct or indirect contact with the index patient other than on the school bus. The duration of exposure of the contacts to the index case during the bus trips was not discussed.

Event 9, TB in bus trip

CT was carried out after transmission of TB in a Japanese commuter bus in 1999 as a result of cumulative exposure to the index case through repeated trips to the workplace [22]. The index case was a 22 year-old woman without cavitation who worked as an employee of an electronics company. Of the 49 commuters exposed to the index case, five seroconverted. However, the study did not exclude workplace contacts.

Event 10, TB in bus trip

Two publications dating from 1962 reported on the same event in the United States: CT was undertaken after transmission of TB from a school bus driver (without cavitation) to students during daily trips [17,23]. Of 266 exposed passengers, 85 (32.0%) seroconverted. In children riding less than 10 minutes per trip, 8 of 37 had a TST conversion. In children riding 40–49 minutes per trip, 7 of 14 children seroconverted, whereas in children following a travel time of at least 50 minutes per trip, 10 of 16 seroconverted [17] (Table 2).

Event 11, TB in bus trip

Between November 1994 and April 1995, students in two counties in New York were exposed to five school bus drivers with pulmonary TB [24]. A relative risk of 39.3 (95% CI: 8.8–174.8) for a positive TST was significant only in students exposed to driver 3. A total of 101 students exposed to driver 3 were screened: 17 were defined as close contacts; of those, 11 were TST positive. There was no clear evidence of transmission of M. tuberculosis to students from drivers 1, 2, 4 or 5. No student was potentially exposed to more than one driver. However, evidence suggests that driver 3 transmitted TB not only to students, but also to bus driver 4, who developed active disease. Drivers 3 and 4 worked for the same bus company and often sat together in the closed bus of driver 3 while waiting for students to leave school and enter their buses. M. tuberculosis isolates of driver 3 and 4 were indistinguishable by DNA fingerprinting.

Event 12, TB in bus trip

A TB outbreak in an Alabama high school in the United States in 1969 led to CT of 379 persons: of 27 students

Table 3

Review results: contact tracing after exposure to cases with tuberculosis in repeated bus trips

Event number	Type of bus-transport	Duration of travel or frequency of exposure	Number of infected contacts/ number of tested contacts (transmission rate)/ number of passengers with active disease	Diagnostic tests carried out or information collected	Other potential factors influencing transmission (e.g. duration of travel, ventilation system, distance to index case)	Location	Reference
4	School bus	10–40 minutes daily[a]	70/212 (33.0%)[b]	– TST – X-ray – sputum culture	Bus generally carried twice as many persons as there were seats. Those getting on at stops closer to the school were crowded in the bus aisles.	Italy	Ariano et al. 1994 [16]
5	School bus	– Index case: 75 minutes in the mornings, daily – Exposed passengers: 35–75 minutes daily	10/32 (31.2%)/ active disease: 2	– TST – X-ray – sputum culture – DNA-fingerprinting	–	USA	Curtis et al. 1999 [18]
6	School bus	Mean duration of exposure >24 hours	18/33 (54.5%)/ active disease: 4	– IGRA – sputum culture	Closed ventilation system, combined with a heating system that blew hot air towards the infectious driver and then into the remainder of the bus	UK	Neira-Munoz et al. 2008 [19]
7	School bus	Daily	7/27 (26%)/ active disease: 1	– TST – X-ray – sputum culture	–	USA	Phillips et al. 2004 [20]
8	School bus	Daily	17/29 (58.6%)[c] 8/17 (47.1%)[d]	– TST – X-ray	–	USA	Sacks et al. 1985 [21]
9	Commuter bus	Daily	5/49 (10.2%)/ active disease: 2	– TST – X-ray – sputum culture	The air conditioning used a closed recirculation system with insufficient ventilation	Japan	Yagi et al. 1999 [22]
10	School bus	<10 to >50 minutes daily[a]	85/266 (32%)/ active disease: 52	– TST – X-ray	Two fan-type heaters, two fans deflecting air from the front to the rear. Capacity: 55 seats, 11 standing	USA	Rogers et al. 1962 [17] Mahady et al. 1961 [23]
11	School bus	25–35 minutes daily After arrival at the school, additional 15–20 minutes in the bus	11/101 (10.9%)[e]/ active disease: 1	– TST – X-ray – sputum culture – sputum AFB smear – demo-graphic info – DNA fingerprinting	Winter, closed windows, poor ventilation	USA	Yusuf et al. 1997 [24]
12	School bus	Daily	22/27 (81.5%)[f] active disease: 0	– TST	Poor ventilation	USA	Darney et al. 1971 [25]

AFB: acid-fast bacilli; IGRA: interferon-gamma release assay; TST: tuberculin skin test: UK: United Kingdom; USA: United States of America.

[a] See Table 2 for details.
[b] Bus contact was independent factor through multivariate analysis.
[c] Total of 17 reactors (with additional contacts in a choir, bus and school).
[d] Of the 17 reactors, 8 had no other direct or indirect contact with the index patient other than the school bus.
[e] Of 101 tested contacts 17 were close contacts. Exposed to driver 3 only. No definite transmission from other infected bus drivers (bus drivers 1, 2, 5) .

who travelled on the school bus with the index case, 22 seroconverted. The index case was a 17 year-old male in the 11th grade (ages 16–17 years). Six of the 10 positive reactors in grades 7 to 9 (12–13 years to 14–15 years) rode the bus, but only 11 of the 67 positive reactors in grades 10 to 12 (15–16 years to 17–18 years) were bus riders. The school bus riders thus accounted for a much larger proportion of the positive reactors in grades 7–9 than they did in grades 10–12. The contact of the students from grades 7–9 with the index case was largely limited to travel on the school bus, which was poorly ventilated [25].

Results from CT following exposure to TB on repeated bus trips (events 4–12) are summarised in Table 3.

Event 13, meningococcal disease in bus trip
A letter to the editor described the transmission of Neisseria meningitidis (serogroup B) to two of 132 co-passengers (1.5%) in a crowded school bus in Australia in June 2005. All co-passengers were successfully traced [26].

Event 14, meningococcal disease in bus trip
In the course of a study in the United States on the effect of influenza to predispose towards meningococcal disease in 1986, five of 72 students were found to have developed meningococcal disease following exposure to the index case in a school bus [27]. The average amount of time spent on the bus the previous two weeks was 8 hours 4 minutes (cumulative) for each of the five affected children. The students had assigned seats and generally used the same seat each day. All five students reported influenza-like symptoms around 5-15 days (mean: 10.6 days) before the development of meningococcal disease. Results from CT following exposure to meningococcal disease on repeated trips on school buses (events 13 and 14) are summarised in Table 4.

Non-scientific literature

Our search of non-scientific literature yielded 55,325 hits. This search was complementary to the scientific literature search to detect information on events that might not be reflected in the scientific literature. Non-scientific sources, in the absence of any scientific peer-review process, cannot be given equal standing with the scientific literature. Nevertheless, it seemed important to check for reports in other sources given the low number of scientific publications. Of the first 200 hits from each keyword combination with each search engine, 34 potentially relevant reports were identified. Of these, we selected 17 publications dating from 1998 to 2008 on eight events – either descriptive reports of the incident followed by CT or press releases produced as part of a CT strategy. They described the potential transmission of TB, meningococcal disease, SARS or rubella during bus or railway trips. No publications on transmission of airborne infectious diseases in metros and trams were found. Only one event (event 6) picked up by the non-scientific literature search

Table 4
Review results: contact tracing after exposure to cases with meningococcal disease in repeated bus trips

Event number	Means of transport	Diagnostic tests	Number of Infected contacts/ number of tested contacts (trans-mission rate)	Cumulative exposure	Other potential factors influencing trans-mission (e.g. duration of travel, ventilation, distance to index case)	Location	Reference
13	School bus	PCR of meningococcal DNA in CSF, followed by porA/ porB genotyping	2/132 (1.5%)	Yes	Bus crowded (usually carried 78 students: 53 seated, 25 standing)	Australia	Beard et al. 2006 [26][a]
14	School bus	CSF cell count; blood, pharyngeal culture	5/72 (6.9%)	Yes	Total roundtrip 2 hours 10 minutes. Some students spent less than 2 hours on the bus; average amount of cumulative ex-posure during pre-vious 2 weeks was 8 hours 4 minutes. Students had assigned seats.	USA	Harrison et al. 1991 [27]

CSF: cerebrospinal fluid; PCR: polymerase chain reaction; USA: United States of America.
[a] Letter to the editor.

[28,29] was also picked up by the scientific literature search [19].

TB in bus trips

Eight publications describe three events linked to transmission of TB as a result of bus travel. Two of those publications report on transmission of TB from a bus driver to students in the United Kingdom [28,29]. This event was also reported in the scientific literature (event 6) [19]. One of the publications describes the exposure to a bus driver infected with TB in a school bus in the United States [30]. Both school bus events are related to repeated bus trips. Five of the publications are dedicated to two different incidents in Canada concerning single-trip exposure to TB in a long-distance travel bus [31-35].

SARS in railway trip

Two publications discuss one event in a train linked to the SARS outbreak in Canada in 2003 [36,37].

Meningococcal disease in railway trips

Six publications in German newspapers describe the occurrence of meningococcal disease related to railway trips in 1998 and 2008. In 1998, three publications reported on a case of meningococcal disease on a train: an 18 year-old student became symptomatic on a railway trip from Rome (Italy) to Munich (Germany) [38-40]. On transit through Austria, co-passengers received post-exposure prophylaxis. On arrival in Germany, the train was stopped and put under quarantine. The publications did not mention whether or not the index case transmitted the disease to co-passengers on the train.

We also selected three publications from 2008 on exposure to an 18 year-old Swiss student with meningococcal disease travelling by train from Zurich (Switzerland) to Berlin (Germany) [41-43]: two of the publications were released as part of a CT media strategy: persons potentially in contact with the index case were invited to contact their local health department [41,43]. This event was also reported in the scientific literature [44]; however, it was not picked up by our scientific literature search, since disease transmission was not evident.

Rubella in bus trip

We selected a publication on CT in 2008 of 700 potentially exposed persons to a woman infected with rubella in a shuttle bus in the United States [45]. The woman commuted to work not knowing that she was infected.

Environmental factors potentially influencing the risk of pathogen transmission in public ground conveyances

Of the 15 selected scientific publications, 11 contain information on potential environmental risk factors such as poor ventilation, closed ventilation systems and proximity to the index case [13,14,16,17,19,22-27]. The scientific publications related to the events 3, 5, 7, and 8 and the selected non-scientific publications do not provide information on environmental factors related to pathogen transmission.

A study related to the combined bus and train trip (event 1) in 1996 in the United States describes the air circulation on the train as an air-conditioning system with filter [13]. The air exchange rate was 10–15 times per hour and filters were changed every 15 days. Windows could not be opened in any of the carriages. Each train was composed of coach cars (at least one sleeper car and one dining car). Interviews with the passengers and index TB patient indicated that transmission resulted rather from brief contact (face-to-face contact or when seated near the ill passenger while he was dining and speaking) than from extended sharing of train airspace. With the exception of a brief stay in the dining car, the index case remained seated in his assigned seat. The passenger had several episodes of haemoptysis, covered his mouth with the hood of his jacket when coughing and avoided contact with other passengers [13].

Related to a single-trip exposure of passengers to TB (event 2), poor ventilation (windows closed, no air conditioning) due to low outside temperature was reported as a factor potentially influencing transmission [14]. In total 21 persons were infected (19 students and two teachers). Of the 19 infected students, 10 were sitting no more than two rows away from the index case [14].

The TB outbreak in northern Italy (event 4) highlights that those students getting on the bus carrying the index case at the stops closer to the final destination were crowded in the bus aisles [16]. Crowding was seen as a potential factor influencing the transmission of disease in the study on an outbreak of meningococcal disease (event 13) in a school bus [26]. The publication on event 14, reports on assigned seats for students (in general they sat in the same seat each day) in a school bus within the frame of CT related to meningococcal disease after an influenza respiratory infection [27].

The TB outbreak in an Alabama high school in 1969 (event 12) with high transmission rates especially in school bus passengers was related to poor ventilation of the bus [25]. The report of transmission of TB in a Japanese commuter bus (event 9) described a closed recirculation system with insufficient ventilation [22]. In event 6, a high transmission rate of TB was also linked to a closed ventilation system, combined with a heating system that blew hot air toward the infectious driver and then into the rest of the bus [19].

In the report from 1962 of event 10, there was a detailed description of the environment of a bus in which TB was transmitted extensively from a school bus driver to students [17]. The bus was equipped with two fan heaters, one situated to the left beside the bus driver and the other midway in the bus. There was a defroster at the base of the windscreen and two fans were installed (one on either side of and directed at the

windscreen). When in use, those would move air from the front to the rear of the bus.

An investigation on CT related to bus drivers with pulmonary TB (event 11) provides some information on potential environmental factors [24]. Even though the extent of ventilation in all buses was not known, it was seen as likely that the windows were closed due to wintertime. However, according to the school policy, the driver (with pulmonary TB) was not allowed to let the children off when the bus had arrived early. Therefore, the children waited on the bus with the driver for 15–20 minutes (in addition to a trip duration of 25–35 minutes), during which time the windows remained closed. This may have contributed to prolonged cumulative exposure of the students in a poorly ventilated environment. No information concerning the seating of the children on the buses was provided. It was not possible to draw any conclusion regarding seat position and exposure.

Discussion and conclusions

Our review of the scientific literature revealed 14 events (15 publications) of documented human-to-human transmission of airborne infectious disease related to public ground transport. Most of the scientific publications we selected report on transmission of TB, a few on meningococcal disease and one on measles: reports on transmission of other pathogens are lacking. In our review we address various factors potentially influencing disease transmission such as length of exposure, proximity to index case and type of ventilation. Complementary to the review of scientific literature, we conducted a web-based search of non-scientific literature in order to ensure a broader search and to assess the potential for publication bias. Through the non-scientific literature search we identified eight events, two of which were reported in the scientific literature, but only one of them [19] was picked up by our scientific literature search.

Close to half a billion citizens in the 27 countries of the European Union enjoy access to various means of transportation [1]. Given the large number of passengers travelling by public ground transport, the number of reported incidents appears to be very low [1,2]. The anonymous nature of contact between passengers makes it unlikely that an infectious disease diagnosed after a trip will trigger warnings or investigations with reference to travel-related exposure, unless unusual circumstances such as 'dramatic' illness (e.g. loss of consciousness in meningococcal disease) are involved. The lack of evidence of disease transmission related to use of public ground transport and the lack of guidance documents may be reasons for the limited number of publications in this field.

The World Health Organization guidelines for air travel recommend CT of passengers exposed to people with pulmonary TB who sat in adjacent rows for longer than eight hours (including ground delays) [46,47]. These guidelines refer to single trips whereas in public ground transport, repeated (daily) and short trips to and from school or the workplace, for example, also take place.

Cumulative exposure related to repeated bus trips can lead to high transmission rates of TB and to transmission of meningococcal disease. We identified reports describing an association between the duration of exposure to TB through repeated trips and seroconversion in contact persons (Table 2): generally speaking, the longer the travel duration, the higher the rate of seroconversion [16,17].

Environmental characteristics such as space and air (re)circulation may influence the risk of disease transmission. It is known that droplet nuclei may be transported through ventilation systems, as has been documented for TB [48]. Indoors, bacilli are potentially trapped, disperse within a room, and may remain viable and suspended in the air for a prolonged period of time [49-52]. Dilution of infectious particles through local air circulation and overall room ventilation can direct exposure into spaces that were not even visited by the index patient [53-56]. Comprehensive information on factors potentially influencing the risk of disease transmission is lacking for travel in public ground conveyances. Detailed information on ventilation and air circulation has been given in two publications: however, the factors were not systematically evaluated [17,19]. Given the low number of publications dedicated to infectious disease transmission and ventilation systems, we included studies dating back to the 1960s when air conditioning systems were not commonly in use on buses. Findings based upon older studies might therefore not be applicable to newer systems.

Crowding of passengers in public or school buses may act as a triggering factor on the transmission of TB and meningococcal disease [16,26]. Transmission through brief but intensive contact has been described for TB [57-62]. In a cohort study with a random sample of 142 commuters on the association between public commuter transport in Peru and pulmonary TB in workers, the authors concluded that the use of minibuses increased the risk of pulmonary TB due to overcrowding, cumulative exposure to persons with productive coughs while commuting twice daily five days a week, closed windows on minibuses, combined with a high prevalence of pulmonary TB [63]. Furthermore, persons with pulmonary TB have more productive coughs in the mornings, hence increasing the risk for transmission of TB to other passengers presumably during morning travel [64], as has already been suggested by other studies in developing and industrialised countries [16,65,66]. While it is recognised that overcrowding in confined spaces increases the risk of transmission, this risk has not been quantified [64]. Not only in settings such as public transport, the relation between overcrowding, duration of exposure including cumulative exposure, ventilation and other environmental

characteristics and disease transmission remains poorly understood.

CT after potential disease transmission in public ground transport is hampered by logistic hurdles. The follow-up of passengers, especially in urban settings, is unfeasible or, at best, limited since passenger data (e.g. name, telephone number, email address), in metros, trams and short-distance bus trips are mostly not collected. Anonymous transport seems to be one of the main hurdles for the initiation of CT. If passenger data are indeed collected, limited storage, lack of useful data, transport company policies and accessibility of data may be further obstacles.

In national long-distance or international railway or bus trips, passenger data may also not be collected routinely. We identified only one scientific publication where CT was performed on the basis of passenger lists for a single railway trip [13]. Without passenger data, CT has to rely on media appeals to inform potentially affected co-passengers. A case of invasive meningococcal disease with fatal outcome in a Swiss student visiting Berlin (Germany) on a class trip by train in 2008 demonstrates the ability to identify contacts in an anonymous transport system [44]. Since no passenger data were collected, it was decided to perform CT through a press release informing the public about meningococcal disease. It also asked the woman who had travelled in the same train compartment as the patient to contact the local health department to receive chemoprophylaxis, which she did.

Contact investigations require a substantial amount of financial and human resources. In none of the retrieved studies was the cost of CT provided nor was the effectiveness of interventions to prevent the transmission of infectious diseases evaluated. Concerning air travel, two publications report on the cost of investigations related to the estimated number of passengers with TB [67,68]. The authors concluded that in the case of TB, contact investigations in aircrafts are highly inefficient. Nevertheless, CT in air travel receives a high level of attention, which is reflected in international regulations and recommendations [46,47]. Taking into account the substantial logistic hurdles, it seems likely that CT after exposure to infectious diseases in public ground transport is inefficient.

All selected contact investigations attempted to discriminate between contact persons infected while travelling with the index case and transmission in other settings, e.g. schools or workplaces. Some investigations may demonstrate stronger evidence than others: in some, contacts were clearly limited to a bus since the index case was a bus driver [17,19,24], while other reports identified bus transport as an independent risk factor through multivariate analysis [14,16]. Conclusions that can be drawn from most of the identified CT investigations are limited by the small number of exposed individuals. A few publications, however, provide some evidence due to a relatively high number of tested contact persons [13,16,17].

Evidence on transmission of infectious diseases is limited by the quantity and quality of the reported CT studies. The publications we selected describe observational studies, which lack a control group and an attempt to minimise bias. Most of the investigations we selected were related to cumulative exposure in school buses where CT was obviously feasible. Only three relevant publications on single-trip exposure were found. Further we could locate only one publication describing CT following a railway trip [13]. The transmission rates may underestimate or conversely overestimate the actual transmission rates since not all contact persons were traced. Concerning the only publication on CT following travel of a TB case on a single railway trip, the train operator's records allowed 77% of all passengers on the trip to be located. However, only 49% of located passengers were evaluated, hence the possibility of more extensive transmission cannot be excluded.

The lack of evidence on disease transmission in public ground transport as well as logistic hurdles related to CT may be the main reasons for the limited number of relevant publications we could identify. We assume that transmission of airborne infectious diseases in public ground transport takes place but does not result in scientific publications, or reports do exist but have not been published. Thus the risk of infectious disease transmission as well as the public health impact of transmission of airborne communicable diseases during travel in railways or buses/coaches remains largely unknown. Even though the risk of infectious disease transmission in ground transport may be higher than in air transport, our investigations did not generate evidence that transmission of infectious diseases in public ground transport is an issue of great public health importance. Taking into account the logistic hurdles and probably limited effectiveness of CT, we conclude that only circumstances such as dramatic illness or organised trips would justify CT in public ground transport. This contrasts with the high profile CT of air passengers has in international regulations and recommendations and raises the question whether indications for CT should be revisited after a risk– benefit assessment and a comprehensive analysis taking into account exposures in both ground and air transport.

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Retrospective screening of serum and cerebrospinal fluid samples from patients with acute meningo-encephalitis does not reveal past Japanese encephalitis virus infection, Emilia Romagna, Italy, 2011

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To the editor:

A recent publication by Ravanini et al reported the detection of a Japanese encephalitis virus (JEV) RNA sequence in one pool of *Culex pipiens* mosquitoes, collected in 2010 in the province of Bologna (Emilia-Romagna region) [1]. In that study, a partial genomic sequence of 167 bp was shown to have 100% similarity to the NS5 region of the JEV genotype III genome. Confirmatory specific RT-PCR targeting the envelope, NS3 and NS5 regions of the JEV genome and attempts at virus isolation in cell culture were repeatedly negative.

Another retrospective study by Platonov et al., conducted in bird samples collected 10 years earlier, had investigated the presence of JEV RNA [2]. In particular, the authors had amplified a 215 bp fragment of the flavivirus NS5 gene in six of seven birds positive for JE group antigens in immunohistochemistry. Based on these findings, the possible introduction of JEV in a new area, and in particular in southern Europe, has been hypothesised and discussed [1-3]. We think that the detection of genomic RNA fragments (167 and 157 bp from the flavivirus NS5 gene and 552 bp from the JEV E gene in the above papers) cannot confirm the presence and circulation of JEV in Europe, and Italy in particular.

We therefore investigated the possibility of human cases of neurological infection caused by JEV in a retrospective serological study. Sera and cerebrospinal fluid (CSF) samples were obtained from 38 subjects with clinical symptoms of acute meningoencephalitis, collected in the province of Bologna between 1 January and 31 December 2011. The specimens were referred to the Regional Reference Centre for Microbiological Emergencies (Centro di Riferimento Regionale per le Emergenze Microbiologiche; CRREM) at St. Orsola-Malpighi Hospital, Bologna, as part of the regional surveillance programme for West Nile virus infections that was started in 2009 [4]. To evaluate the presence of JEV-specific IgM or IgG antibodies, the samples were tested by a commercial indirect immunofluorescence assays (IFA, Euroimmun, Lübeck, Germany). Following the guidelines issued by the World Health Organization, the diagnosis of JEV should preferably be achieved by detection of specific IgM antibodies in the CSF, while the detection of the JEV genome (in serum, plasma, blood or CSF), or of JEV-related antigens in tissue by immunofluorescence/immunohistochemistry or virus isolation can be used in addition or as confirmatory test [5]. None of these CSF or serum samples was IgG- or IgM-positive by IFA, indicating that none of them contained specific antibodies against JEV.

In conclusion, our findings clearly indicate that no human cases of meningoencaphilitis due to JEV occurred in Bologna in the months following the reported detection of a short JEV genomic sequence in *C. pipiens* pool collected in the same area [1]. A recent study conducted on different mosquito species collected between 2007 and 2010 in a larger area of the Emilia Romagna region, identified the presence of several flaviviruseses closely related to JEV by RT-PCR targeting the flavivirus NS5 region; the analysis of these sequences, however, was unable to identify precisely and without doubt whether or not they corresponded to the JEV genome [6]. Moreover, 269,686 mosquitoes (of which 233,074 were C. pipiens) and 1,486 wild birds (418 of which were collected passively) obtained in 2011 in the context of the regional surveillance plan in Emilia Romagna, were tested with the described flavivirus-specific RT-PCR, and no JEV sequences were detected (data not shown). In addition, we are

at present still monitoring flaviviruses in mosquitoes and birds, and further amplicons belonging to the JEV genome have not been detected.

Based on these findings, the hypothesis proposed by Platonov et al. [2] of a new flavivirus, closely related to JEV, appears the most consistent. However, our findings cannot definitively exclude the possible circulation of JEV or other human pathogenic JEV-related flaviviruses in the province of Bologna and consequently, extensive human, entomological and veterinary screening with molecular techniques, will be carried out, to confirm or to rule out the possible circulation of new flaviviruses in Italy.

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