Healthcare-associated infections in neonates and children in the first European point prevalence survey - THELANCETID-D-16-01041-R3

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Abstract

Background: In 2011/2012, the European Centre for Disease Prevention and Control (ECDC) conducted the first Europe-wide point prevalence survey (PPS) of healthcare-associated infections (HAIs) in acute care hospitals. We conducted an analysis of specifically paediatric data from this ECDC PPS.

Methods: Patients present on the ward at 8:00 AM on the day of the survey and not discharged at the time of the survey were included. Data were collected by locally trained healthcare workers according to a patient-based or unit-based protocol. HAI prevalence and distribution of HAI-types among countries and clinical settings were the main outcomes. HAI prevalence and its corresponding 95% confidence intervals, we calculated by clustering at the hospital and country level.

Findings: In total, 17,273 children from 29 countries were analysed. Seven-hundred-seventy HAIs were reported in 726 children corresponding to a prevalence [95%CI] of 4.2% [3.7-4.8] with bloodstream infections (BSIs) being the leading type (343/770), followed by infections of the lower respiratory tract (171/770), gastrointestinal infections (64/770), eye ear nose and throat infections (55/770), urinary tract infections (37/770), and surgical site infections (34/770). HAI prevalence was highest in paediatric intensive care units (122/788) and neonatal intensive care units (244/2283). Neonates and infants in their first 11 months of life, ultimately and rapidly fatal McCabe scores, prolonged length of stay, and the use of invasive medical devices were independent risk factors for HAI. Three-hundred-ninety-two microorganisms were reported for 342 HAIs, with Enterobacteriaceae being the most frequently reported (113/392).

Interpretation: This analysis represents the largest multi-national study on HAI prevalence in children. BSI was the most frequent type of HAI. Infection prevention and control strategies in children should focus on BSI prevention, particularly among neonates and infants.

Funding: The ECDC PPS 2011-2012 was coordinated by ECDC and performed by each EU/EEA Member State with its own funding. ECDC funded several meetings of experts and Member State contact points to develop the methodology, provide training, and discuss results. No specific funding was provided by ECDC for this analysis of paediatric data.

Research in context

Evidence before this study

Point prevalence surveys have been used for the surveillance of healthcare-associated infections (HAIs) for many years. We searched PubMed with the search terms "cross infection" [MeSH], "healthcare-associated infection$", "nosocomial infection$", and "hospital-acquired infection$") in combination with "prevalence", with age restriction (0-18 years) but without time restriction (up to June 2016). Of 928 titles and abstracts, 15 reports were multicentre national or multi-national prevalence surveys in high-income countries. One report was the pilot testing of the European Centre for Disease Prevention and Control (ECDC) point prevalence survey in 2010. Two national surveys (UK-Scotland, Poland) were part of the ECDC point prevalence survey 2011/2012 reported in this study. Most surveys were performed in acute-care adult or mixed adult-paediatric healthcare settings. Only one multi-national point prevalence survey reported paediatric data. Between 1983 and 1987, the World Health Organization conducted a multinational prevalence survey in 47 hospitals of 14 high- and upper-middle-income countries showing that, among a total of 28,861 patients, 3147 were children with a pooled HAI prevalence in children of 8.7%. Nine surveys were conducted in a general population in which children were included, two addressed neonatal intensive care only, and one was performed in general paediatric wards. Finally, one study in the UK and Ireland focused exclusively on respiratory tract infections in children.

Added value of this study

This analysis of paediatric data from the ECDC point prevalence survey 2011/2012 represents the largest multi-national study on HAI prevalence in children. The adjusted prevalence [95%CI] was 4.2% [3.7-4.8%]. The survey confirms that the burden of HAIs is the highest in the first year of life and in neonatal and paediatric intensive care units. Bloodstream infection was the most common type of HAI, not only in neonates and infants in their first 11 months of life but throughout childhood. With older age, infections such as lower respiratory tract infections or surgical site infections were more common. The variation of HAI

prevalence among European countries (1.2-10.4%) could neither be explained by the distribution of paediatric settings, nor did it follow a geographical or socio-economic pattern. Only five countries were statistically significant high or low outliers.

Implications of all the available evidence

Given the high prevalence of HAIs among neonates and small infants, in both neonatal and paediatric intensive care settings, and bloodstream infection being the most common type of HAI, infection prevention and control should focus on the prevention of bloodstream infections in the youngest age groups, particularly in neonatal and paediatric intensive care units.

Introduction

For many years, point prevalence surveys (PPSs) have been used for healthcare-associated infection (HAI) surveillance.[1] The pioneering Study on the Efficacy of Nosocomial Infection Control (SENIC) project, initiated in the 1970s by the US Centers for Disease Control and Prevention (CDC) used repeated PPSs to study the benefit of establishing infection prevention and control (IPC) teams in US hospitals.[2] In the following years, the US National Nosocomial Infection Surveillance (NNIS) system established prospective HAI surveillance in intensive care units, which was taken up by national surveillance networks in other countries. Incidence surveillance has become the gold standard for HAI surveillance in high-risk areas such as intensive care, oncology, or neonatal care, and for selected HAIs such as ventilator-associated pneumonia, catheter-associated urinary tract infections, and catheter-associated bloodstream infections. However, incidence surveillance is almost never performed for all HAI types because it is cumbersome and resource demanding. PPSs offer an alternative to estimate the hospital-wide burden of HAIs within a reasonable budget.[1] Thus, it can be applied to a wider range of settings including institutions with limited resources and allows for broadening the comparison of HAI rates across a wider range of socio-cultural contexts. In July 2008, the coordination of the EU-funded network Improving Patient Safety in Europe (IPSE) and its HAI surveillance component (previously Hospitals in Europe Link for Infection Control through Surveillance - HELICS) were transferred to the European Centre for Disease Prevention and Control (ECDC) to form a new Healthcare-Associated Infections surveillance Network (HAI-Net), which, in 2009, started planning the first EU-wide PPS about HAI and antimicrobial use in European acute care hospitals.[3]

In 2011–2012, the EU Member States, Iceland, Norway and Croatia participated in this ECDC PPS. Data on 273,753 patients from 1149 hospitals were submitted to ECDC and, in order to obtain similar precision in HAI prevalence estimates for all participating countries, a representative sub-sample of hospitals was drawn from the data for countries that were overrepresented such as Belgium, Portugal, and Spain. A total of 231,459 patients from 947 hospitals remained in the final ECDC PPS database.[3] The prevalence of patients with one or

more HAIs was 6.0% (country range 2.3–10.8%).[3] When extrapolated to the average daily number of occupied beds per country, the adjusted overall HAI prevalence was estimated at 5.7% [95% confidence interval (95%CI) 4.5–7.4%]. The most frequent types of HAI were lower respiratory tract infections (LRTIs, i.e. pneumonia 19.4% and other lower respiratory tract infections 4.1%), followed by surgical site infections (SSIs; 19.6%), urinary tract infections (UTIs; 19.0%), bloodstream infections (BSIs; 10.7%), and gastro-intestinal infections (GIs; 7.7%).[3]

We report the results of an analysis of data from paediatric patients that were enrolled in the ECDC PPS. The objectives of this study were: a) to calculate HAI prevalence among hospitalised children of different age groups in Europe; b) to describe the distribution of HAI types in different paediatric settings and age groups; and c) to determine risk factors for HAI among hospitalised children in Europe.

Methods

Data reporting was done according to the STROBE Guidelines.[4] National PPS contact points in EU Member States, Iceland, Norway and Croatia agreed to organise a PPS of HAI and antimicrobial use in acute care hospitals in their country based on a standardised study protocol developed by ECDC.[5] These national PPSs took place during one of the following periods: May–June 2011, September–October 2011, May–June 2012, or September–November 2012. These periods were chosen to fall outside winter (when there is a higher antimicrobial use) and outside summer (when there is a lower staffing rate). The national PPSs could be performed according to two methods for data collection: a patient-based protocol (referred to as the standard protocol) and a unit-based protocol (light protocol). In the standard protocol, demographic and risk factor data were collected for every single patient. In the light protocol, denominator data were aggregated at the ward level and for each specialty (e.g. total of paediatric surgical patients in the ward), and demographic and risk factor data were collected individually for each patient with at least one HAI. Data were collected by locally trained healthcare workers and submitted to the national PPS coordinators, who themselves submitted the data to ECDC. Additional information about the ECDC PPS methodology is available in the ECDC PPS report.[3]

As part of the ECDC PPS, all children hospitalised in general paediatrics, in paediatric surgery, in a paediatric intensive care unit (PICU), in a neonatal care unit, or in a neonatal intensive care unit (NICU) were eligible for the PPS if admitted to the ward before 8:00 AM on the day of the survey. Children in day-care wards, long-term-care wards, and healthy newborns in maternity wards were excluded from the PPS. Data on patients and HAIs were retrieved from patient charts and/or other sources (e.g. hospital information system, laboratory database) using standardised data collection forms.

HAI prevalence was defined as the proportion of paediatric patients with one or more HAI among all paediatric patients. HAI data included the type of HAI according to the HAI case definitions,[5] the date of onset of the HAI, the presence of invasive devices in the 48 hours before onset of HAI (for LRTIs, UTIs, and BSIs), the isolated microorganisms and

selected antimicrobial resistance data. HAI definitions were based on definitions from the German Krankenhaus Infektions Surveillance System (KISS) for neonatal infections,[6] and from the European Society for Clinical Microbiology and Infectious Diseases Study Group for *Clostridium difficile* (ESGCD) for *Clostridium difficile* infections.[7] The definitions of HAIs used for paediatric patients are shown in the supplementary table 1.

HAI prevalence and distribution of HAI-types among countries and clinical settings were the main outcomes and were calculated based on the combined data obtained following the standard and the light protocol. To report HAI prevalence and its corresponding 95% confidence intervals (95%CIs), we used two nested levels of clustering at the hospital level and country level to take into account the correlation of data within the levels. Patient characteristics, exposure, and clinical settings were secondary outcomes and a descriptive analysis was performed on data obtained following the standard protocol. Categorical variables were compared using the chi-square test; continuous variables were summarized as means or medians and compared using the Student's t-test or the Wilcoxon's rank sum test where appropriate. Adjusted risk factor analysis was performed on data obtained following the standard protocol. To estimate the risk factors for HAI, we used a generalised linear mixed-effects model with a logit link function. In the multivariable model, we adjusted for the following confounders: gender, age stratified into five age groups (<1 month, 1-11 months, 1-4 years, 5-10 years, ≥11 years), McCabe score (nonfatal, ultimately fatal, i.e. fatal outcome within the next 5 years, rapidly fatal, i.e. fatal outcome within the next 6 months),[14] use of any invasive medical device (central catheter, peripheral line, urinary catheter, ventilation) alone or combined, and length of hospital stay defined as the days before and including the day of the point prevalence survey for controls (or as before and including the first day of HAI for HAI cases) and stratified into four categories (<4 days, 4-7 days, 8-14 days, >14 days). Patients with missing data were not included in this analysis. No consistent information was available about the size of the paediatric settings or whether the participating hospitals were free standing children's hospitals. As a proxy we stratified the analysis according to the number of children enrolled in the survey by category: ≤25 children, 26-40 children, 41-70 children, >70 children.

Ethical approval was at the discretion of each national public health and government body in charge each national PPS. Anonymised patient and hospital level data were shared with ECDC.

Role of the funding source: The ECDC PPS 2011-2012 was coordinated by ECDC and performed by each EU/EEA Member State with its own funding. ECDC funded several meetings of experts and Member State contact points to develop the methodology, provide training, and discuss results. No specific funding was provided by ECDC for this analysis of paediatric data. The Member States had no role in study design, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Of the 231,459 patients included in the final ECDC PPS database, 17,273 (7.5%) were children and were reported by 29 countries. They were hospitalised in 1356 wards of 618 hospitals, of which 148 (23.9%) were primary hospitals, 260 (42.1%) secondary hospitals, 146 (23.6%) tertiary hospitals, 39 (6.3%) specialised hospitals, and 25 (4.1%) with unknown status. Most children were hospitalised in general paediatric wards (8298, 48.0%), followed by neonatal units (4467, 25.9%), NICUs (2283, 13.2%), paediatric surgery wards (1437, 8.3%), and PICUs (788, 4.6%). The country-wide distribution of clinical settings is shown in figure 1 (left-hand side). Of the 17,273 children, 16,237 (94.0%) were registered following the standard protocol, and 1036 (6.0%) following the light protocol. Patient characteristics are summarized in table 1. The distribution of children by age groups was as follows: <1 month: 5587 (34.4%); 1-11 months: 4024 (24.8%); 1-4 years: 2970 (18.3%); 5-10 years: 1753 (10.8%); ≥11 years: 1864 (11.5%); data about age were missing for 39 (0.2%) children. In the unadjusted descriptive analysis, children with HAI were of lower age, were more likely to have a rapidly fatal McCabe score, had previous surgery, had any invasive device in place 48 hours before HAI or on the day of survey, had prolonged length of stay up to the survey, and were more likely to be hospitalised in a PICU or a NICU (table 1).

A total of 770 HAIs were reported in 726 children corresponding to an HAI prevalence [95%CI] of 4.2% [3.7-4.8]. The country range was 1.2% to 10.4% (figure 1; supplementary table 2). Three countries had a HAI prevalence above the upper limit of the 95%CI and two countries had a HAI prevalence below the lower limit of the 95%CI (figure 1). PICUs (15.5% [11.6-20.3]) and NICUs (10.7% [9.0-12.7]) were the two clinical settings with the highest HAI prevalence, followed by neonatology (3.5% [2.8-4.5]), paediatric surgery (3.4% [2.3-4.9]), and general paediatrics (1.8% [1.4-2.4]). Predicted HAI prevalence stratified by clinical settings and taking into account the number of children contributed to the database is summarized in supplementary table 3.

Paediatric centres contributing >70 children to the database had the highest HAI prevalence (6.5% [6.1-6.8]) compared to centres contributing 41-70 (4.9% [4.6-5.2]), 26-40

(3.2% [3.0-3.5]), and ≤25 children (2.4% [2.2-2.5]) to the database, respectively. Paediatric patients from centres contributing more children also had less favourable McCabe scores (4.0% rapidly fatal cases), were more likely to be hospitalised in NICU (16.8%) or PICU 6.9%), had more invasive medical devices (49.6% children with ≥1 device), and were hospitalised longer (21.2% children hospitalised >14 days) (supplementary table 4).

The HAI prevalence per age group was as follows: <1 month: 5.1% (95%CI: 4.5-5.7); 1-11 months: 6.5% (5.7-7.2); 1-4 years: 2.2% (1.6-2.7) 5-10 years: 2.1% (1.4-2.8); ≥11 years: 2.8% (2.0-3.5). BSI was the most common type of HAI (44.6% [41.0-48.1]), followed by LRTI (22.2% [19.3-25.2]), GI (8.3% [6.4-10.3]), eye ear nose and throat infection (EENT) (7.1% [5.3-9.0]), UTI (4.8% [3.3-6.3]), and SSI (4.4% [3.0-5.9]). The distribution of the different types of HAIs varied depending on the country and this could not be explained by the distribution of the different paediatric settings (supplementary figure 1; supplementary table 5). Most HAIs (592/770, 76.9%) were identified in infants in their first 11 months of life. BSI was the most common type of HAI in neonates (57.1%), in the first 11 months of life (44.3%), between 1-4 years of age (25.4%), and ≥11 years of age (25.9%) (figure 2). Only in the age group of 5-10 years of age were LRTIs (26.2%) more common than BSIs (21.4%). UTIs were uncommon in neonates (0.7%), but contributed to 6.9–9.9% HAIs in older age groups. SSIs became gradually more frequent in older age groups.

Table 2 summarizes the independent risk factors for having at least one HAI at the time of the survey. Compared to neonates, older age groups, particularly after the first 11 months of life, were less likely to suffer from a HAI. Both ultimately and rapidly fatal McCabe scores were significantly associated with having at least one HAI. Length of stay up to the day of the survey was a time-dependent risk for HAI for all time categories (4-7 days, 8-14 days, >14 days) compared to the first category (<4 days). Having one or more invasive medical devices in place (within 48h before onset of HAI) was highly associated with having a HAI.

A total of 392 microorganisms were reported in 342 (44.4%) of the 770 HAIs: 343 (87.5%) were bacteria, 28 (7.1%) fungi, and 21 (5.4%) viruses. Enterobacteriaceae were the most commonly isolated microorganisms (28.8%), followed by coagulase-negative

staphylococci (20.9%) and *Staphylococcus aureus* (10.5%) (table 3). Coagulase-negative staphylococci were the most common microorganism in neonates and infants <12 months of age (table 3). The proportion of *Staphylococcus aureus* isolates that were resistant to meticillin was 18.8%. The proportions of Enterobacteriaceae isolates that were resistant to 3rd-generation cephalosporins and to carbapenems were 44.4% and 8.6%, respectively (supplementary figure 2). Of the few reported viruses, rotaviruses were the most frequently identified (13/21).

Discussion

We performed an analysis of the largest multinational dataset of HAIs in paediatric patients. Our results confirmed that the burden of HAIs was the highest in the first year of life and demonstrated the importance of BSI as being the most common type of HAI in children from all age groups. LRTIs and particularly SSIs were more frequent in older age groups and the distribution of HAIs in children aged 5 years or older was close to the distribution of HAIs in adults.[1, 3, 8, 9] These findings suggest that age-adapted strategies are needed for infection prevention and control in paediatric settings, focussing on the prevention of BSI. We observed variations in HAI prevalence and the distribution of HAI-types among European countries. These variations could neither be explained by the distribution of paediatric settings in the database, nor did they follow a geographical pattern. Although the range of HAI prevalence (1.2-10.4%) was wide, only a few countries were significant high or low outliers. No specific conclusion on the effectiveness of national infection prevention and control practices could be drawn from our results. Age as well as ultimately and rapidly fatal McCabe scores were identified as independent risk factors for HAI. No information was available about the size of the participating paediatric settings or about whether the institutions were free-standing children's hospitals. As a proxy we stratified the analysis by the number of enrolled children and found that indeed, hospitals that had enrolled more children had a higher HAI prevalence. The low HAI prevalence in the age group <1 month was unexpected. A closer look revealed that this was due to the fact that, in the sample of paediatric settings that participated in the ECDC PPS, (non-intensive) neonatal units contributed 66.2% of the neonatal population. Indeed, most neonates were hospitalised in regular non-intensive care neonatology units. This is of interest because, in the published literature, studies among preterm neonates in NICUs are more common than studies in other neonatal units and thus, may contribute to a perceived high risk for HAI in the neonatal population as a whole. However, a number of neonates with prolonged hospital stay were classified in the age group of 1-11 months, and thus, contributed to the high prevalence in this age group.

Very few recent reports of cross-national PPSs including paediatric data have been published. Between 1983 and 1987, the World Health Organization conducted a multinational PPS in 47 hospitals from 14 countries (Australia, China, Czechoslovakia, Denmark, Egypt, Greece, Kuwait, Malaysia, Nepal, Netherlands, Singapore, Spain, Thailand, United Kingdom).[10] A total of 28,861 patients were included of which 3147 (10.9%) were children. The HAI prevalence in the four age groups of children (< 1 month, 1-11 months, 1-4 years, 5-14 years) were 8.8%, 13.5%, 9.3%, and 6.7%, respectively. More information can be obtained from national PPSs. Table 4 summarizes the findings of 14 previously published national and multi-national PPS in high-income countries in comparison with that of the ECDC PPS 2011/2012.[8, 11-24] One PPS was the ECDC pilot survey in 2010.[24] Eight national PPSs were conducted in a general patient population in which children were included;[8, 11, 13, 15, 17-21] two specifically addressed NICUs;[16, 22] and one was performed in general paediatric wards.[23] One study in the UK and Ireland focused exclusively on LRTIs in children.[14] The largest paediatric dataset was from a national PPS conducted in France in 2001 and included 305,656 patients of which 21,596 (7.1%) were children.[18] In this French PPS, the prevalence of HAI among children was 2.4% [2.2-2.6%] overall, 1.2% [1.0-1.5%] for neonates and 3.3% [3.0-3.6%] for children in non-neonatal settings. The group of neonates also included new-borns in maternity units, which may be the reason for the low HAI prevalence in this group. In addition, the proportion of laboratory confirmed HAIs (456/562; 81.1%) was unusually high, which raises concerns about the possible underestimation of HAI prevalence, in particular LRTIs and clinical sepsis.

As in our study, BSI was the most common type of HAI in these other reports (range: 22.1-52.6%).[13, 16, 17, 25] However, although the vast majority of BSIs in our study were reported in neonates and infants in their first 11 months of life, the proportion of BSIs among all HAIs remained high also in other age groups. LRTIs and SSIs were more frequent in children of 5 years or older. UTIs were not common and overall less important than GIs and EENTs, particularly in older age groups. Our results suggest that neonates and infants requiring intensive care are at high risk for HAI. Other reports identified risk factors for HAI similar to that identified in our study: young age and surgery,[13] presence of an invasive device and

prolonged length of stay,[25] central venous catheter or mechanical ventilation,[19] and again young age and an ultimately or rapidly fatal McCabe score.[17] In our study, all tested risk variables were independently and significantly associated with HAI but the highest effects were found for the use of invasive medical devices and for length of stay >14 days up to the day of the PPS (or for HAI cases up to the first day of infection) with odds ratios of 15.3 (95% CI, 11.9-19.7) and 14.9 (95% CI, 11.0-20.1), respectively.

The two most common groups of microorganisms in HAI among children in our study were Enterobacteriaceae and coagulase-negative staphylococci, which was similar to findings in France (Enterobacteriaceae: 21.9%; coagulase-negative staphylococci: 21.9%),[18] Switzerland (Enterobacteriaceae; 50.0%; coagulase-negative staphylococci: 29.2%),[17] and the USA (Enterobacteriaceae: 25.6%; coagulase-negative staphylococci: 31.6%).[16] In a Mexican study, the most common pathogen in HAI among children was *Klebsiella pneumoniae* (31.0%).[26] The proportion of meticillin-resistant *Staphylococcus aureus* (MRSA) in HAI in children in the French PPS was 26.7%.[18] No MRSA was reported in paediatric patients in the Swiss study.[17] The relatively low number of microbiologically documented HAIs was due to the high proportion of HAI-types that did not require microbiology testing, such as clinical sepsis or pneumonia.

Our study has some limitations. First, data were collected by many individuals in different countries. Training was provided in all participating countries but data validation based on samples of sufficient size was not possible due to resource limitations. Second, the results of this study may not be representative for the paediatric acute care patient populations in all European countries. Future PPSs should take representativeness of subgroups of paediatric patients into account. Third, conducting the national PPSs at four different time periods may have introduced bias in the case-mix of patients, in particular because they took place in different seasons and over two years. However, these time periods of the ECDC PPS were outside winter and summer seasons where paediatric settings are particularly prone to either low or high ward occupancy. Fourth, the data collection forms had limited fields for paediatric data. For example, more information about

birth weight and prematurity would have been needed to adjust for relevant risk factors for HAI in neonates, specific information about the paediatric settings (e.g. free standing children's hospital, level of care, case-mix), that were missing in the ECDC PPS 2011/2012 database. Fifth, only microbiology data available on the day of the PPS was included and thus, both the distribution of microorganisms and antibiotic resistance data may not be representative. Although having incomplete microbiology data does not interfere directly with identifying a HAI, it may have consequences in sub-categorising the type of infection. Sixth, healthy newborns may have been coded as belonging to a non-intensive neonatal unit, instead of being newborns in gynaecology-obstetrics. We assume that this proportion was low but may have had an impact on the overall prevalence of HAI in neonatal wards. Seventh: Calculating weighted EU/EEA estimates as reported in the ECDC PPS report for the overall PPS[3] was not possible because no specific information on the number of paediatric beds and patient-days in the countries were available.

Our analysis of paediatric data from the ECDC point prevalence survey 2011/2012 represents the largest multi-national study on HAI prevalence in children conducted so far. Despite its limitations, it provides detailed information on the prevalence and distribution of HAIs among hospitalised children in Europe. Our results show that the prevalence of HAIs in NICUs and PICUs in Europe remains unacceptably high. BSIs in neonates and children are associated with a high mortality and long-term adverse neurological outcomes.[27] Prevention of HAIs in children in Europe would require a multi-national quality improvement programme, with a focus on NICUs and PICUs and on healthcare-associated BSIs.

Contributors

CS was the coordinator of the ECDC-PPS and CS, SH and the ECDC PPS study group members were involved in the design and the overall plan for data analysis of the ECDC PPS. SH and the ECDC PPS study group members participated in the coordination of the national surveys and the data collection at the national level. WZ, AGA, CS and MS planned the paediatric data analysis for this manuscript, and WZ and AGA performed this analysis. WZ wrote the first draft of the manuscript. WZ, AGA, SH, AH, MS, CS and the ECDC PPS study group members reviewed and contributed to subsequent drafts and approved the final version for publication.

Conflict of interest statement

Elisabeth Presterl from the ECDC PPS study group received grants from the Austrian Federal Ministry of Health and Women's Affairs during the conduct of the study. Nina Sorknes from the ECDC PPS study group received grants from the Norwegian Nurses Association during the conduct of the study. The other authors declare no competing interests.

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Table 1. Patient characteristics, exposures and clinical areas – Paediatric data, standard protocol, ECDC point prevalence survey 2011-2012

	All (N = 16,237)	**Without HAI (N = 15,511)**	**With HAI (N = 726)**	***P*-value**
Patient characteristics				
Female gender, % [95%CI]	46.0 [45.3-46.8]	46.2 [45.4-47.0]	42.5 [38.8-46.2]	0.055
Age (months), median [IQR]	3 [0-48]	3 [0-48]	1 [0-7]	<0.001
Neonates, % [95%CI]	33.2 [32.5-33.9]	32.9 [32.2-33.6]	39.8 [36.1-43.4]	<0.001
Rapidly fatal McCabe score, % [±SD]	0.7 [0.6-0.8]	0.6 [0.4-0.7]	3.9 [2.4-5.3]	<0.001
Exposures				
Surgery*, % [95%CI]	9.1 [8.7-9.6]	8.5 [8.0-8.9]	23.9 [27.1]	<0.001
Central catheter*, % [95%CI]	7.1 [6.7-7.5]	5.8 [5.4-6.1]	36.9 [33.3-40.5]	<0.001
Peripheral line*, % [95%CI]	38.7 [37.9-39.4]	37.4 [36.6-38.2]	67.2 [63.8-70.7]	<0.001
Urinary catheter*, % [95%CI]	2.2 [2.0-2.4]	1.8 [1.6-2.0]	11.6 [9.2-14.0]	<0.001
Ventilation*, % [95%CI]	3.0 [2.8-3.3]	2.2 [1.9-2.5]	22.0 [19.0-25.1]	<0.001
Length of stay (days)**, median [IQR]	4 [2-8]	4 [2-8]	12 [6-26]	<0.001
Clinical areas				
Paediatric intensive care, % [95%CI]	3.6 [3.3-3.9]	3.1 [2.8-3.4]	15.3 [12-6-18.0]	<0.001
Neonatal intensive care, % [95%CI]	11.2 [10.7-11.7]	10.4 [9.9-10.9]	27.9 [24.6-31.2]	<0.001
Neonatology, % [95%CI]	27.8 [27.1-28.4]	27.7 [27.0-28.4]	27.9 [24.6-31.2]	0.930
Paediatric surgery, % [95%CI]	8.1 [7.6-8.5]	8.1 [7.7-8.5]	7.2 [5.2-9.1]	0.364
General paediatrics, % [95%CI]	49.4 [48.6-50.2]	50.6 [49.8-51.4]	21.7 [18.7-24.8]	<0.001

*Before or on the day of the point prevalence survey
**Before and including the day of the point prevalence survey
95%CI: 95% confidence interval; ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection; IQR: interquartile range

Table 2. Independent risk factors for HAI – Multivariable model of paediatric data, standard protocol, ECDC point prevalence survey 2011-2012

	OR	95%CI	*P*-value
Gender			
Girl	1.0	-	-
Boy	1.1	1.0-1.4	0.150
Age group			
<1 month	1.0	-	-
1-11 months	0.6	0.5-0.7	<0.001
1 – 4 years	0.2	0.2-0.3	<0.001
5 – 10 years	0.2	0.1-0.3	<0.001
≥11 years	0.2	0.2-0.3	<0.001
McCabe classification			
Nonfatal	1.0	-	-
Ultimately fatal	2.3	1.3-4.1	0.003
Rapidly fatal	2.5	1.7-3.6	<0.001
Length of stay (days)*			
<4	1.0	-	-
4-7	3.3	2.4-4.5	<0.001
8-14	6.7	4.9-9.1	<0.001
>14	14.9	11.0-20.1	<0.001
Presence of at least one invasive medical device			
No	1.0	-	-
Yes	15.3	11.9-19.7	<0.001

*For cases: before and including the first day of HAI. For controls: before and including the day of the point prevalence survey.
95%CI: 95% confidence interval; ECDC: European Centre for Disease Prevention and Control; HAI: healthcare-associated infection; OR: odds ratio

Table 3. Identified microorganisms – Paediatric data, ECDC point prevalence survey 2011-2012

Microorganism	Age group					
	All	**<1 month**	**1-11 months**	**1-4 years**	**5-10 years**	**≥11 years**
Coagulase-negative staphylococci	82 (21.0%)	33 (31.4%)	38 (21.3%)	3 (7.0%)	1 (3.1%)	7 (21.9%)
Staphylococcus aureus	41 (10.5%)	15 (14.3%)	14 (7.9%)	4 (9.3%)	4 (12.5%)	4 (12.5%)
Escherichia coli	37 (9.5%)	7 (6.7%)	17 (9.6%)	4 (9.3%)	4 (12.5%)	5 (15.6%)
Klebsiella spp.	37 (9.5%)	6 (5.7%)	21 (11.8%)	7 (16.3%)	2 (6.3%)	1 (3.1%)
Enterobacter spp.	27 (6.9%)	14 (13.3%)	10 (5.6%)	2 (4.7%)	0 (0.0%)	1 (3.1%)
Pseudomonas aeruginosa	26 (6.7%)	3 (2.9%)	10 (5.6%)	7 (16.3%)	4 (12.5%)	2 (6.3%)
Candida spp.*	23 (5.9%)	3 (2.9%)	12 (6.7%)	3 (7.0%)	1 (3.1%)	4 (12.5%)
Viruses	21 (5.4%)	3 (2.9%)	13 (7.3%)	4 (9.3%)	1 (3.1%)	0 (0.0%)
Enterococcus spp.	20 (5.1%)	5 (4.8%)	12 (6.7%)	2 (4.7%)	1 (3.1%)	0 (0.0%)
Streptococcus spp.	18 (4.6%)	6 (5.7%)	5 (2.8%)	1 (2.3%)	4 (12.5%)	2 (6.3%)
*Stenotrophomonas malthophilia**	12 (3.1%)	0 (0.0%)	8 (4.5%)	1 (2.3%)	3 (9.4%)	0 (0.0%)
Serratia marcescens	8 (2.1%)	4 (3.8%)	3 (1.7%)	1 (2.3%)	0 (0.0%)	0 (0.0%)
Acinetobacter baumannii	7 (1.8%)	3 (2.9%)	4 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Clostridium difficile	4 (1.0%)	0 (0.0%)	1 (0.6%)	1 (2.3%)	2 (6.3%)	0 (0.0%)
Haemophilus influenzae	4 (1.0%)	0 (0.0%)	1 (0.6%)	1 (2.3%)	1 (3.1%)	1 (3.1%)
Moraxella catarrhalis	4 (1.0%)	0 (0.0%)	2 (1.1%)	1 (2.3%)	1 (3.1%)	0 (0.0%)
Proteus mirabilis	4 (1.0%)	0 (0.0%)	1 (0.6%)	1 (2.3%)	1 (3.1%)	1 (3.1%)
Aspergillus fumigatus	3 (0.8%)	0 (0.0%)	2 (1.1%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Other	12 (3.1%)	3 (2.9%)	4 (2.2%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
Total	390 (100.0%)	105 (100.0%)	178 (100.0%)	43 (100.0%)	32 (100.0%)	32 (100.0%)

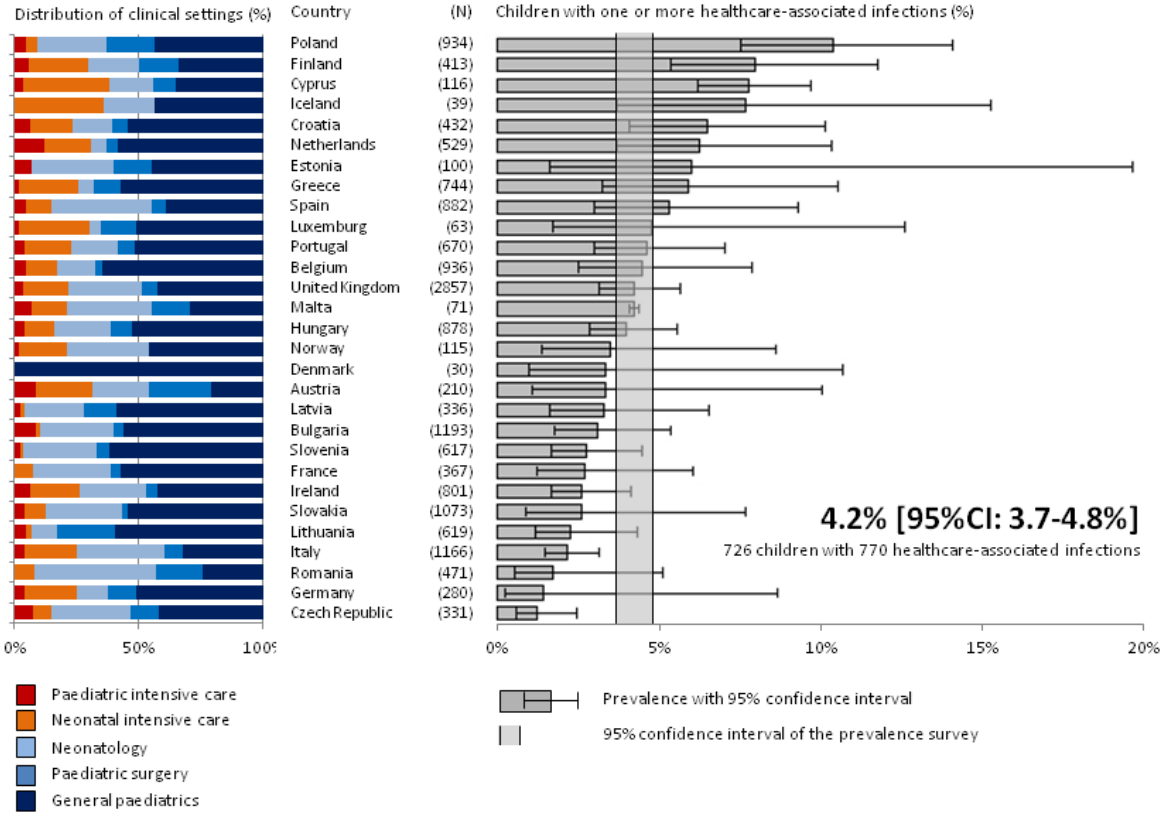
*Missing data about age for one isolate
ECDC: European Centre for Disease Prevention and Control

Table 4. Paediatric data of national and multi-national prevalence surveys in high-income countries

Survey	Setting	Patients (N)	Children (N)	Prevalence, by age group [§]			
				All (% [95%CI])*	**Neonates** (% [95%CI])*	**Infants** (% [95%CI])*	**Children** (% [95%CI])*
Moro, Italy, 1983 [11]	Adult/children	34,577	3099	7.7 [6.8-8.7]	-	11.5 [9.6-13.5]	5.8 [4.8-6.9]
Campins, Spain, 1990† [12, 13]	Adult/children	38,489	4081	8.5 [8.2-8.7]	-	-	8.5 [7.6-9.3]
Kelsey, UK/Ireland, 1993/1994 [14]	LRTI/children	6183	6183	1.3 [1.1-1.7]	-	1.7 [1.3-2.2]	0.7 [0.4-1.2]
Gikas, Greece, 1999 [15]	Adult/children	3925	332	9.9 [6.9-13.7]	-	19.7 [13.2-27.7]	3.9 [1.7-7.5]
Sohn, USA, 1999 [16]	NICU	827	827	11.4 [9.3-13.8]	11.4 [9.3-13.8]	-	-
Mühlemann, Switzerland, 2000 [17]	Adult/children	520	520	6.7 [4.7-9.2]	6.9 [3.0-13.1]	10.1 [6.2-15.1]	4.7 [2.6-7.6]
Branger, France, 2001 [18]	Adult/children	305,656	21,596	2.4 [2.2-2.6]	1.2 [1.0-1.5]	-	3.3 [3.0-3.6]
Gravel, Canada, 2002† [19, 20]	Adult/children	6747	997	10.0 [9.4-10.8]	18.5 [13.9-23.9]	2.2 [1.0-4.4]	8.0 [6.4-9.9]
Valinteliene, Lithuania, 2003/2005/2007 [21]	Adult/children	10,102	3733	3.3 [2.7-3.9]	-	-	-
Sarvikivi, Finland, 2008/2009 [22]	NICU	2562	2562	6.4 [5.4-7.4]	6.4 [5.4-7.4]	-	-
Rutledge, Canada, 2009 [23]	Children	1353	1353	9.2 [7.7-10.9]	4.8 [2.9-7.4]	14.0 [10.7-17.8]	10.9 [7.4-15.4]
Zarb, Europe, 2010 [24]	Adult/children	19,888	1024	7.1 [6.7-7.4]	-	7.8 [6.0-9.9]	3.7 [2.6-5.1]
Magill, USA, 2011 [8]	Adult/children	11,282	1611	3.4 [2.6-4.4]	-	3.1 [2.2-4.3]	4.1 [2.5-6.4]
ECDC PPS 2011/2012 [‡]	Adult/children	231,459	16,237	4.2 [3.7-4.8]	5.1% [4.5-5.7]	6.5 [5.7-7.2]	2.3 [2.0-2.7]

*95% confidence intervals were calculated from published data
†Added numbers from separate publications of adult and children data of the same national prevalence survey
‡Data from the standard protocol
§Age groups: neonates: 1 month of life; infants: <1 year of life; children: 1 year and older
95%CI: 95% confidence interval; LRTI: lower respiratory tract infection; NICU: neonatal intensive care unit

Figure 1. Prevalence of children with one or more healthcare-associated infections and clinical settings – Paediatric data, ECDC point prevalence survey 2011-2012



N: Number of children included in the point prevalence survey; 95%CI: 95% confidence interval

Figure 2. Distribution of healthcare-associated infections in children, by age group – Paediatric data, standard protocol, ECDC point prevalence survey 2011-2012