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Early intervention in pertussis outbreak with high attack rate in cohort of adolescents with complete acellular pertussis vaccination in Valencia, Spain, April to May 2015

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Forty-three pertussis cases reported in May 2015 in Valencia were linked to a school outbreak where 90% of the students had been vaccinated. Cases were diagnosed upon paediatrician consultation and in hospital emergency units. Approximately half of the cases were students born in 2002, the first age cohort with complete shift to acellular pertussis vaccine. Public health intervention, visiting school premises to conduct interviews, sample collection and early antibiotic prophylaxis stopped further spread in the community.

Event description

In early May 2015, two suspected cases of pertussis in twins raised the alert in a school in Valencia, Spain. On 6 May, the school headmaster contacted the local public health authorities to report other students with persistent cough. A team of epidemiologists performed an investigation at the school premises on the following day, as a pertussis outbreak was suspected. During two further visits within the coming four days, the team detected a high incidence of pertussis cases among students in the first grade of secondary school, born in the years 2001 and 2002, including 10 laboratory-confirmed cases. Rapid risk assessment guided further intervention to tackle the spread of the disease.

Epidemiological investigation

The epidemiology units in the Valencian Community are responsible to monitor and respond to alerts from a computerised mandatory notification system (AVE, Análisis de Vigilancia Epidemiológica) and from laboratories in public hospitals (RedMiva, Red de Vigilancia Microbiológica de la Comunidad Valenciana). Epidemiologists also have access to the primary healthcare (PHC) computer system (SIA, Sistema de Información Ambulatoria) and to the vaccine information system (SIV, Sistema de Información Vacunal). During the outbreak described here, the overall surveillance system (individual systems are described on the website of the General Directorate of Public Health of Valencian Community [1]) allowed daily identification and follow-up of notified cases.

Information on the type and duration of treatment, on the date of symptom onset, on disease evolution, number of vaccine doses administered, was entered in the AVE which was used as database for this outbreak investigation.

Case definition

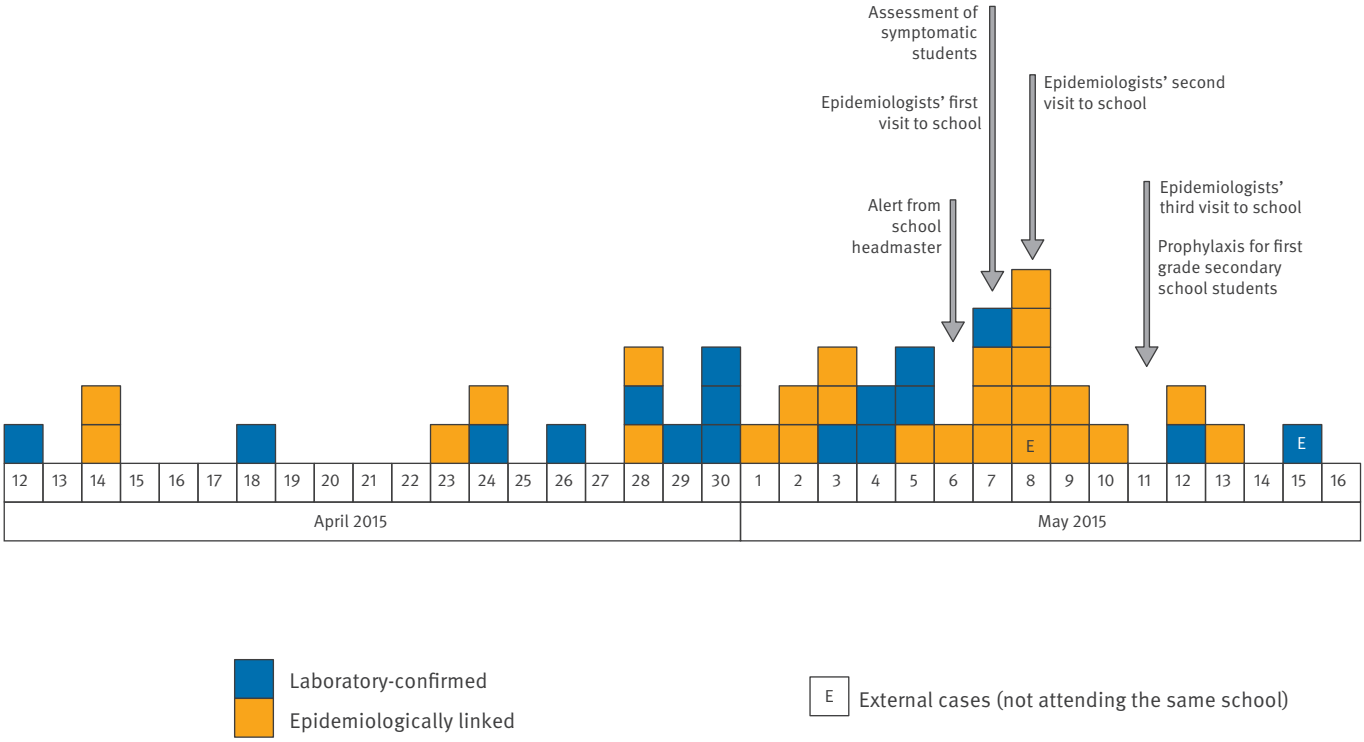
For the outbreak investigation, an adapted version of the Spanish case definition for pertussis was used [2]. The notified cases in the AVE were defined as 'laboratory-confirmed' (if PCR or serology were positive) or as 'epidemiologically-linked' when having clinical symptoms compatible with pertussis and history of contact with a laboratory-confirmed case. Individuals who did not fulfil the criteria above were dismissed as 'non-cases'. For notification purposes, all initial probable cases were re-defined when included in AVE as 'epidemiologically linked'.

Case investigation

The epidemiology unit team from Valencia assessed the situation at school premises, among the 395 students and 47 teachers. They conducted interviews with 50 symptomatic students, after having received verbal consent from their parents, and five teachers; in addition, they collected microbiological samples (nasopharyngeal smears) to confirm the outbreak that reached a total of 43 cases. The majority of the cases was fully vaccinated (Table).

Figure 1

Number of cases by date of symptom onset, pertussis school outbreak, Valencia, Spain, April–May 2015 (n=43)



Among the 43 cases, 40 were students and one was a school teacher; there were two additional cases, in other students who shared common after-school activities, and were thus classified as 'epidemiologically linked' cases. Among school students just over half of the cases were in males and median age was 13 years, ranging from 12 to 17 years. Information on vaccination coverage was available for grades in which cases occurred: 243 of 275 (88.4%) children in these grades were vaccinated with at least four doses; 89.4% (67/75) vaccination coverage was recorded in students in the first grade of secondary school; 95.2% (40/42) of student cases had been vaccinated, of which 90.4% had been fully vaccinated with five doses.

Here, we describe the evolution of the outbreak cases according to the date of symptom onset (Figure 1).

The investigation confirmed a higher attack rate (37%) in students the first grade of secondary school (28/75), of which 23 were born in 2002, the first age cohort with complete shift to acellular pertussis vaccine in our region (Figure 2).

In 2008, the last pertussis vaccination dose was administered in the 2002 cohort.

Control measures

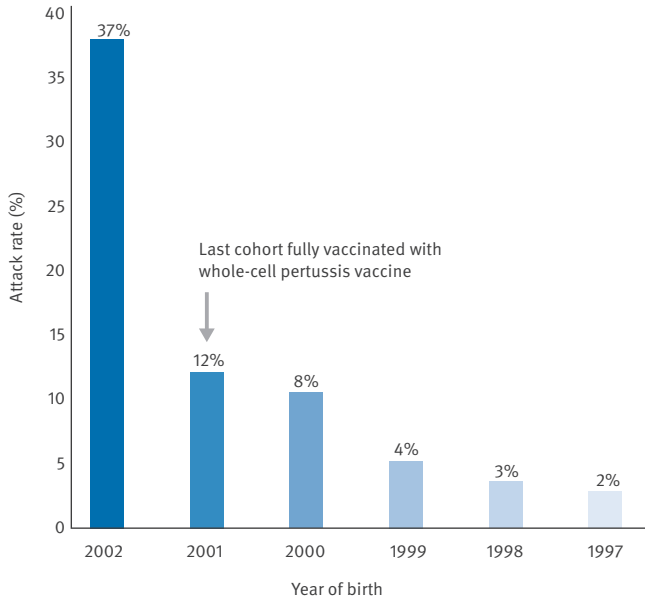
After confirmation of the outbreak, students, staff, parents, local GPs and paediatricians were informed about it either directly by telephone or by a letter given to the school's headmaster to give to children's parents. In an initial stage, all symptomatic children were referred to their paediatricians for diagnostic and treatment with recommendations from the public health authorities to undertake antibiotic treatment, delay return to school until after completion of treatment, and follow up and prophylaxis of close contacts. As new cases were confirmed, decision was taken to extend prophylaxis to all students in the first grade of secondary school, with recommendation to treat with azithromycin for five days (500 mg on the first day and 250 mg on the following days) [2]. In addition to antibiotic treatment, they were recommended isolation for five days and vaccination if they had not completed five doses. Following these recommendations, 63 of the first grade students had received prophylactic antibiotic treatment. There was additionally an active investigation to identify risk groups, (pregnant women and infants under one year old), but the team did not identify any of them among contacts linked to outbreak cases.

Epidemiological context

Pertussis shows a characteristic cyclic pattern peaking every three to four years. In recent years, an increase in the number of cases has been noticed in different European countries, including Spain, in spite of good vaccination coverage [3,4]. Studies have also indicated a decline in antigenic response to acellular vaccine already few years after vaccination booster and

Figure 2

Attack rate by age cohort, pertussis school outbreak, Valencia, Spain, April–May 2015 (n=40[a])



[a] One teacher and two external cases not included.

Table

Description of cases and vaccination coverage, pertussis school outbreak, Valencia, Spain, April–May 2015 (n=43)

		Number
Sex	Men	24
	Women	19
Age (years[a])	Median (range) 13 (12–17)	
Case classification	Students	40
	Teachers	1
	External cases	2
Case confirmation	Laboratory	17
	PCR	15
	Serology	2
	Epidemiological	26
Vaccination with pertussis vaccine	Yes	40
	Complete[b]	38
	Incomplete	2
	No	1
	Not recorded	2

[a] Students only, one teacher aged >45 years not included here.
[b] Five doses.

this could result in the near future in vulnerable age cohorts vaccinated exclusively with it [5,6]. This highlights that even a full course of acellular vaccine in line with the present vaccination schedules and good coverage may not confer sufficient protection to adolescents, and that there continues to be a risk of epidemic waves each three to four years [7,8].

In Spain, the vaccination schedules for pertussis vary little among regions, with doses given at 2–4–6 and 18 months and a booster at five to six years of age. Only two regions have included a sixth booster dose at 14 years of age, although most paediatricians suggest a booster for 11-12 year-old children [9]. The type of vaccine changed in the Valencian Community since 2001 for the booster dose, when acellular vaccine was included in the programme. It completely replaced the cellular vaccine also for the first doses in 2004. In practical terms this last substitution was implemented for birth cohorts 2002 and 2003.

Discussion

During April and May 2015, we have seen an increase of pertussis cases in the city of Valencia, which follows the cyclic pattern of pertussis. The last pertussis epidemic had occurred in 2011 and led to 249 cases in 12 months [10]. Incidence in 2015 has surpassed, up to 6.5 times during week 22, the expected number of cases in a normal season for Valencian Community as a whole [11]. In the city, this seemingly seasonal [12] manifestation clearly has increased incidence and transmission in school children and has presented in form of small outbreaks in primary and secondary educational institutions (age 9 to 13 years) besides the one described in this communication. In these outbreaks prophylactic early intervention in close contacts (same class) have been crucial in stopping further transmission. The rapid intervention in this outbreak has achieved an interruption of transmission within two weeks of implementation of control measures with a last case reported on 28 May, only two cases of onward transmission to community members outside the affected school were noted and no cases were detected in vulnerable individuals.

In general, the awareness of a situation with susceptible individuals has triggered other vaccination strategies like cocooning or more recently to expand vaccination to pregnant women [13-15]. The Valencian Community has implemented such changes too [16].

Conclusions

Our investigation highlights the potential increased risk in the first age cohorts with complete vaccination with acellular pertussis. This is consistent with the results of other studies where risk is seen to increase three years after the last acellular dose [5]. These findings should be incorporated into vaccination strategies decisions and they should promote research on new anti-pertussis vaccine components with greater effectiveness and longer protection. Experience with this

early intervention brings evidence that rapid response to public health alerts after suspicion of pertussis cases allows early diagnosis and intervention to stop transmission to core vulnerable groups (i.e. pregnant women and children under one year of age).

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Conflict of interest

None declared.

Authors' contributions

Ana Míguez Santiyán: Public health intervention in school, cases' identification, sample collection and follow up; notification of cases and data collection; inclusion in the regional system for Analysis of Epidemiological Surveillance; recommendations for management of cases and contacts based on Spanish national guidelines to children and staff; data base development and data analysis; figures and tables; article writing and review.

Rafael Ferrer Estrems: Public health intervention in school, cases' identification, sample collection and follow up; database development and data analysis; figures and tables; literature review and bibliography preparation; article writing and editing.

Jose Luis Chover Lara: Public health intervention in school, cases' identification, sample collection and follow up; notification of cases and data collection; inclusion in the regional system for analysis of epidemiological surveillance; recommendations for management of cases and contacts based on Spanish national guidelines to children and staff; article review.

Juan Alberola Enguídanos: laboratory samples processing; diagnostic and notification of laboratory results; article review.

Jose Miguel Nogueira Coito: Laboratory samples processing; diagnostic and notification of laboratory results; article review.

Antonio Salazar Cifre: Public health intervention in school, cases' identification, sample collection and follow up; notification of cases and data collection; inclusion in the regional system for analysis of epidemiological surveillance; recommendations for management of cases and contacts based on Spanish national guidelines to children and staff; article review.

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Assessing the risk of observing multiple generations of Middle East respiratory syndrome (MERS) cases given an imported case

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To guide risk assessment, expected numbers of cases and generations were estimated, assuming a case importation of Middle East respiratory syndrome (MERS). Our analysis of 36 importation events yielded the risk of observing secondary transmission events at 22.7% (95% confidence interval: 19.3–25.1). The risks of observing generations 2, 3 and 4 were estimated at 10.5%, 6.1% and 3.9%, respectively. Countries at risk should be ready for highly variable outcomes following an importation of MERS.

Middle East respiratory syndrome (MERS) has continued to spread globally [1]. A large cluster of MERS cases has been observed in the Republic of Korea since May 2015 [2]. Until 1 July 2015, so-called quaternary cases (i.e. generation 3 counting from the index case as generation 0) have been reported in South Korea [2]. Although the inter-human transmission potential of MERS is considered to be too low to cause large-scale epidemics [3-5], high variability and heterogeneity in the transmission potential have been underscored [6]. As MERS continues to spread globally, it is vital that risk assessment involves an evaluation of the potential outcomes following MERS importation events [7]. Among a total of 23 importation events in countries outside the Middle East region, there have been four MERS case importations that have given rise to at least one secondary transmission event [2].

While the basic reproduction number R_0, i.e. the average number of secondary cases produced by a primary case in a fully susceptible population, is less than 1 for MERS and a major epidemic may therefore not occur immediately, it is critical to quantitatively assess several risks of MERS transmission following an importation event, e.g. the expected numbers of cases and generations. The present study aims to analyse the observed importation events of MERS and estimate the expected size of MERS clusters and the number of generations using a stochastic epidemic model.

Importation data

Using secondary data sources [2,7-11], we extracted the numbers of secondary cases and generations for each reported importation event of MERS. We excluded data from the Kingdom of Saudi Arabia, Qatar and the United Arab Emirates from the analysis because cases in these endemic countries have frequently experienced exposures to a domestic animal reservoir (e.g. dromedary camels). Moreover, it has not been possible to fully track the transmission trees (i.e. via contact tracing data) in these countries. Including Middle East countries other than those, a total of 36 importation events were analysed. Of these, 13 events occurred in the Middle East, reported from Egypt, Iran, Jordan, Kuwait, Lebanon, Oman, Turkey and Yemen. In the present study, statistical estimation of parameters was done using two different sets of data, i.e. using all 36 importation events and restricting the analysis to the 23 importation events observed in areas outside of the Middle East. The latter data were analysed separately because the dynamics of case importation including the frequency of exposures and local contact patterns for those 23 events may not be fully comparable with the remaining 13 events.

Mathematical model

The importation event data were analysed using a branching process model which allowed us to jointly estimate the transmissibility, R_0, and the dispersion parameter, k, by assuming that the distribution of secondary cases per single primary case followed a

negative binomial distribution. Using the branching process model, the risk of observing at least one secondary transmission event, the risk of observing each generation of cases and the total number of cases were estimated. Hence, an important assumption to calculate these risks based on observed importation event data is that each importation event was a random sample drawn from the assumed model. For the estimation of the two model parameters, we used two different pieces of likelihood. The first one analyses the distribution of the total number of cases as described by Breban et al. for MERS [4], but the present study specifically focused on importation events [12]. Given the total number of cases z for each importation event, the likelihood to estimate R_0 and k was calculated as

Equation 1:

$$L_1(R_0,k;z)=\begin{cases}\dfrac{1}{\left(1+\frac{R_0}{k}\right)^k}, \text{for } z=1\\ \dfrac{\prod_{j=0}^{z-2}\left(\frac{j}{k}+z\right)}{z!}\left(\dfrac{1}{1+\frac{R_0}{k}}\right)^{zk}\left(\dfrac{R_0}{1+\frac{R_0}{k}}\right)^{z-1}. \text{for } z\geq 2\end{cases}$$

The number of observed importation events was limited to 36 and the sample size was small. To reduce uncertainty, we analysed in addition the number of generations per importation. Considering the concept of generation to extinction, we derived the probability distribution of the number of generations, i.e.

Equation 2:

$$\Pr(g\leq h)=\begin{cases}\dfrac{1}{\left(1+\frac{R_0}{k}\right)^k}, \text{for } h=1\\ \dfrac{1}{\left(1+\frac{R_0}{k}-\frac{R_0}{k\left(1+\frac{R_0}{k}\right)^k}\right)^k}, \text{for } h=2\\ \dfrac{1}{\left(1+\frac{R_0}{k}\left(1-\Pr\left(g\leq h-1\right)\right)\right)^k}-, \text{for } h\geq 3\end{cases}$$

from which we obtained the likelihood function L_2 for the observed number of generations, derived from $\Pr(g\leq h)$-$\Pr(g\leq h\text{-}1)$ for $h>1$, i.e.

and so forth. The total likelihood was given by the product of L_1 and L_2. The maximum likelihood method was employed to statistically infer the parameters, and the profile likelihood-based confidence intervals (CI) were computed. To account for both stochasticity and parameter uncertainty in calculating the outbreak size

Equation 3:

$$L_2(R_0,k;h)=\begin{cases}\dfrac{1}{\left(1+\frac{R_0}{k}\right)^k}, \text{for } h=1\\ \dfrac{1}{\left(1+\frac{R_0}{k}-\frac{R_0}{k\left(1+\frac{R_0}{k}\right)^k}\right)^k}-\dfrac{1}{\left(1+\frac{R_0}{k}\right)^k}. \text{for } h=2\\ \dfrac{1}{\left(1+\frac{R_0}{k}\left(1-\dfrac{1}{\left(1+\frac{R_0}{k}-\frac{R_0}{k\left(1+\frac{R_0}{k}\right)^k}\right)^k}\right)\right)^k}-\dfrac{1}{\left(1+\frac{R_0}{k}-\frac{R_0}{k\left(1+\frac{R_0}{k}\right)^k}\right)^k}, \text{for } h=3\end{cases}$$

distribution and the risk of observing each generation of cases, the covariance matrix was used to draw random samples of R_0 and k from a bivariate normal distribution with the correlation parameter informed by the matrix. The simulations were run 10,000 times, allowing us to take percentile points for the calculation of uncertainty bounds.

Results

Figure 1 illustrates the original data employed to quantify our model.

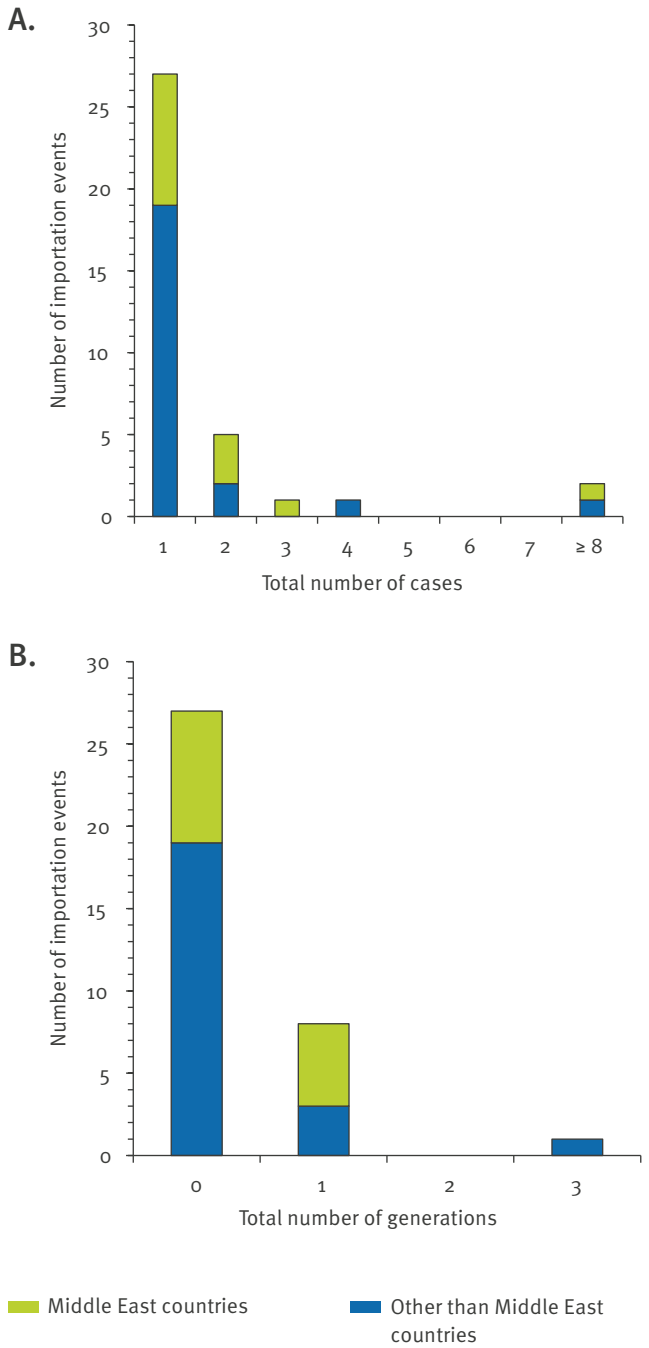
The distribution of the total number of cases was right skewed, including two outbreaks with a total of at least eight cases. Excluding the Middle East countries, only the ongoing South Korean outbreak was the one that involved eight or more cases. With regard to the number of generations, three quarters of the importations (27/36) did not result in any secondary transmission. Secondary transmissions were observed in Iran, Jordan, Kuwait, France, Republic of Korea, Oman (twice), Tunisia and the United Kingdom. Excluding Middle East countries, 19 of 23 importations did not generate any secondary cases (Table 1). Among the total of 36 importations, generation 3 (or the so-called quaternary cases) was observed only for the ongoing South Korean outbreak.

Table 2 shows the estimates of R_0 and k. Based on a total of 36 events, R_0 and k were estimated at 0.75 (95% CI: 0.54–1.09) and 0.14 (95% CI: 0.06–0.32), respectively.

The value of k was substantially smaller than 1, indicating that the distribution of secondary cases per single primary case was highly over-dispersed. Analysing the 23 importation events out of the Middle East countries, the estimates of R_0 and k were 0.81 (95% CI: 0.49–1.46) and 0.07 (95% CI: 0.02–0.21), respectively. These estimates were not significantly different from those obtained using the total set of 36 importation events. For this reason, simulations were conducted using estimates derived from the full set of 36 importation events.

Figure 1

Importation events of Middle East respiratory syndrome (n = 36)



A. The observed number of importation events as a function of the total number of cases. An importation event frequently ends up with only the imported (index) case, i.e. without generating any secondary cases.

B. Observed number of importation events by total number of generations observed for each importation. Generation 0 represents the imported (index) case, generation 1 represents secondary cases produced by the imported case, and so forth.

Table 1

Importation of Middle East respiratory syndrome to the 23 countries outside the Middle East that have experienced case until 1 July 2015 (n = 208 cases)

Country	Generation	Total number of cases
Algeria	0	1
Algeria	0	1
Austria	0	1
China	0	1
France	1	2
Germany	0	1
Germany	0	1
Germany	0	1
Germany	0	1
Greece	0	1
Italy	0	1
Malaysia	0	1
The Netherlands	0	1
The Netherlands	0	1
Philippines	0	1
Philippines	0	1
South Korea	3	181
Thailand	0	1
Tunisia	1	2
Tunisia	0	1
United Kingdom	1	4
United States	0	1
United States	0	1

The generation column represents the total number of generations (e.g. 0 indicates that the imported index case did not generate any secondary cases), while the total number of cases represents the cumulative number of confirmed cases including the index case (e.g. 1 indicates that the imported index case did not generate any secondary cases). For instance, in France, there was a secondary transmission, causing generation 1, but there was only 1 secondary case without tertiary case, and thus, the total number of cases was 2.
According to our classification, Turkey was included in the Middle East.

Figure 2 shows the expected total number of cases and the risk of observing each generation conditional on an importation event.

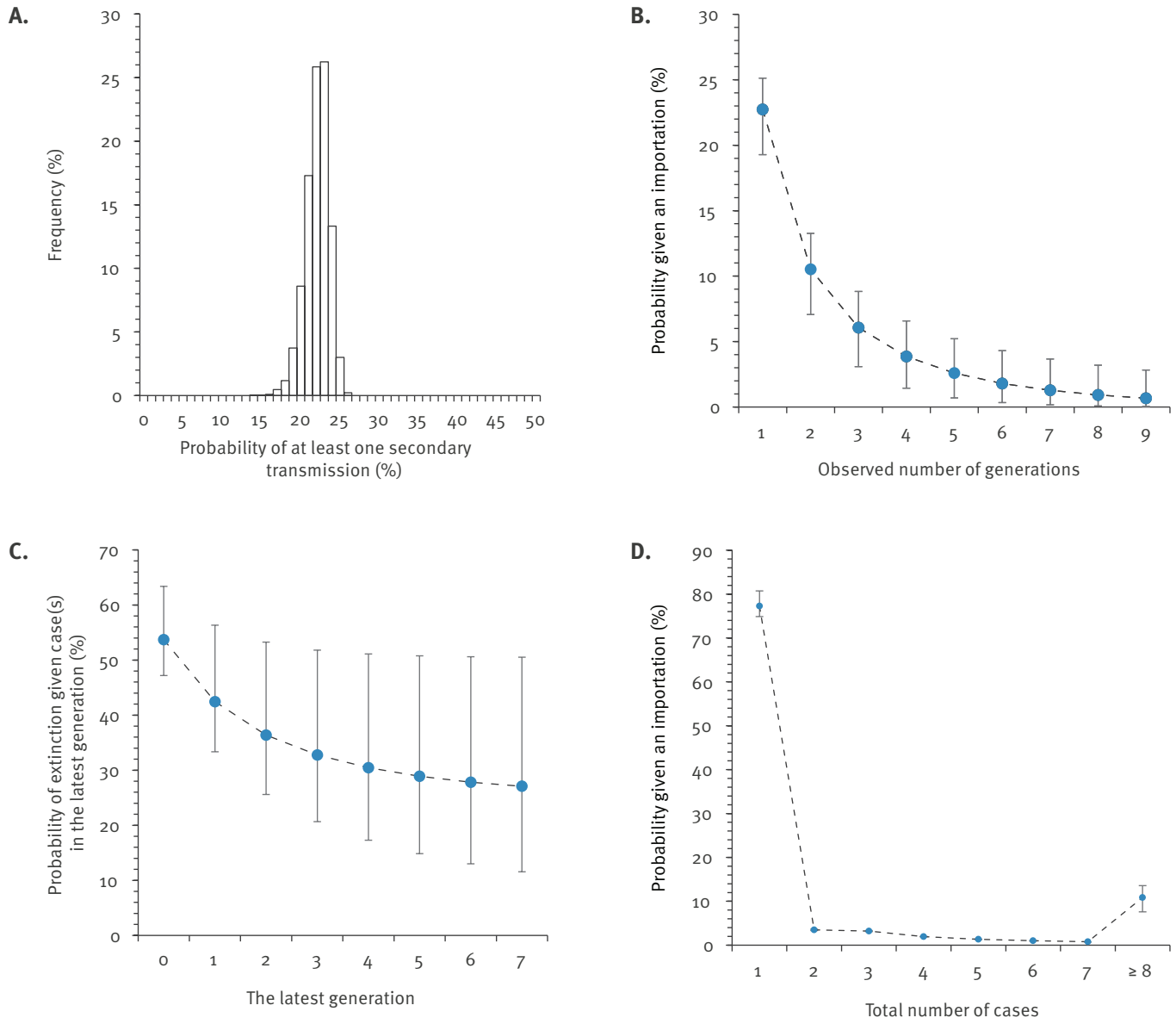
The risk of observing at least one secondary transmission was 22.7% (95% CI: 19.3–25.1) (Figure 2A). The risks of observing generations 2, 3 and 4 were, respectively, 10.5%, 6.1% and 3.9% (Figure 2B). When generation 2 (tertiary cases) was observed, the conditional risk of observing the next generation (quaternary cases) was as large as 63.6% (95% CI: 46.7–74.4) (Figure 2C). The outbreak size distribution appeared to be highly skewed (Figure 2D). Assuming an importation occurred, the risk of observing eight or more cases in total would be 10.9% (95% CI: 7.6–13.6).

Discussion

The present study analysed importation events of MERS with a particular focus on the associated outbreak size

Figure 2

Probabilities of observing multiple generations of Middle East respiratory syndrome cases given one case importation



A. Frequency distribution of the probability of observing at least one secondary case caused by an imported (index) case, based on a total of 10,000 simulation runs.

B. Probability that the transmission survives to a specific generation given an imported (index) case.

C. Conditional probability that the transmission goes extinct at the particular generation given case(s) in the corresponding generation. Until 20 June 2015, cases of MERS up to generation 3 (i.e. or the so-called quaternary cases) have been diagnosed in South Korea.

D. Frequency distribution of the total number of cases given an imported case.

In panels B, C and D, filled circles represent the posterior median of simulations, while whiskers extend to upper and lower 95% credible intervals, based on 10,000 posterior resampling simulation runs.

and number of disease generations arising from each importation event. Our findings indicate that if a case of MERS was imported, at least one secondary transmission event would be observed with a probability of 22.7%. The risk of involving tertiary, quaternary and quinary cases was also calculated (Figure 2B). Although our study only relied upon importation events consisting of a small number of clusters, the estimated R_0 was broadly consistent with published estimates that analysed larger cluster datasets mainly observed in Middle East countries [3-5] and was smaller than estimates derived from the early phase of hospital-associated outbreaks [13]. Considering that countries at risk of importation (i.e. countries without infected animal reservoirs) have had to confront the uncertainty associated with the risk of experiencing a case importation [14,15,16], our modelling analyses could facilitate quantitative risk assessment.

An important outcome of the present study is that the risk of observing multiple generations of MERS cases was estimated at 22.7% and that of a tertiary case at

Table 2

Estimated transmission potential and dispersion parameter of Middle East respiratory syndrome based on imported case data

	Basic reproduction number (95% CI)[a]	Dispersion parameter (95% CI)
All importation events (n = 36)	0.75 (0.54–1.09)	0.14 (0.06–0.32)
Importation events in countries other than Middle East (n = 23)[b]	0.81 (0.49–1.46)	0.07 (0.02–0.21)

CI: confidence interval.

[a] 95% confidence intervals were derived from the profile likelihood.

[b] Excluded Middle East countries are: Egypt, Iran, Jordan, Kuwait, Lebanon, Oman, Turkey and Yemen.

10.5% in our model. Since the distribution of secondary cases per single primary case is highly over-dispersed, superspreading events can occur, and thus, the expected total number of cases is highly variable. The finding echoes a recent re-analysis of clusters of MERS cases reported up to August 2013 [17]. Of course, we can expect that secondary transmission events could be prevented by a combination of contact tracing, monitoring suspected cases, early diagnosis and isolation of infectious individuals. Besides, the present study suggests that countries at risk of importation should keep in mind that a large cluster of cases with multiple generations may well occur, even though R_0 is clearly below the epidemic threshold at 1.0 [18].

In addition to the risk of observing a certain number of generations following an imported case, we also calculated the conditional risk of observing the next generation of case(s). This is in line with a risk assessment in real time: because the exact number of cases in a single generation cannot be manually counted during the course of an outbreak, it is reasonable to calculate the conditional risk given a generation where the conditional probability of observing the next generation is usually greater than 50%.

Two important limitations should be noted. Firstly, our exercise regarded each observed importation event as a random draw governed by the proposed probability model. Indeed, this assumption is unavoidable for fitting a branching process model to the data [3,4]. While the assumption may be common among modelling studies, it did not allow us to account for the variable type and effectiveness of interventions, especially at later generations of cases in each cluster. Secondly, MERS outbreaks have frequently been amplified in healthcare settings [6,19,20], but we limited ourselves to accounting for individual heterogeneity in a general sense. An improvement on this point was difficult, because MERS outbreaks have been seen mostly in healthcare settings without large-scale community transmission. The transmission dynamics in and out of healthcare settings have not been consistently characterised across individual outbreaks of MERS.

Despite these limitations, the present study successfully characterised the risk of observing a certain number of cases and generations given a case importation of MERS. The risk of at least one secondary case in our model was 22.7%, and that of a tertiary case was 10.5%. Once an untraced case is imported, countries at risk should assume that the secondary transmission risk as well as the risk of observing multiple generations of cases exists and should be ready to respond effectively by following their preparedness plans to manage emerging infectious diseases.

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Conflict of interest

None declared.

Authors' contributions

HN conceived mathematical modelling method and analysed the data. HN, YM, GC and MS drafted and revised the manuscript.

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National point prevalence survey of healthcare-associated infections and antimicrobial use in French home care settings, May to June 2012

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In May and June 2012, a national point prevalence survey (PPS) of healthcare-associated infections (HAIs) and antimicrobial use was conducted among French patients under home-based hospital care (HBHC). Data from 5,954 patients in 179 volunteer HBHC providers were collected. Prevalence of patients with at least one active HAI was 6.8% (95% confidence interval (CI): 6.1–7.4). Prevalence of those receiving at least one antimicrobial agent was 15.2% (95% CI: 14.3–16.1). More than a third (35.5%) of HAIs were HBHC-associated, 56% were imported from a healthcare facility and 8.5% of indeterminate origin. The main infection sites were urinary tract (26.6%), skin and soft tissue (17.6%), surgical site (15%), and pneumonia or other respiratory tract infections (13.5%). In multivariate analysis, three risk factors were associated with HBHC-associated infections: urinary catheter, at least one vascular catheter and a McCabe score 1 or 2. The most frequently isolated microorganism was *Staphylococcus aureus* (20.7%), 28.1% of them meticillin-resistant. Non-susceptibility to third-generation cephalosporins was reported in 25.3% of *Enterobacteriaceae*, of which 16.1% were extended spectrum beta-lactamase-producing strains. The most prescribed antimicrobials were fluoroquinolones (16.1%), and third-generation cephalosporins (14.5%). PPS may be a good start in HBHC to obtain information on epidemiology of HAIs and antimicrobial use.

Introduction

Nowadays, healthcare-associated infections (HAIs) may occur at different steps of the care pathway from hospital to home care. Besides the fact that more and more patients receive high-tech home care, including home infusion therapy, tracheostomy care and ventilator support, dialysis and other highly invasive procedures, home care patients may have substantial host risk factors, including advanced age, chronic illness or immunosuppression [1,2]. Surveillance of HAIs is thus important in order to identify patients who are at risk of infection and to develop effective infection control prevention measures [1,2]. In the last decades, the importance of surveillance of HAI in the home care setting has been recognised but literature remains sparse [1-7].

In France, a national point prevalence survey (PPS) of HAIs has been organised in healthcare facilities (HCFs) every five years since 1996 as part of the HAI prevention strategy [8]. However, data are lacking concerning care delivered to patients under home-based hospital care (HBHC). This system is becoming an important part of the French healthcare system: in 2011, ca 300 HBHC have provided home healthcare to 12,000 patients each day, accounting for almost 4 million patient days [9].

The objectives of this paper were to describe the major characteristics of HAIs and antibiotic consumption in HBHC and to identify risk factors associated with HBHC-associated infections, based on the first national PPS conducted on patients under HBHC in 2012.

Methods

Setting

This study was conducted in HBHC providers which were invited to participate in the national 2012 PPS survey. This system is part of hospital care that provides

complex medical and paramedical care to individuals in their home. In France, HBHC has to meet the same requirements as hospitals in terms of accreditation, quality and safety of care and prevention of HAIs [10]. They are general and versatile, public or private. Nevertheless, certain HBHC providers can specialise in a particular area of care (e.g. rehabilitation, obstetric or paediatric). Patients of any age, if covered by the national health insurance system, can be admitted with a family doctor's or hospital prescription [10,11]

The home care system is complex and involves a particular context of cooperation and coordination. Various participants are necessary for continuity of care, including the persons involved in the logistic implementations, the HBHC team (physicians in charge of the coordination, nurses, assistant nurses, midwives, physiotherapists, nutritionists etc.) and the team involved in the patient's wellbeing (e.g. family, home help, psychologist). The HBHC providers operate around the clock. The frequency of visits by a nurse varies according to the type of illness and the medical prescription but all patients receive at least one medical visit a week [10,11].

Study design and data collection

This study used the French national PPS protocol [12], which takes into account the European requirements for PPS [13]. However, the French PPS covered not only acute care hospitals, but also rehabilitation centres, long-term care facilities and HBHC providers. The latter had a specific protocol [14] involving a two-step methodology for data collection. All HBHC providers in France were invited to participate in the study between 14 May and 29 June 2012. Regional coordinating centres for nosocomial infection control (CClin) organised training courses on the use of the study protocol and on data collection, and provided technical assistance to local teams. All participating HBHC providers had up to one week during the study period to collect data from their patients in order to account for the extent of the geographical area they cover. A local coordinator, preferably a member of the hygiene team, was responsible for training and managing an investigation team including infection control practitioners or nurses. A senior nurse was responsible for organising visits to patients at home and for assigning a registered nurse or a midwife to help investigators collect data. Data collection was carried out in two steps. Firstly, at the patient's home, the registered nurse or midwife collected clinical data after informing the patient or their guardian about the study and obtaining verbal consent. Secondly, at the HBHC headquarters, the medical investigator completed the patient's questionnaire and confirmed the HAIs and the antimicrobial treatments by examining the patient's medical records.

Data collected included: date of PPS, date of patient admission to HBHC (starting date of home care), age, sex, clinical condition (whether the patient was immunocompromised or had active/advanced cancer and a McCabe score [13] that classifies the severity of underlying medical conditions, specialty area of the patient's care, presence of invasive devices on the day of the survey and whether the patient had one or more active HAIs and/or received antimicrobial treatment. For HAIs, date of onset, infection site, pathogens, origin of HAI (HBHC-associated, imported from a HCF or with an indeterminate origin) were included. Up to three different HAIs per patient and up to two pathogens per HAI could be recorded. Antimicrobial resistance data were collected for selected bug–drug combinations. For antimicrobial use, the type, number (up to five), route of administration and indication (when listed in the patient's medical record) were collected.

The European Centre for Disease Prevention and Control (ECDC) case definitions were used for most HAIs [13] and the McGeer criteria [15] for the diagnosis of pneumonia and respiratory tract infections. An HAI was considered active when signs and symptoms of the infection were present on the date of the survey or when signs and symptoms were no longer present but the patient was still on antimicrobial treatment for this infection on the survey date. HBHC-associated infections were those occurring in a patient during the process of care, neither present nor incubating at the time of starting home care (Day 1), for which the signs and symptoms became apparent after Day 2 and were not associated with a previous discharge from an HCF. Imported HAIs were those that were already present on Day 1 of starting home care or that developed in a patient before Day 3 and for which a discharge from an HCF had preceded the HBHC services (e.g. surgical site infections that met the case definition of an active HAI and occurred within 30 days of the date of surgery or within a year of the surgery in the case of an infection related to a surgically implanted device). For antimicrobial use, the Anatomical Therapeutic Chemical (ATC) classification system established by the World Health Organization (WHO) was used [16].

Data analysis

Data analysis was performed using Stata 11.2 (StataCorp Texas, US). The prevalence of HAIs was reported as the percentage of patients with at least one active HAI among the total number of patients. Analogously, the prevalence of antimicrobial use was reported as the percentage of patients receiving at least one antimicrobial agent among the total number of patients. Antimicrobial resistance was reported as the percentage of non-susceptible (intermediate or resistant) bacteria among the total number of isolates for which antimicrobial susceptibility testing (AST) results were available. Univariate and multivariate analyses were carried out in order to identify factors independently associated with HBHC-associated infections. Thus, patients with HAIs exclusively imported from an HCF or with an indeterminate origin were excluded from these analyses. In the univariate analysis, comparisons

Table 1

Prevalence of infected patients according to clinical characteristics, national point prevalence survey in home care settings, France, May–June 2012 (n = 5,954)

	Patients	With HAIs	Prevalence ratio (95% CI)	P [a]	Patients[b]	With HBHC-associated infections	Prevalence ratio (95% CI)	P [a]
	n (% column)	n (% row)			n (% column)	n (% row)		
Age group (years)								
<1	149 (2.5)	1 (0.7)	0.1 (0.14–0.80)	**<0.01**	148 (2.6)	0 (0.0)	NA	0.35
1–17	127 (2.1)	4 (3.1)	0.5 (0.18–1.49)		125 (2.2)	2 (1.6)	0.7 (0.16–3.17)	
18–44	650 (10.9)	38 (5.8)	Reference		626 (11.0)	14 (2.2)	Reference	
45–74	2,665 (44.8)	207 (7.8)	1.4 (0.95–1.94)		2,525 (44.3)	67 (2.7)	1.2 (0.67–2.13)	
75–84	1,412 (23.7)	94 (6.7)	1.1 (0.78–1.69)		1,353 (23.7)	35 (2.6)	1.2 (0.62–2.17)	
≥85	951 (16.0)	59 (6.2)	1.1 (0.70–1.62)		920 (16.1)	28 (3.0)	1.4 (0.72–2.63)	
Specialty area of patient's care								
Medical or paediatric	5,476 (92.0)	393 (7.2)	3.6 (1.91–6.83)	**<0.0001**	5,226 (91.7)	143 (2.7)	4.4 (1.4–13.82)	**<0.01**
Other area of care[c]	478 (8.0)	10 (2.1)	Reference		471 (8.3)	3 (0.6)	Reference	
Sex								
Female	2,995 (50.3)	194 (6.5)	Reference	0.37	2,880 (50.6)	79 (2.7)	Reference	0.38
Male	2,959 (49.7)	209 (7.1)	1.1 (0.90–1.34)		2,817 (49.4)	67 (2.4)	0.9 (0.62–1.20)	
McCabe score								
0 Non-fatal disease	1,664 (28.0)	88 (5.3)	Reference	**0.02**	1,596 (28.0)	20 (1.3)	Reference	**<0.0001**
1 Ultimately fatal disease	1,573 (26.4)	114 (7.2)	1.4 (1.05–1.86)		1,510 (26.5)	51 (3.4)	2.8 (1.63–4.64)	
2 Rapidly fatal disease	1,342 (22.5)	108 (8.0)	1.6 (1.17–2.10)		1,283 (22.5)	49 (3.8)	3.1 (1.85–5.29)	
Missing/unknown	1,375 (23.1)	93 (6.8)	NA		1,308 (23.0)	26 (2.0)	NA	
Immunocompromised patients								
No	3,870 (65.0)	244 (6.3)	Reference	**0.01**	3,707 (65.1)	81 (2.2)	Reference	**0.01**
Yes	1,512 (25.4)	127 (8.4)	1.4 (1.09–1.70)		1,437 (25.2)	52 (3.6)	1.7 (1.18–2.39)	
Missing/unknown	572 (9.6)	32 (5.6)	NA		553 (9.7)	13 (2.4)	NA	
Active/advanced cancer								
No	3,483 (58.5)	236 (6.8)	Reference		3,319 (58.3)	72 (2.2)	Reference	
Yes	2,005 (33.7)	148 (7.4)	1.1 (0.89–1.35)	**0.04**	1,926 (33.8)	69 (3.6)	1.7 (1.20–2.34)	**0.001**
Missing/unknown	466 (7.8)	19 (4.1)	NA		452 (7.9)	5 (1.1)	NA	
At least one invasive device								
No	3,457 (58.1)	140 (4.0)	Reference	**<0.0001**	3,365 (59.1)	48 (1.4)	Reference	**<0.0001**
Yes	2,497 (41.9)	263 (10.5)	2.8 (2.26–3.45)		2,332 (40.9)	98 (4.2)	3.0 (2.14–4.30)	
Urinary catheter								
No	5,188 (87.1)	328 (6.3)	Reference	**<0.0001**	4,965 (87.2)	105 (2.1)	Reference	**<0.01**
Yes	766 (12.9)	75 (9.8)	1.6 (1.23–2.09)		732 (12.8)	41 (5.6)	2.8 (1.90–3.98)	
Tracheal intubation or tracheotomy								
No	5,748 (96.5)	384 (6.7)	Reference	0.15	5,505 (96.6)	141 (2.6)	Reference	0.97
Yes	206 (3.5)	19 (9.2)	1.4 (0.88–2.30)		192 (3.4)	5 (2.6)	1.0 (0.41–2.51)	
At least one catheter								
No	4,077 (68.5)	190 (4.7)	Reference	**<0.0001**	3,963 (69.6)	76 (1.9)	Reference	**<0.0001**
Yes	1,877 (31.5)	213 (11.3)	2.6 (2.14–3.21)		1,734 (30.4)	70 (4.0)	2.2 (1.55–2.99)	
Peripheral vascular catheter								
No	5,792 (97.3)	364 (6.3)	Reference	**<0.0001**	5,562 (97.6)	133 (2.4)	Reference	**<0.0001**
Yes	162 (2.7)	39 (24.1)	0.2 (0.14–0.31)		135 (2.4)	13 (9.6)	0.2 (0.13–0.42)	
Central vascular catheter								
No	5,812 (97.6)	380 (6.5)	Reference	**<0.0001**	5,572 (97.8)	139 (2.5)	Reference	**0.03**
Yes	142 (2.4)	23 (16.2)	0.4 (0.23–0.57)		125 (2.2)	7 (5.6)	0.4 (0.20–0.94)	
Peripherally inserted central catheter								
No	5,795 (97.3)	368 (6.4)	Reference	**<0.0001**	5,568 (97.7)	141 (2.5)	Reference	0.34
Yes	159 (2.7)	35 (22.0)	4.2 (2.82–6.15)		129 (2.3)	5 (3.9)	1.6 (0.63–3.85)	
Implantable venous access device								
No	4,823 (81.0)	300 (6.2)	Reference	**0.001**	4,630 (81.3)	107 (2.3)	Reference	**0.01**
Yes	1,131 (19.0)	103 (9.1)	1.5 (1.20–1.91)		1,067 (18.7)	39 (3.7)	1.6 (1.10–2.33)	
Subcutaneous catheter								
No	5,624 (94.5)	380 (6.8)	Reference	0.88	5,378 (94.4)	134 (2.5)	Reference	0.16
Yes	330 (5.5)	23 (7.0)	1.0 (0.67–1.60)		319 (5.6)	12 (3.8)	1.5 (0.84–2.79)	
Total	**5,954**	**403 (6.8)**			**5,697**	**146 (2.6)**		

CI: confidence interval; HAI: healthcare-associated infection; HBHC: home-based hospital care; NA: not applicable.

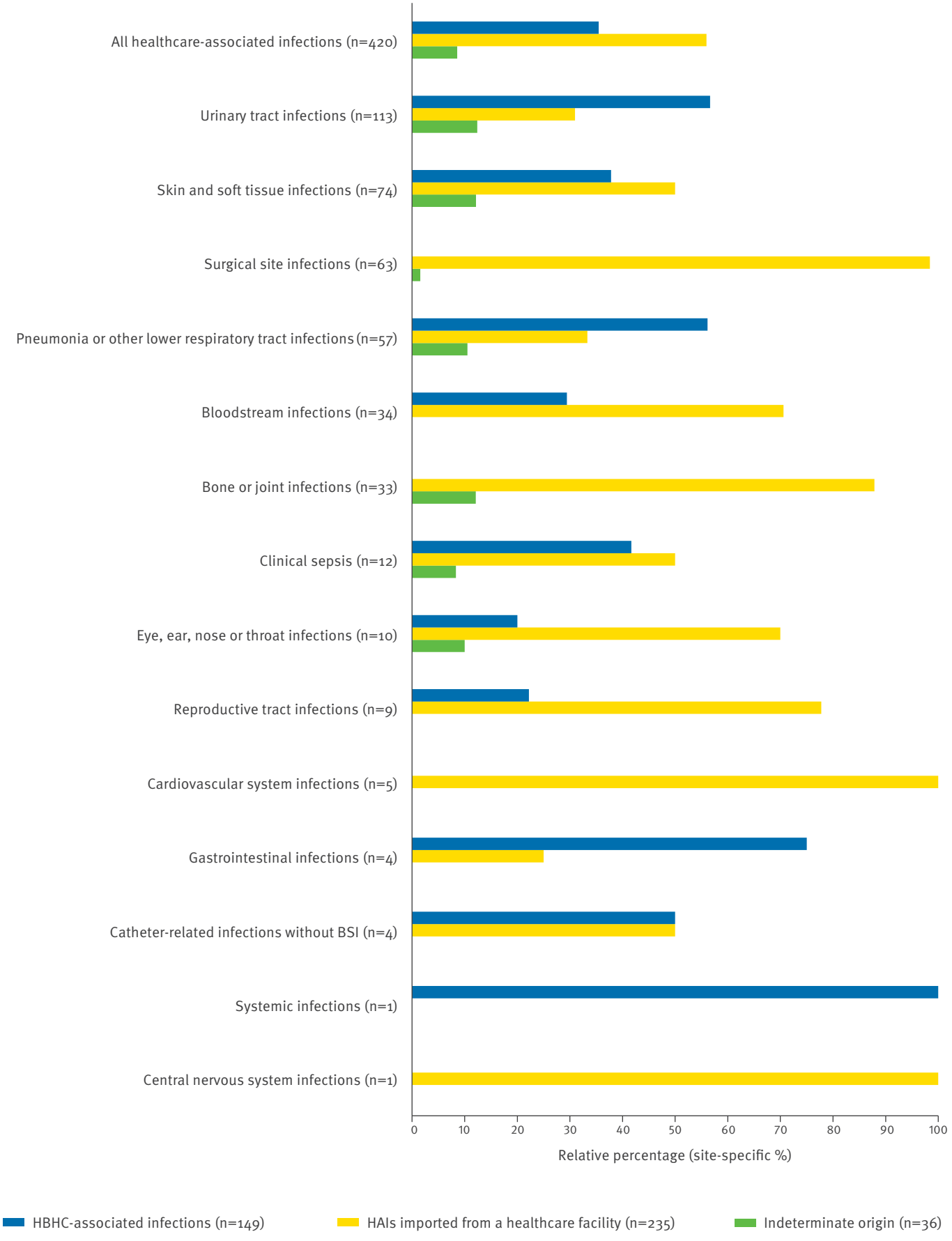
[a] *P* value of Pearson's chi-squared test. Significant values are highlighted in bold.

[b] Patients with HAI exclusively imported from a healthcare facility or with an indeterminate origin were excluded from this analysis (n = 257 patients).

[c] This category covers patients receiving psychiatric/mental healthcare, antepartum or post-partum care, rehabilitation and physical therapy and other care. Among the patients who received psychiatric/mental healthcare or antepartum care, none presented an infection.

Figure 1

Relative percentage (site-specific) of healthcare-associated infections by origin of infection, national point prevalence survey in home care settings, France, May-June 2012 (n = 420)



BSI: bloodstream infection; HAI: healthcare-associated infection; HBHC: home-based hospital care.

Table 2

Independent risk factors of infections associated with home-based hospital care, national point prevalence survey in home care settings, France May–June 2012 (n = 5,656)

Variables	Two-level random intercept model [a]			
	Full model		Final model	
	OR (95% CI)	p	OR (95% CI)	p
Active/advanced cancer	1.15 (0.69–1.89)	0.18	NA	NA
Immunocompromised patients	0.91 (0.11–1.20)	0.32	NA	NA
Receiving medical or paediatric care	2.10 (0.58–7.52)	0.26	NA	NA
McCabe score 1 or 2	1.61 (0.91–2.87)	0.10	1.82 (1.07–3.08)	0.03
Urinary catheter	2.35 (1.58–3.49)	<0.0001	2.38 (1.61–3.52)	<0.0001
At least one vascular catheter	1.82 (1.24–2.66)	0.002	1.89 (1.33–2.70)	<0.0001
	Model validation results			
	Full model		Final model	
Log likelihood	−626.99		−629.91	
Level 2 intercept variance (uoj)	0.73; SE (0.27)		0.74; SE (0.27)	
Intra-class correlation	0.18; SE (0.05)		0.18; SE (0.05)	
Likelihood-ratio test of rho (p)	<0.0001		<0.0001	
Akaike information criterion (AIC)	1,275.97		1,271.81	
Bayesian information criterion (BIC)	1,349.02		1,311.65	
Total number of patients	5,656		5,656	
Number of home care providers	160		160	
Number of patients with HBHC-associated infections	145		145	

CI: confidence interval; HBHC: home-based hospital care; NA: not applicable; OR: odds ratio; SE: standard error.

[a] Output model obtained by retaining the significant variables (p<0.05).

Patients with healthcare-associated infections exclusively imported from a healthcare facility or with an indeterminate origin were excluded from this analysis, as were HBHC that included fewer than five patients (nine HBHC and 41 patients).

between infected and non-infected patients were performed using the chi-squared test and expressed as prevalence ratios. Multivariate analysis was conducted using logistic regression with all variables that had p<0.2 in the univariate analysis. Multivariate analysis was completed by a two-level random intercept logistic model, considering patients clustered in their respective HBHC. The Stata command *xtmelogit* was used to run analyses and data from HBHC that included more than five patients. The final model was computed with a manual stepwise backward elimination. All tests were considered as significant at p<0.05 in the whole analysis. The −2 log likelihood ratio test and lowest Akaike information criterion score were evaluated in order to determine the model with the best fit.

Results

Data from 5,954 patients in 179 HBHC providers were collected. More than half (55%) of participating providers were public, 35% were private for-profit and 10% were private non-profit. Private for-profit providers included most patients (45.6%). The median number of patients per HBHC was 19 (interquartile range (IQR): 10–35). Most patients (88.4%) received medical care, 3.6% paediatric care, 3.3% psychiatric or mental healthcare, 3.2% antepartum or post-partum care, 1.2% rehabilitation and physical therapy and 0.3% received other care. The median length of home healthcare was 35 days (IQR: 12–96) and only 4.3% had received home healthcare for less than two days on the day of survey.

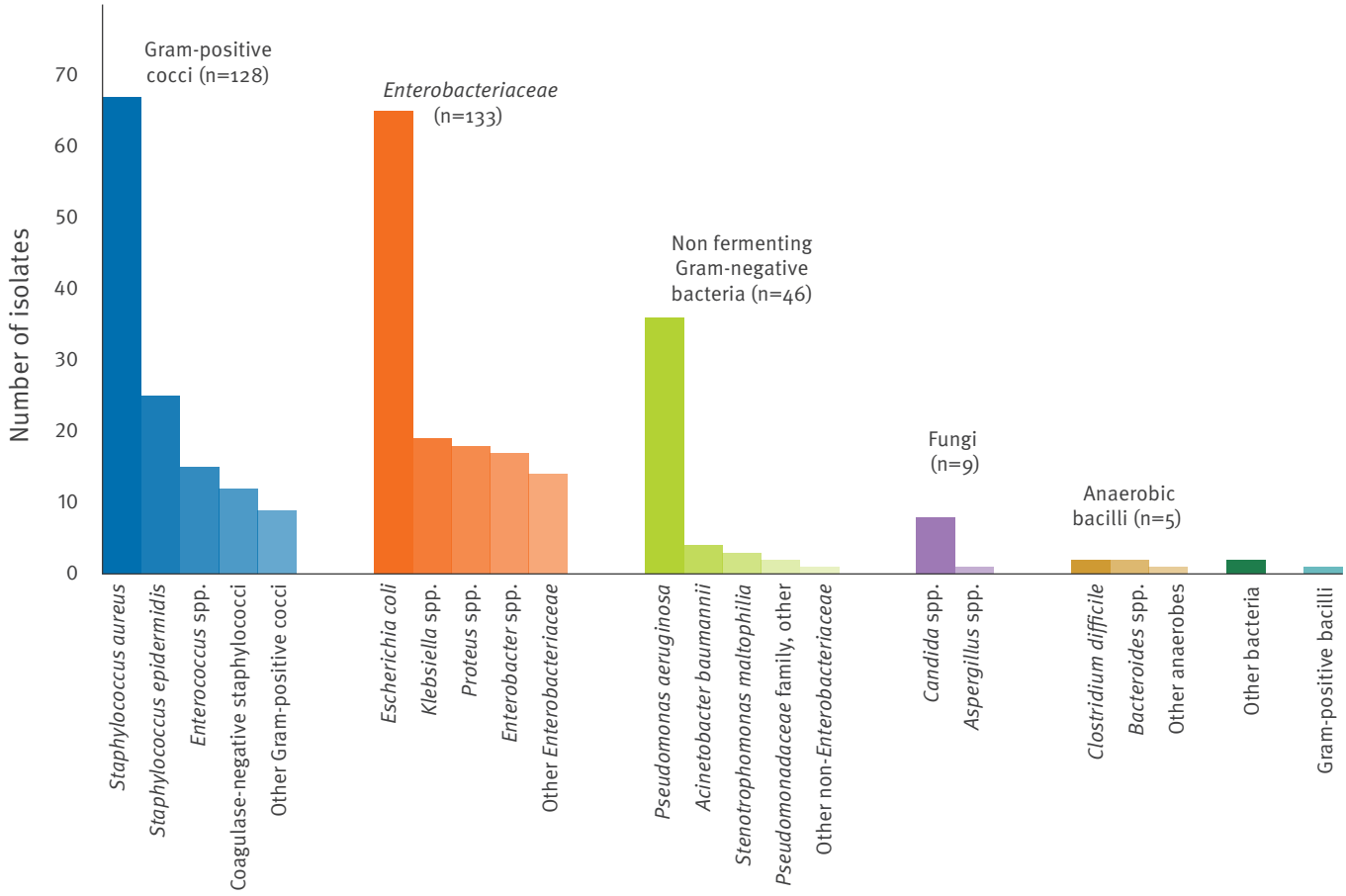
The median patient age was 69 years (IQR: 55–81) and the male-to-female sex ratio was 1. A quarter of patients were immunocompromised, a third presented an active or advanced cancer and nearly a half (48.9%) were classified as having fatal prognosis (McCabe score 1 or 2). On the day of the survey, 42% of patients presented at least one invasive device, 31.5% at least one vascular or subcutaneous catheter (mostly an implantable venous access device in 19% of patients), 13% a urinary catheter and 3.5% a tracheal intubation or tracheostomy (Table 1).

Healthcare-associated infections

A total of 420 HAIs in 403 patients were reported. The prevalence of patients with at least one active HAI was 6.8% (95% confidence interval (CI): 6.1–7.4). Most of the infected patients (n=387, 96.0%) had only one HAI, 15 (3.7%) had two HAIs and one patient (0.3%) had three HAIs on the day of the survey. The prevalence of patients with at least one HAI was not significantly different for HBHC with different ownership status. Among the patients who received psychiatric/mental healthcare or antepartum care, none presented an infection. The HAI prevalence was significantly lower (p<0.001)

Figure 2

Distribution of microorganisms isolated from healthcare-associated infections, national point prevalence survey in home care, France, May-June 2012 (n = 324)



in patients younger than 18 years (1.8%) than in patients 18 years and older (7%). Overall, 149 (35.5%) infections in 146 patients were HBHC-associated infections (prevalence: 2.5%; 95% CI: 2.1–2.9), 235 (56%) infections in 228 patients were imported from a healthcare setting (mainly from acute care facilities) and 36 infections (8.5%) in 34 patients had an indeterminate origin. The most common HAIs were urinary tract infections (UTIs), followed by skin and soft tissue infections (SSTIs), surgical site infections (SSI) and pneumonia or other lower respiratory tract infections (LRTIs). UTIs and pneumonia or other LRTIs were the most frequent infections reported as HBHC-associated (Figure 1). Surgical site infections accounted for 26.4% of the 235 infections reported as imported from an HCF.

Risk factors for HBHC-associated infection

Several patient characteristics were associated with higher risk in the univariate analysis: patients who received medical or paediatric care, McCabe score › 0, immunocompromised patients, active/advanced cancer, at least one invasive device, a urinary catheter or at least one vascular catheter (Table 1). When these factors were analysed using a two-level random effect logistic model, the presence of a urinary catheter (odds ratio (OR) = 2.38; 95% CI: 1.61–3.52), the presence of at least one vascular catheter (OR = 1.89; 95% CI: 1.33–2.70) and McCabe score 1 or 2 (OR = 1.82; 95% CI: 1.07–3.08) were the independent factors associated with HBHC-associated infections (Table 2).

Isolated microorganisms and antimicrobial susceptibility

A positive microbiology result was available for 274 (65.2%) HAIs (any origin): a single microorganism was reported for 224 HAIs (53.3%); two or more were reported for 50 (11.9%). Among the 324 microorganisms isolated, the most common were *Enterobacteriaceae* (41%) followed by Gram-positive cocci (40%). *Staphylococcus aureus* was the most frequently isolated microorganism (21%), mainly in skin and soft tissue infections, followed by *Escherichia coli* (20%), mostly in urinary tract infections (Figure 2).

Among the 257 isolates concerned by selected bug–drug combinations, 181 (70%) had available AST results. Listing only strains with at least 20 isolates tested, the available results were: 57 of 67 S. aureus isolates, 23 of 36 *Pseudomonas aeruginosa* isolates and 87 of 133 *Enterobacteriaceae* isolates, mainly *E. coli* isolates (46 of 87 with known AST results). Meticillin resistance was reported in 16 of 57 S. aureus isolates with known AST results, including two vancomycin non-susceptible

Table 3

Antimicrobial use: prevalence, indication, route of administration and reason in patient charts/notes, national point prevalence survey in home care settings, France, May–June 2012 (n = 179 home-based hospital care providers, n = 5,954 patients)

	Patients under antimicrobial treatment[a]		Antimicrobial agents	
	n	Prevalence (95% CI)[b]	n	Relative %[c]
Total	**906**	**15.2 (14.3–16.1)**	**1,163**	**100**
Indication of antimicrobial treatment				
Treatment intended for community infection	346	5.8 (5.2–6.4)	462	39.7
Treatment intended for healthcare-associated infection	343	5.8 (5.2–6.4)	446	38.3
Medical prophylaxis	115	1.9 (1.6–2.3)	129	11.1
Other indications[d]	48	0.8 (0.6–1.0)	53	4.6
Surgical prophylaxis[e]	17	0.3 (0.1–0.4)	20	1.7
Unknown indication	47	0.8 (0.6–1.0)	53	4.6
Route of administration				
Oral	605	10.2 (9.4–10.9)	718	61.7
Intravenous	302	5.1 (4.5–5.6)	387	33.3
Intramuscular	23	0.4 (0.2–0.6)	23	2.0
Subcutaneous	26	0.4 (0.3–0.6)	27	2.3
Unknown	7	0.1 (0.0–0.2)	8	0.7
Reason in patient's medical record				
Yes	743	12.5 (11.6-13.3)	973	83.7
No	150	2.5 (2.1-2.9)	164	14.1
Missing data in the questionnaire	21	0.4 (0.2-0.5)	26	2.2

CI: confidence interval.

[a] Patients receiving a least one antimicrobial agent.

[b] Prevalence of antimicrobial use in each category.

[c] Percentage among total number of antimicrobials (relative percentage).

[d] This category included antimicrobials used for other indications: e.g. erythromycin as prokinetic agent or when the same antimicrobial agent was prescribed for more than one indication.

[e] Surgical intervention does not occur in home-based hospital care, however, surgical prophylaxis was reported for 17 patients of whom 16 received surgical prophylaxis for longer than two days.

The sum of patients treated, by indication, route of administration or reason of antimicrobial treatment, may not be equal to the total number of patients treated with at least one antimicrobial, as the same patient could have had more than one antimicrobial treatments.

(intermediate) isolates. Resistance to third-generation cephalosporins was reported in eight of 23 P. aeruginosa isolates and in 22 of 87 *Enterobacteriaceae*, 14 of them were extended spectrum beta-lactamase (ESBL)-producing strains. Non-susceptibility to carbapenems was reported in six of 23 *P. aeruginosa* isolates and in two of 87 *Enterobacteriaceae* (which were *E. coli* strains).

Antimicrobial use

A total of 906 patients received at least one antimicrobial agent (prevalence: 15.2%; 95% CI: 14.3–16.1). Among them, 687 (75.9%) patients received one antimicrobial agent, 187 (20.6%) received two antimicrobials and 32 (3.5%) received three or more antimicrobial agents. A total of 1,163 antimicrobial prescriptions were reported (68 different molecules), which corresponds to an average of 1.3 antimicrobial agents per patient receiving an antimicrobial treatment. On the day of the survey, 85% of patients with an HAI received at least one antimicrobial. The prevalence of patients receiving at least one antimicrobial agent was highest in patients between 1 and 17 years of age (32.3%) and lowest among patients younger than 1 year (4.0%). It was also significantly higher ($p < 0.0001$) among men than among women (17.3% vs 13.2%) and highest among immunocompromised patients (20.8%). Furthermore, patients were more likely to receive at least one antimicrobial agent when they had at least one invasive device (23.3% with invasive device vs 9.4% without) or at least one catheter (26.6% with catheter vs 10% without) or a urinary catheter (18.7% with urinary catheter vs 14.7% without).

Antimicrobials were most frequently prescribed for treatment of an infection (78.1%): community-acquired infection (39.7%) or HAI (38.3%). Medical prophylaxis was the indication in 11.1% of prescriptions (Table 3). The most common infections treated were: SSTI (23.8%), pneumonia and LRTI (20.3%), bone or joint infections (17.3%) and UTI (14.6%). The route of administration was mostly oral (61.7%) and the reason for antimicrobial use was documented in the patient's medical records for 83.7% (Table 3).

Table 4

Distribution of antimicrobial agents by main indication, national point prevalence survey in home-care settings, France May–June 2012 (n = 1,163)

Top antimicrobial agents (accounting for 95.2% of use) n (%)	All indications	Treatment for community infections	Treatment for healthcare-associated infections	Medical prophylaxis	Other[a] indications
	n (%)	n (%)	n (%)	n (%)	
Antimicrobial agents, total	**1,163 (100)**	**462 (39.7)**	**446 (38.3)**	**129 (11.1)**	**53 (4.6)**
Fluoroquinolones (J01MA)	187 (16.1)	77 (16.7)	80 (17.9)	10 (7.8)	7 (13.2)
Ciprofloxacin (J01MA02)	72 (6.2)	29 (6.3)	36 (8.1)	3 (2.3)	2 (3.8)
Ofloxacin (J01MA01)	61 (5.2)	25 (5.4)	23 (5.2)	3 (2.3)	2 (3.8)
Levofloxacin (J01MA12)	40 (3.4)	16 (3.5)	17 (3.8)	2 (1.6)	3 (5.7)
Third-generation cephalosporins (J01DD)	169 (14.5)	72 (15.6)	67 (15.0)	11 (8.5)	11 (20.8)
Ceftriaxone (J01DD04)	109 (9.4)	47 (10.2)	40 (9.0)	7 (5.4)	9 (17.0)
Cefixime (J01DD08)	26 (2.2)	10 (2.2)	12 (2.7)	1 (0.8)	2 (3.8)
Ceftazidime (J01DD02)	18 (1.5)	8 (1.7)	9 (2.0)	1 (0.8)	NA
Combinations of penicillins, incl. beta-lactamase inhibitors (J01CR)	153 (13.2)	74 (16.0)	48 (10.8)	14 (10.9)	6 (11.3)
Amoxicillin and enzyme inhibitor (J01CR02)	127 (10.9)	61 (13.2)	35 (7.8)	14 (10.9)	6 (11.3)
Piperacillin and enzyme inhibitor (J01CR05)	25 (2.1)	13 (2.8)	12 (2.7)	NA	NA
Combinations of sulfonamides and trimethoprim, incl. derivatives (J01EE)	95 (8.2)	22 (4.8)	20 (4.5)	42 (32.6)	7 (13.2)
Sulfamethoxazole and trimethoprim (J01EE01)	95 (8.2)	22 (4.8)	20 (4.5)	42 (32.6)	7 (13.2)
Penicillins with extended spectrum (J01CA)	83 (7.1)	37 (8.0)	29 (6.5)	8 (6.2)	2 (3.8)
Amoxicillin (J01CA04)	81 (7.0)	37 (8.0)	27 (6.1)	8 (6.2)	2 (3.8)
Streptogramins (J01FG)	51 (4.4)	15 (3.2)	30 (6.7)	1 (0.8)	2 (3.8)
Pristinamycin (J01FG01)	51 (4.4)	15 (3.2)	30 (6.7)	1 (0.8)	2 (3.8)
Carbapenems (J01DH)	49 (4.2)	20 (4.3)	26 (5.8)	NA	1 (1.9)
Imipenem and enzyme inhibitor (J01DH51)	36 (3.1)	16 (3.5)	17 (3.8)	NA	1 (1.9)
Antibiotics for treatment of tuberculosis (J04AB)	42 (3.6)	12 (2.6)	27 (6.1)	NA	2 (3.8)
Rifampicin (J04AB02)	41 (3.5)	12 (2.6)	26 (5.8)	NA	2 (3.8)
Triazole derivatives (J02AC)	35 (3.0)	16 (3.5)	10 (2.2)	3 (2.3)	1 (1.9)
Fluconazole (J02AC01)	30 (2.6)	14 (3.0)	9 (2.0)	2 (1.6)	NA
Other antibacterials (J01XX)	35 (3.0)	12 (2.6)	22 (4.9)	NA	NA
Daptomycin (J01XX09)	19 (1.6)	4 (0.9)	15 (3.4)	NA	NA
Imidazole derivatives (J01XD)	33 (2.8)	19 (4.1)	4 (0.9)	6 (4.7)	2 (3.8)
Metronidazole (J01XD01)	33 (2.8)	19 (4.1)	4 (0.9)	6 (4.7)	2 (3.8)
Glycopeptide antibacterials (J01XA)	31 (2.7)	13 (2.8)	18 (4.0)	NA	NA
Vancomycin (J01XA01)	21 (1.8)	8 (1.7)	13 (2.9)	NA	NA
Other aminoglycosides (J01GB)	31 (2.7)	14 (3.0)	12 (2.7)	2 (1.6)	2 (3.8)
Macrolides (J01FA)	30 (2.6)	11 (2.4)	7 (1.6)	8 (6.2)	3 (5.7)
Beta-lactamase-resistant penicillins (J01CF)	23 (2.0)	8 (1.7)	10 (2.2)	1 (0.8)	1 (1.9)
Lincosamides (J01FF)	23 (2.0)	10 (2.2)	11 (2.5)	1 (0.8)	NA
Beta-lactamase-sensitive penicillins (J01CE)	20 (1.7)	3 (0.6)	NA	13 (10.1)	1 (1.9)
Tetracyclines (J01AA)	17 (1.5)	7 (1.5)	2 (0.4)	3 (2.3)	4 (7.5)

NA: not applicable.

[a] This category included antimicrobials used for other indications: e.g. erythromycin as prokinetic agent or prescription of a same antimicrobial agent for more than one indication.

Only levels 4 and 5 of the Anatomical Therapeutic Chemical classification system [16] are shown. Individual sums may not add up to the totals because only the most frequent antimicrobials are shown here.

The categories 'unknown indication' and 'surgical prophylaxis' represented 4.6% and 1.7% of the total, respectively, and are included in the first column.

Antibacterials for systemic use (ATC group J01) accounted for 91.6% of all reported antimicrobials. Antimycotics for systemic use (ATC group J02) accounted for 4.0% of the total reported antimicrobials. The most widely used antimicrobial agents at ATC level 4 [16] were fluoroquinolones (16.1%), followed by third generation cephalosporins (14.5%) and combinations of penicillins with beta-lactamase inhibitors (13.2%), mainly prescribed for the treatment of infections. For medical prophylaxis, combinations of sulphonamides and trimethoprim were the most common group (32.6%). At ATC level 5, the most frequently prescribed antimicrobial agent was amoxicillin, with enzyme inhibitor representing 10.9% of all antimicrobials. It was the most frequently used drug in treatment of community infections, followed by ceftriaxone (9.4%) and sulfamethoxazole with trimethoprim (8.2%), mainly prescribed for medical prophylaxis (Table 4).

Discussion

To our knowledge, our study is the first to provide estimates of HAIs and antimicrobial use in HBHC in a European country based on a large multicentre patient-based sample. The prevalence of patients with at least one HAI was slightly higher in our study than those found in the PPS conducted in HCFs [17], however only a third of the total were HBHC-associated infections. Our home care population was at high risk for HAIs with heavy underlying conditions, including diseases with poor prognosis, and with frequent exposure to invasive procedures (especially urinary and vascular catheters) and to antimicrobial agents for either community infection or HAI (mainly fluoroquinolones and third-generation cephalosporins). In addition, our study provides critical data on antimicrobial susceptibility, especially MRSA and ESBL-producing strains.

Our study covered almost 60% of HBHC providers registered in France by the National Agency for Information on Hospital Care (ATIH) [9]. To date, few HAI prevalence studies in HBHC settings have been published despite the growing use of home care services in the recent years [1,4,9]. This could be partly explained by the fact that data collection in the home care setting is more difficult than in HCFs owing to the geographical dispersion of homes, difficulty in tracking clinical and laboratory data, and the multiple healthcare workers. In our study, data collection was facilitated by a two-step methodology, previously tested in 2007 in a French pilot HBHC [18] and by the technical and methodological support provided by regional reference centres. Dwyer et al. [19], in a recently published study in the United States on a national sample representative of people receiving home care, reported that 11.5% of individuals had an infection at the time of the survey, which is higher than the rate found in our study. However, the most common infections including UTIs, pneumonia and cellulitis were the same as ours. However, in the study by Dwyer et al., the study design did not allow determining whether infections were resolved or ongoing or whether infections were associated with the community or with a previous healthcare exposure or with the current home care. In our study, the origin of HAIs was recorded: HBHC-associated infections were defined as those occurring in a patient during the process of care, neither present nor incubating at the time of starting home care (Day 1), for which the signs and symptoms became apparent after Day 2 and were not associated with a previous discharge from an HCF. In another American study, Manangan et al. [4] reported that 16% of home care patients had infections during the study period; 8% of these infections were reported as being acquired at home, which differs significantly from our study. Compared with the *Healthcare Associated infections and antimicrobial use in Long-Term care facilities* (HALT) study conducted in Europe in LTCFs and nursing homes (NHs) [20], the prevalence of infected residents in French NHs was similar to our prevalence of HBHC-associated infections.

Compared with included patients from HCFs [17], our studied patients were older, more likely to have been exposed to at least one invasive device, more frequently immunocompromised or suffering from an active cancer and more likely to have a diagnosis that was rapidly or ultimately fatal than patients included from HCFs. In our study, many individual patient characteristics were associated in the univariate analysis with a HBHC-associated infection, but only the presence of invasive devices and underlying conditions was associated with HAI in the multivariate analysis. This result was obtained using a two-level random intercept logistic model allowing adjustment of the risk estimates for random variations among HBHC, meaning that the results were not influenced by differences between HBHC providers.

In our study, a microbiological diagnosis was made in two thirds of HAIs, as most of the case definitions of HAIs were mainly based on clinical criteria. In addition, AST results were available for the majority of selected bug–drug combinations. Among the few published prevalence studies in home care, only two French pilot studies [5,18] reported microbiological data on HAIs. *S. aureus* was the main pathogen isolated in our study, in contrast to results found in PPS in HCFs where *E. coli* was most frequently isolated [17]. The rates of ESBL-producing strains as well as carbapenemase-producing *P. aeruginosa* were as high in HBHC as in HCF. Emerging ESBL-producing strains and carbapenemase-producing bacteria remain a rare but scrutinised phenomenon in France. The higher antimicrobial non-susceptibility estimated in our study should therefore be interpreted with caution because the number of isolated microorganisms with information on AST was small.

With regard to antimicrobial use, our study is, to our knowledge, the first published study which presents data about antimicrobial use in the HBHC setting. Some studies reported data on antimicrobial use in nursing home residents [20-24] and others focused only on outpatient parenteral antimicrobial therapy.

Most of these studies are not directly comparable with our study because of different patient populations and different antimicrobial classification. For instance, in the 2010 HALT study [20], the prevalence of residents in French NHs receiving at least one antimicrobial agent was lower than the prevalence of patients who received at least one antimicrobial agent in our study. Penicillins, quinolones and other beta-lactams were the most frequently prescribed antimicrobials in the HALT study [20]. In addition, the prevalence of patients receiving at least one antimicrobial agent was slightly lower in our study when compared with those in HCFs [17]. More guidance on the use of antimicrobials for infection or prophylaxis is needed. Overuse and misuse of antimicrobials have resulted in the emergence of multidrug-resistant organisms; monitoring the use of antimicrobials has become a concern in all HCFs, and home care settings should not be an exception.

As is usual in prevalence study designs, some methodological issues have to be raised. Firstly, this study does not allow assessment of the temporal relationship between exposure and outcome, as in other point-prevalence studies, resulting in a possible overrepresentation of infections of long duration (e.g. skin and soft tissue infections) and underestimation of more time-limited infections (e.g. infectious diarrhoea) [25,26]. Secondly, there was a potential risk of selection bias because the HBHC participating were not a random sample of HBHC settings in France. Finally, due to the large-scale patient-based approach, we could only investigate certain risk factors and may have missed some confounding factors (e.g. parenteral nutrition, comorbidities, some patient characteristics or potential health and safety hazards in the home) [1,2,27,28]. On the other hand, data quality of the survey was controlled by training investigators, searching for missing data, validation of clinical diagnosis by a supervisor and support from regional reference centres. Standardised criteria for infection diagnosis were based on ECDC case definitions for most HAIs and on the McGeer criteria [15] for the diagnosis of pneumonia and respiratory tract infections. Indeed, radiological diagnosis for the latter infections may not be available in HBHC settings. In addition, variability due to HBHC differences was taken into account using a two-level random logistic regression analysis. One additional benefit of this study is that it reinforced awareness about infection control among the large number of participating home care staff and that the impact of this study could encourage more staff to participate in future PPS.

In conclusion, PPS may be a good start in HBHC to obtain information on the epidemiology of HAIs and to quantify the burden of HAIs and antimicrobial use. Programme initiatives in such settings should include surveillance of the more critical HAIs, staff training and awareness, allocation of sufficient resources for infection control teams, fostering the safety culture of healthcare staff, patient empowerment and definitions of priorities at the national level.

Ethical considerations

According to the French law for biomedical research and human experimentation, an individual written consent from the patients or their relatives was not required for data collection. However, all patients were informed about the study by the nurse before their inclusion.

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Conflict of interest

None declared.

Authors' contributions

All authors have contributed directly to the intellectual content of the paper and have agreed to have their name listed as an author on the final, revised version. Their own substantive contribution to the paper is as follows: Katiuska Miliani developed the concept of the manuscript, managed the national database, analysed the data and wrote the first draft of the manuscript. Brigitte Migueres contributed to the concept of the manuscript, interpreted the results critically and revised the article to ensure important intellectual content. Delphine Verjat-Trannoy critically reviewed the article and provided important feedback on the article. Sophie Vaux provided critical revision of the article for important content. Jean-Michel Thiolet reviewed the article and contributed to the final version. Pascal Astagneau, is the head of the research team, he provided epidemiological expertise and also contributed to final revision.
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