Impact factor 7.1

Eurosurveillance

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Special edition:

Antimicrobial use and prevalence of healthcare-associated infections in acute and long-term care facilities

December 2018

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RESEARCH ARTICLES

Antimicrobials in acute and long-term care: a point in time along the way to improved use

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Citation style for this article:
Neuhauser Melinda M., Weber J. Todd. Antimicrobials in acute and long-term care: a point in time along the way to improved use. Euro Surveill. 2018;23(46):pii=1800607. https://doi.org/10.2807/1560-7917.ES.2018.23.46.1800607

Article submitted on 08 Nov 2018 / accepted on 15 Nov 2018 / published on 15 Nov 2018

Antimicrobial use is the most important modifiable factor contributing to resistance [1]. One key strategy against antimicrobial resistance that has the potential to improve patient outcomes is to optimise antimicrobial use. Understanding how antimicrobials are being used informs stewardship efforts in acute care, long-term care and outpatient settings [2]. In the acute care setting, stewardship programs encompass tracking and reporting aggregate antimicrobial use metrics, such as days of therapy or defined daily doses. Benchmarking use within and across facilities is helpful in identifying where action is needed. Antimicrobial use point prevalence surveys (PPS) complement the aggregate metrics by providing information on patient-level use, such as indication and site of infection during the specified time period [3,4]. This approach is able to reveal more targeted quality improvements and enables comparisons of antimicrobial use at the national, regional or local level. PPS may be particularly useful for resource-limited hospitals and long-term care facilities (LTCF) with restricted capabilities for capturing use data on a continual basis [5,6]. Since PPS evaluate antimicrobial use during a single time period, they need to be repeated at regular intervals to monitor trends over time.

On the occasion of the European Antibiotic Awareness Day on 18 November, this issue of Eurosurveillance is dedicated to several studies presenting results from European PPS based on the European Centre for Disease Prevention and Control (ECDC) healthcare-associated infections (HAI) and antimicrobial use protocol for acute care hospitals and the HAI and antimicrobial use protocol for LTCF [7,8].

Plachouras et al. describe the outcomes from the second European Union/European Economic Area (EU/EEA)-wide PPS conducted in acute care hospitals [3]. In this survey, the weighted prevalence of antimicrobial use was 30.5% (95% confidence interval (CI): 29.2–31.9%) in 1,209 acute care hospitals in 28 EU/EEA countries [3].

Since 2009, as part of a Transatlantic Taskforce on Antimicrobial Resistance, ECDC and the United States (US) Centers for Disease Control and Prevention (CDC) have collaborated to share and, where possible, harmonise methodologies for conducting PPS focused on HAI and antimicrobial use [9]. The European hospital-based antimicrobial use PPS coordinated by ECDC took place in 2011–12 and 2016–17; the CDC-led ones in the US were conducted in 2011 and 2015. In an analysis of a subset of the data from the US CDC's hospital-based PPS conducted in 2015, a higher proportion of patients (non-weighted prevalence: 50.1%; 4,590/9,169) received at least one antimicrobial [10], compared to those in European hospitals (non-weighted prevalence: 32.9%; 102,093/310,755) [3]. Variation in methodologies between Europe and the US, including the definition of the prevalence time period (1 day vs 2 days) and data collectors, may have influenced these results. However, there was large variability in the point prevalence of antimicrobial use across European countries. Greece had the highest percentage at 55.6%, while Hungary had the lowest at 15.9% [3]. In the 2011 US PPS, variability by geographic region was not described [11]. The US also had a higher percentage of patients (50%) receiving two or more drugs [11], compared with most recent findings from European countries (30%) [3]. Overall, the antimicrobial use prevalence was similar between the first and second PPS in Europe, as well as when the US compared their results to the first and most recent US PPS survey. Both the European and US PPS revealed declining fluoroquinolone use, however, when compared with their first surveys [3,10].

In another study in this issue of Eurosurveillance, Karki et al. present results from the third point prevalence survey of HAI and antimicrobial use in European LTCF. The observed prevalence of antimicrobial use was

4.9% (95% CI: 4.8–5.1%) in 1,788 LTCF in 23 EU/EAA countries [4].

In the long-term care setting, the first US large-scale antimicrobial use PPS in 2017 comprised 15,295 residents in 161 nursing homes [12]. The results showed that 8.2% (95% CI: 7.8–8.7%) of residents received at least one antimicrobial at the time of the survey [12], compared with 4.9% (95% CI: 4.8–5.1%) of residents in the European prevalence survey [4]. In general, the European and US survey methodologies were more similar for the PPS in LTCF compared with that in acute care hospitals. The target population had notable differences; in the US, only nursing homes were surveyed, while in Europe nursing homes, residential homes and mixed LTCF were surveyed. Similar to acute care hospitals, prevalence in European LTCF varied geographically, with the highest values in Spain and Denmark (10.5%) and the lowest in Lithuania (0.7%) [4]. The urinary tract was the most common infection site listed as the source in both the US and European LTCF [4,12].

Descriptive antimicrobial use data from PPS are informative to guide stewardship efforts, but have limitations in addressing quality of prescribing for more targeted interventions. In order to address quality of prescribing, the CDC expanded data collection for the acute care PPS conducted in 2015 to describe the quality of antimicrobial drug prescribing in selected clinical circumstances, i.e. community-acquired pneumonia and urinary tract infection, and vancomycin and fluoroquinolone use [13]. The CDC, with input from external experts, is working to refine prescribing quality assessment pathways to describe opportunities for improvement in hospital prescribing practices.

The European Commission and the CDC have released recommendations regarding the key elements of antimicrobial stewardship programs in the acute care, long-term care and outpatient settings [14-17]. European Commission recommendations also target other key stakeholders such as local governments, prescribers, researchers and the pharmaceutical industry. The European healthcare-associated infections and antimicrobial use PPS included structure and process indicators for antimicrobial stewardship [3,4]. In acute care hospitals, approximately half of the hospitals have less than 0.1 full-time equivalent antimicrobial stewardship consultants per 250 beds, and approximately half of the European hospitals had a formal procedure for post-prescription review [3]. In the European LTCF survey, 39.4% of facilities had guidelines for appropriate antimicrobial use, 24.0% had a restrictive list of antimicrobials and 20.7% had annual training on appropriate antimicrobial prescribing [4]. In comparison, 59% of US nursing homes had guidelines for appropriate use, 25% had a restrictive list of antimicrobials and 73% had training for nursing staff (but 'annual' frequency was not specified in the questionnaire) [18]. Dedicating necessary resources in both acute care and LTCF settings is important to advance antimicrobial stewardship interventions.

In the US, stewardship programs in hospitals often target optimising antimicrobial therapy for commonly encountered infections such as community-acquired pneumonia, UTI, and skin and soft tissue infections [15]. Studies have demonstrated a number of interventions to improve antimicrobial use for each of these, making them likely high-yield targets for improvement.

Several important findings from the studies published in this issue can guide targeted stewardship program efforts. In the acute care PPS, surgical prophylaxis exceeded more than one day in 54.2% of the courses [3]. As noted by the authors, one preoperative dose is recommended for most surgical procedures, so optimising duration of therapy for surgical prophylaxis represents a stewardship opportunity to reduce unnecessary antimicrobial use, development of resistance and costs [3]. Further, documented indications for antimicrobials were frequently (19.8%) missing in the medical chart, which can be a barrier to improving use. The LTCF survey results showed that almost half (46.1%) of antimicrobials were prescribed for the urinary tract and the majority (74.0%) of antimicrobials were prescribed for prophylaxis of UTI [4]. Although quality of prescribing was not evaluated, optimising antimicrobial therapy for UTI represents another stewardship opportunity to reduce unnecessary prescribing for asymptomatic bacteriuria or medical prophylaxis.

The European PPS have contributed to our knowledge by highlighting that ca 30% and 5% of patients received at least one antimicrobial in acute care hospitals [3] and LTCF [4], respectively. Antibiotic use PPS provide a standardised methodology and data collection tool for facilities to extract and analyse data. These data can be used at the national, regional or local level to guide stewardship interventions. Examples for improving surgical prophylaxis duration in the hospital setting may include implementing standardised surgical prophylaxis protocols in collaboration with surgery and key stakeholders [19]. Often, more detailed quality assessment through a medication use evaluation (i.e. retrospective evaluation of clinical course for quality improvement) may be warranted to further identify more targeted interventions for commonly used antimicrobials or infections.

Identifying opportunities to streamline data collection is necessary, as PPS are currently performed by labour-intensive manual chart abstraction. As electronic health records continue to advance, leveraging electronic means to capture prevalence of HAI, antimicrobial use and quality of prescribing should be an aspiration. For example, the US Department of Veterans Affairs Salt Lake City IDEAS Center has begun to capture electronic medication use evaluations for community-acquired pneumonia [20] and other common clinical conditions.

Although PPS are complicated and time-consuming efforts, they are likely more feasible for resource-limited hospitals and LTCF than creating a prospective antimicrobial use surveillance system. With many countries around the world performing antimicrobial use PPS, there is an opportunity for global collaboration in order to share information and knowledge towards the goal of more judicious use of precious, lifesaving antimicrobials.

Acknowledgements

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conflict of interest

None declared.

Authors' contributions

Dr. Neuhauser and Dr. Weber made substantial contributions to the design of the editorial. Dr. Neuhauser drafted the editorial and both authors revised it critically for content. Both authors had final approval of the published version and are accountable for all aspects of the work.

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Antimicrobial use in European acute care hospitals: results from the second point prevalence survey (PPS) of healthcare-associated infections and antimicrobial use, 2016 to 2017

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Citation style for this article:
Plachouras Diamantis, Kärki Tommi, Hansen Sonja, Hopkins Susan, Lyytikäinen Outi, Moro Maria Luisa, Reilly Jacqui, Zarb Peter, Zingg Walter, Kinross Pete, Weist Klaus, Monnet Dominique L., Suetens Carl, the Point Prevalence Survey Study Group. Antimicrobial use in European acute care hospitals: results from the second point prevalence survey (PPS) of healthcare-associated infections and antimicrobial use, 2016 to 2017. Euro Surveill. 2018;23(46):pii=1800393.

Article submitted on 18 Jul 2018 / accepted on 16 Oct 2018 / published on 15 Nov 2018

Antimicrobial agents used to treat infections are life-saving. Overuse may result in more frequent adverse effects and emergence of multidrug-resistant microorganisms. In 2016–17, we performed the second point-prevalence survey (PPS) of healthcare-associated infections (HAIs) and antimicrobial use in European acute care hospitals. We included 1,209 hospitals and 310,755 patients in 28 of 31 European Union/European Economic Area (EU/EEA) countries. The weighted prevalence of antimicrobial use in the EU/EEA was 30.5% (95% CI: 29.2–31.9%). The most common indication for prescribing antimicrobials was treatment of a community-acquired infection, followed by treatment of HAI and surgical prophylaxis. Over half (54.2%) of antimicrobials for surgical prophylaxis were prescribed for more than 1 day. The most common infections treated by antimicrobials were respiratory tract infections and the most commonly prescribed antimicrobial agents were penicillins with beta-lactamase inhibitors. There was wide variation of patients on antimicrobials, in the selection of antimicrobial agents and in antimicrobial stewardship resources and activities across the participating countries. The results of the PPS provide detailed information on antimicrobial use in European acute care hospitals, enable comparisons between countries and hospitals, and highlight key areas for national and European action that will support efforts towards prudent use of antimicrobials.

Background

Antimicrobials are commonly used in acute care hospitals for the treatment of both community-acquired and healthcare-associated infections (HAIs), and for surgical prophylaxis [1]. Studies have indicated that some antimicrobial use may be unnecessary and in instances when use is required, the selection, dose, route of administration and duration of treatment may be inappropriate [2,3]. Through selection pressure, antimicrobials contribute to the emergence and spread of antimicrobial resistance (AMR) [4]. Moreover, antimicrobial use has adverse consequences, including HAIs caused by *Clostridium difficile* [5,6], multidrug-resistant organisms [7] and fungi [8].

Data on antimicrobial consumption in acute care hospitals are necessary to assess the magnitude, the reasons and determinants of antimicrobial use and to inform public health policies that are promoting prudent use of antimicrobials. In June 2017, the European Commission published the European guidelines for the prudent use of antimicrobials in human medicine [9]. These guidelines recommend establishing antimicrobial stewardship programmes in all healthcare facilities. Although antimicrobial consumption in hospitals is measured at a national level by some EU/EEA countries, methodologies are not always consistent between countries and therefore preclude valid comparisons. The European Surveillance of Antimicrobial

Table 1a

Prevalence of antimicrobial use, structure and process indicators of antimicrobial stewardship, by country, 28 European Union/European Economic Area countries[a] and Serbia, 2016–2017

Country	Number of hospitals	Number of eligible patients	Antimicrobial use				Antimicrobial stewardship consultant in the hospital			Formal procedure for post-prescription review in the hospital[b]		Participation in a national or regional hospital antimicrobial consumption surveillance network	
			Number of patients with at least one antimicrobial	Observed prevalence % (95% CI)	Predicted prevalence %	DDD per 100 patients	Total number replied	Mean FTE per 250 beds	Median FTE per 250 beds	Total number replied	Number with procedure	Total number replied	Number with participation
Austria	49	13,461	3,663	27.2 (24.3–30.2)	31.9	40.3	49	0.14	0	49	31	9	9
Belgium	43	11,800	3,320	28.1 (26.6–29.7)	30.2	45.5	35	0.33	0.23	41	18	25	18
Bulgaria	12	2,200	995	45.2 (39.8–50.3)	38.7	54.3	12	0.63	0.50	11	9	3	2
Croatia	34	10,466	3,263	31.2 (26.6–35.8)	33.8	42.0	31	0.60	0	34	12	25	20
Cyprus	8	1,036	475	45.8 (42.9–48.8)	42.3	70.6	8	0	0	8	1	5	0
Czech Republic	45	15,117	4,386	29.0 (27.2–30.8)	36.9	48.1	45	0.49	0.28	5	2	45	0
Estonia	23	4,220	1,059	25.1 (21.2–29.0)	29.6	38.0	14	0.13	0.13	20	11	15	2
Finland	51	9,079	3,485	38.4 (35.0–41.7)	34.8	49.8	35	0.28	0.08	46	23	9	9
France	50	16,522	3,259	19.7 (17.9–21.5)	26.6	26.5	50	0.67	0.25	50	46	50	44
Germany	49	11,324	2,437	21.5 (17.2–25.8)	28.2	31.8	46	0.14	0	49	12	49	16
Greece	42	9,401	5,227	55.6 (53.1–58.1)	42.1	N	27	0.14	0.09	27	18	36	18
Hungary	38	20,588	3,282	15.9 (13.2–18.6)	23.9	19.8	38	0.16	0	35	5	8	8
Iceland	2	633	190	30.0 (28.5–31.5)	28.3	35.4	2	0	0	2	0	1	0
Ireland	60	10,333	4,104	39.7 (37.4–42.0)	35.2	68.2	56	0.54	0.60	58	43	60	46
Italy	56	14,773	6,579	44.5 (42.6–46.5)	40.0	64.6	55	0.42	0	55	21	53	20
Latvia	14	3,807	1,459	38.3 (35.1–41.6)	34.7	51.0	11	0.11	0	14	2	14	1
Lithuania	62	12,415	3,370	27.1 (23.9–30.4)	26.6	37.9	60	0.35	0	61	34	62	60
Luxembourg	12	2,018	516	25.6 (19.4–31.7)	27.7	39.8	12	0.71	0	12	3	9	7
Malta	4	961	385	40.1 (37.8–42.4)	35.1	64.8	4	0.16	0	4	1	4	1
The Netherlands	19	4,441	1,471	33.1 (31.5–34.7)	37.8	49.7	7	0.03	0	4	3	12	10

CI: confidence interval; DDD: defined daily dose; EU/EEA: European Union/European Economic Area; FTE: full-time equivalent; N: not available; NA: not applicable; UK: United Kingdom.

[a]For the UK, data for England, Northern Ireland, Scotland and Wales are presented separately.

[b]Review of the appropriateness of prescribed antimicrobials within 72 hours (three calendar days) from the initial order, in at least one of the hospital wards.

The three EU/EEA countries that did not participate were Denmark, Lichtenstein and Sweden.

Table 1b

Prevalence of antimicrobial use, structure and process indicators of antimicrobial stewardship, by country, 28 European Union/European Economic Area countries[a] and Serbia, 2016–2017

Country	Number of hospitals	Number of eligible patients	Antimicrobial use				Antimicrobial stewardship consultant in the hospital			Formal procedure for post-prescription review in the hospital[b]		Participation in a national or regional hospital antimicrobial consumption surveillance network	
			Number of patients with at least one antimicrobial	Observed prevalence % (95% CI)	Predicted prevalence %	DDD per 100 patients	Total number replied	Mean FTE per 250 beds	Median FTE per 250 beds	Total number replied	Number with procedure	Total number replied	Number with participation
Norway	43	9,628	2,868	29.8 (28.0–31.4)	34.7	55.0	24	0.22	0.08	24	18	24	24
Poland	80	21,712	6,073	28.0 (25.7–30.2)	33.4	36.7	80	0.16	0.07	79	32	43	4
Portugal	93	16,982	6,722	39.6 (36.9–42.3)	37.2	51.7	81	0.22	0	93	37	60	38
Romania	40	11,443	4,829	42.2 (38.7–45.7)	35.4	53.7	36	0.54	0.24	40	27	36	34
Slovakia	50	9,145	2,641	28.9 (26.2–31.6)	30.2	42.6	46	0.50	0	50	32	29	4
Slovenia	20	5,720	1,787	31.2 (28.8–33.7)	37.4	45.3	20	0.07	0	20	3	20	12
Spain	96	19,546	9,054	46.3 (44.8–47.9)	39.3	66.4	80	0.46	0.12	72	29	78	30
UK – England	32	20,148	7,533	37.4 (35.3–39.5)	35.2	64.2	32	0.58	0.45	32	32	32	32
UK – Northern Ireland	16	3,813	1,385	36.3 (32.3–40.3)	36.6	68.8	16	0.53	0.55	16	14	16	16
UK – Scotland	45	11,623	4,093	35.2 (33.3–37.1)	35.1	69.2	42	0.58	0.29	45	28	45	39
UK – Wales	21	6,400	2,186	34.2 (32.0–36.4)	34.5	56.9	21	0.75	0.32	19	17	21	17
EU/EEA	**1 209**	**310,755**	**102,093**	**30.5 (29.2–31.9)[c]**	**NA**	**46.0**	**1,075**	**0.37**	**0.08**	**1,075**	**564**	**898**	**541**
Serbia	66	14,982	6,185	41.3 (38.9–43.7)	36.9	53.1	61	0.32	0	66	24	8	7

CI: confidence interval; DDD: defined daily dose; EU/EEA: European Union/European Economic Area; FTE: full-time equivalent; N: not available; NA: not applicable; UK: United Kingdom.

[a]For the UK, data for England, Northern Ireland, Scotland and Wales are presented separately.

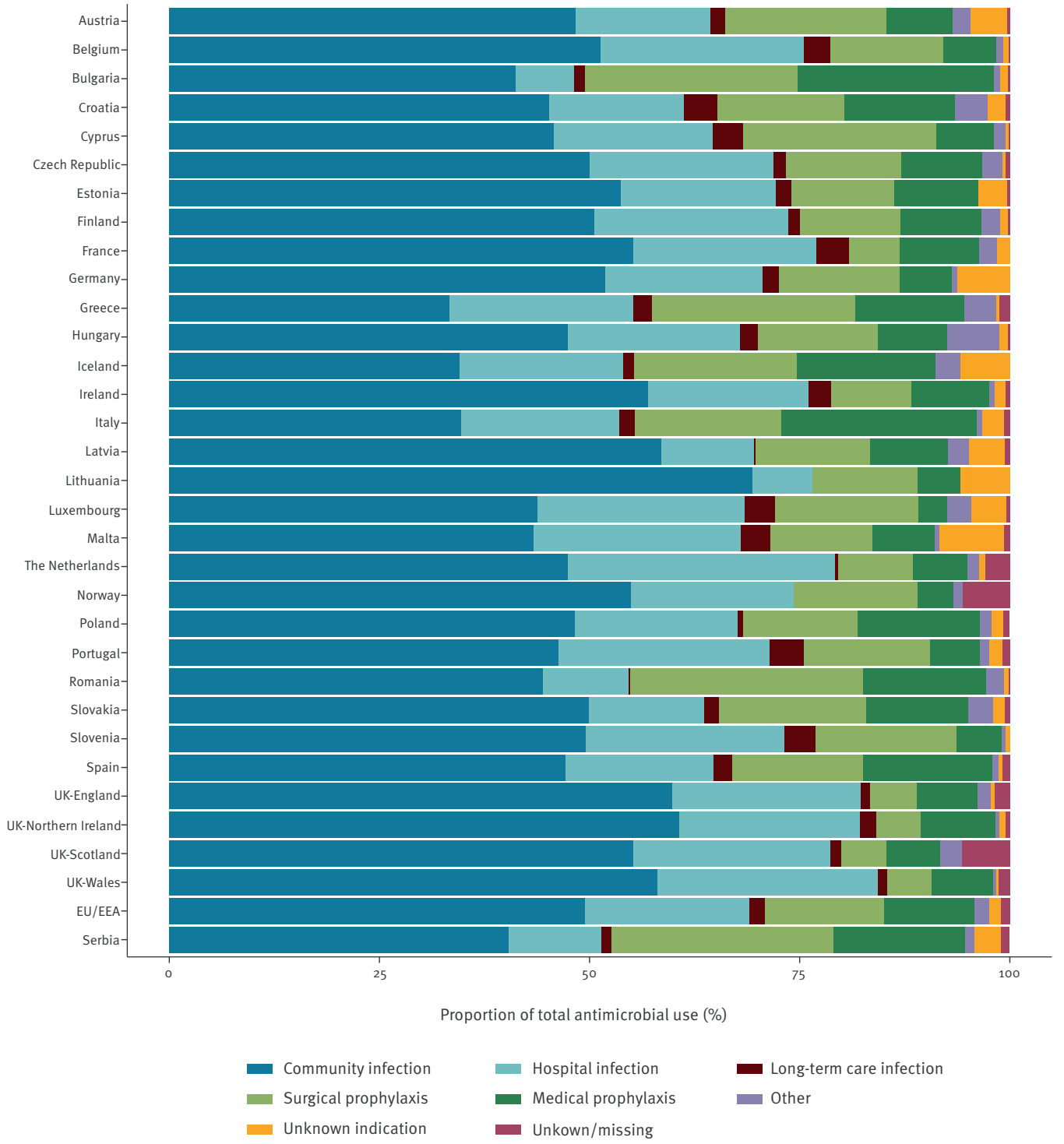
[b]Review of the appropriateness of prescribed antimicrobials within 72 hours (three calendar days) from the initial order, in at least one of the hospital wards.

[c]Observed prevalence is weighted.

The three EU/EEA countries that did not participate were Denmark, Lichtenstein and Sweden.

Figure 1

Indications for antimicrobial use in acute care hospitals, 28 European Union/European Economic Area countries[a] and Serbia, 2016–2017



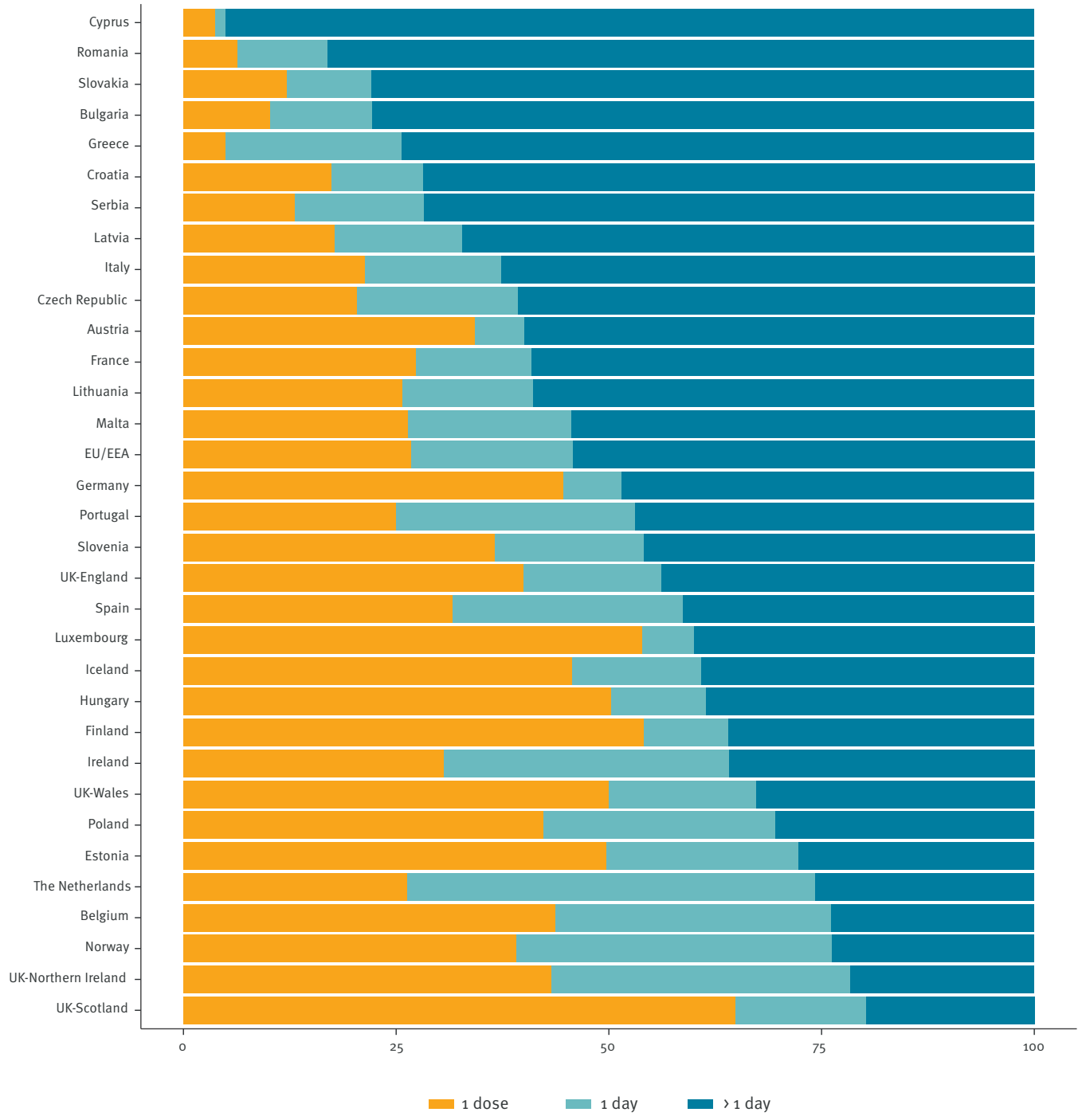
UK: United Kingdom.

[a]For the UK, data for England, Northern Ireland, Scotland and Wales are presented separately.

The three EU/EEA countries that did not participate were Denmark, Lichtenstein and Sweden.

Figure 2

Surgical prophylaxis in acute care hospitals, by dose and duration, 28 European Union/European Economic Area countries[a] and Serbia, 2016–2017



UK: United Kingdom.

[a]For the UK, data for England, Northern Ireland, Scotland and Wales are presented separately.

The three EU/EEA counties that did not participate were Denmark, Lichtenstein and Sweden.

Consumption Network (ESAC-Net) monitors the use of antimicrobials in the EU/EEA, but does not provide uniform information on antimicrobial use in hospitals and does not include clinical data to assess the appropriateness of antimicrobial prescriptions [10].

Point prevalence surveys (PPSs) are a feasible method to assess antimicrobial use in hospitals, and their value in identifying targets for interventions has been demonstrated [2,11]. The European Centre for Disease Prevention and Control (ECDC) PPS of HAIs and antimicrobial use in European acute care hospitals applies a standardised methodology for the estimation of the prevalence of both HAIs and antimicrobial use across the EU/EEA. The first ECDC PPS in 2011–12 indicated that 32.7% of patients in acute care hospitals received one or more antimicrobial agents on the day of the survey, which translated to more than 450,000 patients receiving at least one antimicrobial agent on any given day in European acute care hospitals [1].

In this study, based on data from the second PPS in 2016–17, we aimed at estimating the prevalence of antimicrobial use and describing the indications and the prescribed antimicrobial agents. Further, we aimed to raise awareness, identify targets for improvement and provide a standardised tool for evaluating the effect of local, regional and national policies on strengthening prudent use of antimicrobials in European acute care hospitals.

Methods

Survey design

The PPS was performed in 28 EU/EEA countries and one EU candidate country, Serbia. The countries were recommended to select the participating acute care hospitals by systematic random sampling. Data were collected by trained staff on 1 day per ward during four possible periods in 2016–17. The periods were selected to be out of the winter period (December–February) when antimicrobial use is the highest and out of the summer holiday season (July–August) when staffing at hospitals is usually low.

All participating countries applied a standardised protocol updated from a version used in an earlier PPS conducted in 2011–12 [12]; the main update was the addition of a larger number of structure and process indicators for the prevention of HAIs and for antimicrobial stewardship. All patients admitted to the ward before or at 0800 on the day of the PPS and were still present at the time of the PPS were included. It was also possible to provide aggregated denominator data at ward level ('light' protocol).

Data collection

Data collected included; hospital type and size, ward specialty, patient demographic data and risk factors and whether the patient was receiving one or more antimicrobial agent at the time of the PPS.

For patients receiving one or more antimicrobials additional data were collected for each antimicrobial prescribed including; the agent, the route of administration, the dosage and indication based on prescriber judgement (treatment of community, hospital or long-term care acquired infection, surgical or medical prophylaxis), diagnosis by anatomical site in case of treatment (e.g. pneumonia, urinary tract infection etc.), documentation of the reason for antimicrobial prescription in the medical records, and whether the current antimicrobial regimen was the same as the one that had been initiated. In case of change, the reason for change had to be indicated (escalation, de-escalation, switch from intravenous to oral, adverse effects, other or unknown).

Prevalence of antimicrobial use and the number of Defined Daily Doses

The 2018 version of the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) index of the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology was used for calculating the prevalence of antimicrobial use and the number of DDDs per 100 patients on the day of PPS [13]. Antimicrobial agents for systemic use within ATC groups A07AA (intestinal antiinfectives), D01BA (dermatological antifungals for systemic use), J01 (antibacterials for systemic use), J02 (antimycotics for systemic use), J04 (antimycobacterials) as second-line treatment of e.g. meticillin-resistant *Staphylococcus aureus* (MRSA) infections (rifampicin) or for treatment of mycobacteria other than tuberculosis (MOTT) and P01AB (nitroimidazole-derived antiprotozoals) were included. Antiviral agents and antimicrobials for the treatment of mycobacteria were not included. For the calculation of the number of DDD per 100 patients, children and adolescents (< 18 years of age) and neonates were excluded, as DDDs are defined for adults only.

Structure and process indicators

Data on the structure and process indicators in relation to antimicrobial stewardship were collected at hospital level including; number of full-time equivalent antimicrobial stewardship consultants, existence of a formal hospital procedure for post-prescription review of the appropriateness of an antimicrobial within 72 hours (3 calendar days) from the initial order and participation in a national or regional hospital antimicrobial consumption surveillance network.

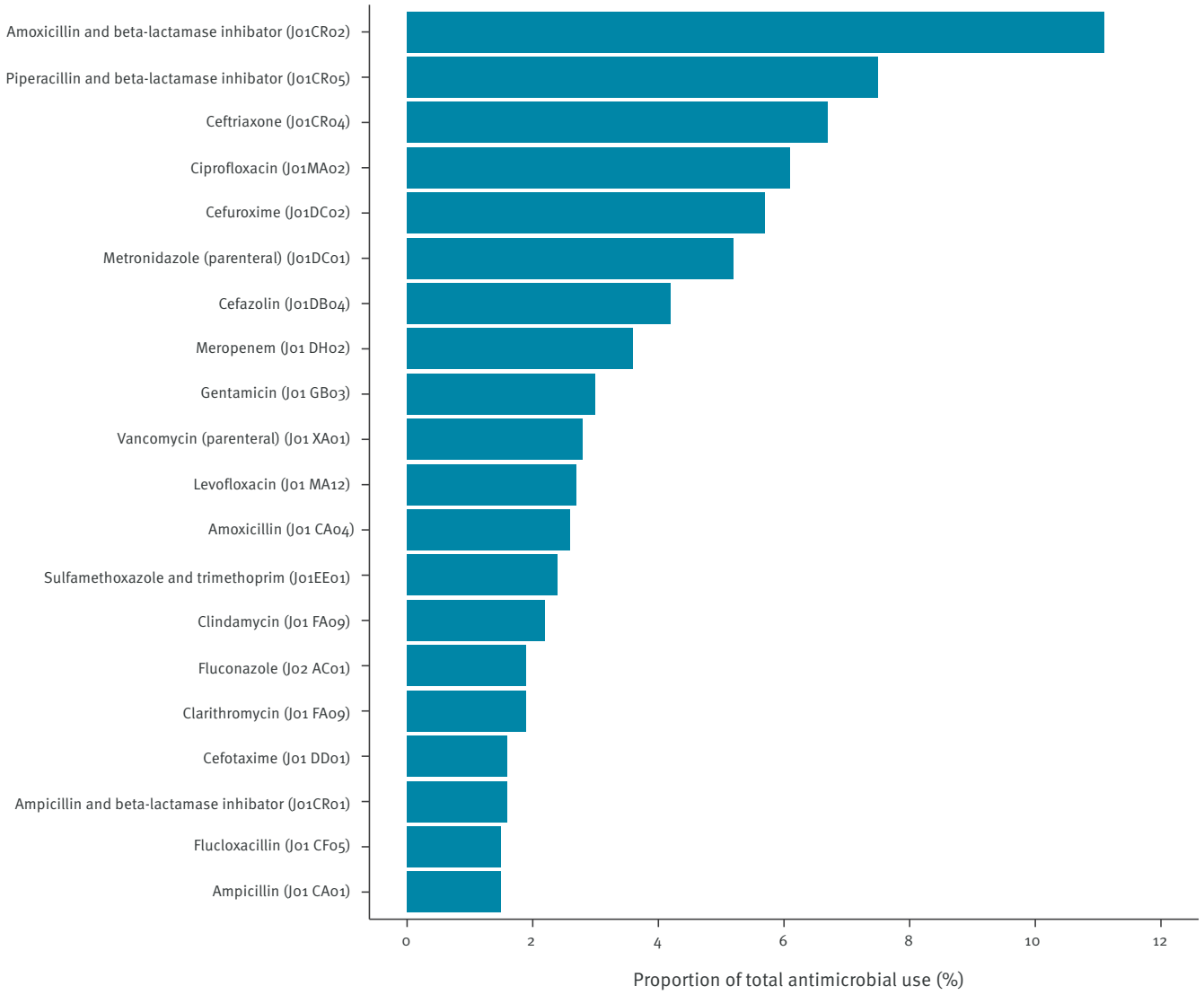
Data from the United Kingdom (UK) were reported separately for the four administrations: UK-England, UK-Northern Ireland, UK-Scotland and UK-Wales.

Descriptive analysis

All analyses were performed with R, version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria). Country representativeness of the sample was considered 'optimal' if the recommended systematic random sampling of hospitals was used, 'good' if a sufficient number of representative hospitals was selected

Figure 3

Antimicrobial agents (ATC code) accounting for 75% of antimicrobial use (Drug Utilisation 75%) in acute care hospitals, European Union/European Economic Area countries, 2016–2017



ATC: Anatomical Therapeutic Chemical.

The three EU/EEA counties that did not participate were Denmark, Lichtenstein and Sweden.

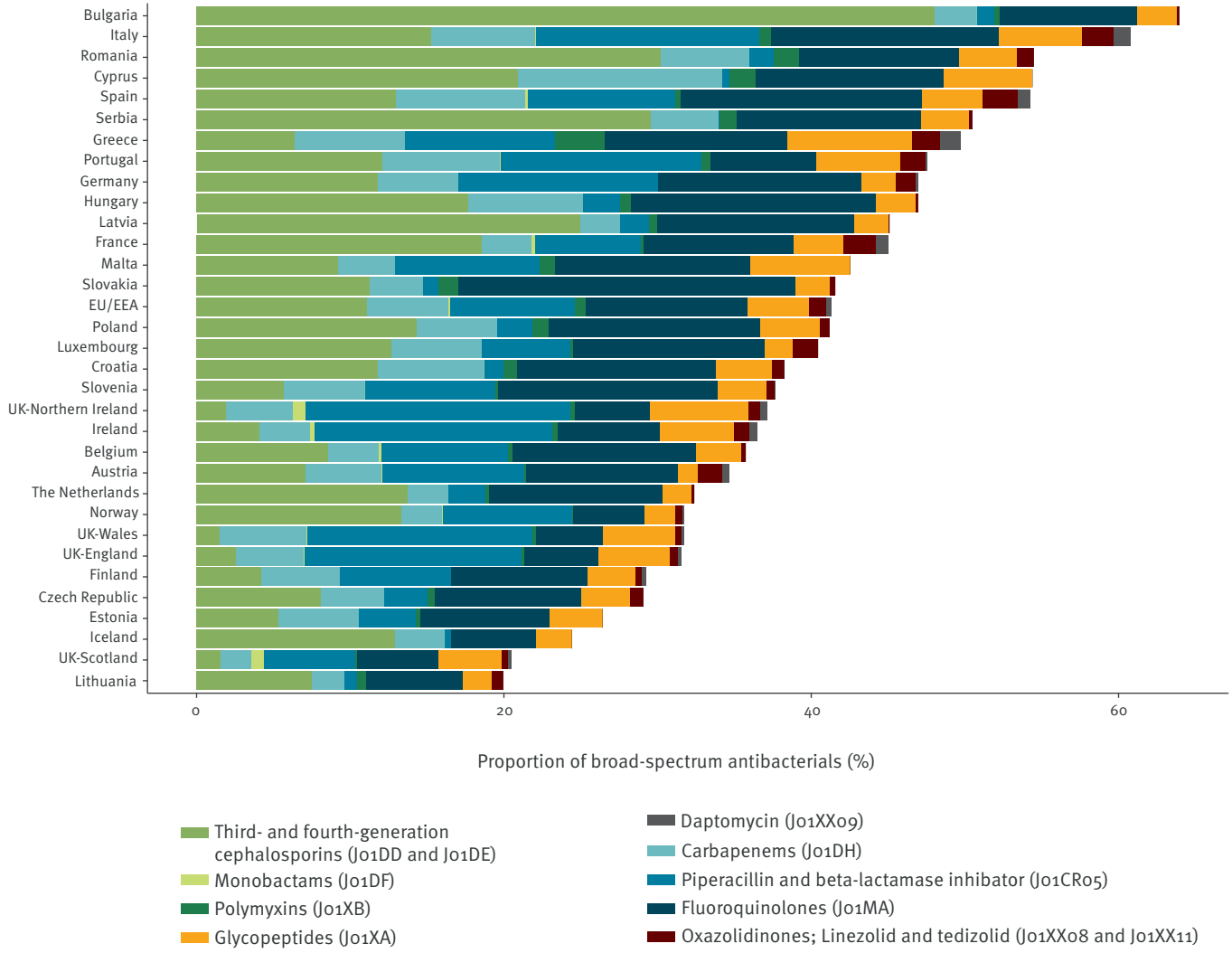
applying a different methodology or 'poor' if there was no systematic selection of a representative sample hospitals. For countries contributing to the survey with more than 20,000 patients, a randomised sub-sample was used in the final analysis to avoid over-representation of these countries when making analyses for the EU/EEA overall.

The prevalence of antimicrobial use was reported as the percentage of patients receiving at least one antimicrobial agent on the day of the survey. Antimicrobial groups and agents were classified according to the ATC/DDD index at the level of the chemical group (4^{th} ATC level) and the chemical substance (5^{th} ATC level). The relative frequencies of antimicrobial groups (4^{th} ATC level) were calculated. In addition, the relative frequencies of individual antimicrobial agents (5^{th} ATC level) that represented the Drug Utilisation 75% (DU75%), i.e. describing the agents that made 75% of total antimicrobial use in the participating hospitals, were also reported [14].

The proportion of the broad-spectrum antibacterials, among all antibacterials for systemic use (ATC J01), was also calculated – as proposed in the ECDC, European Food Safety Authority (EFSA) and European Medicines

Figure 4

Proportion of broad-spectrum antibacterials[a] among all antibacterials for systemic use (J01), 28 European Union/European Economic Area countries[b] and Serbia, 2016–2017



UK: United Kingdom.

[a]As defined in the European Centre for Disease Prevention and Control, European Food Safety Authority and European Medicines Agency Joint Scientific Opinion: piperacillin and beta-lactamase inhibitor (ATC J01CR05), third- and fourth-generation cephalosporins (J01DD and J01DE), monobactams (J01DF), carbapenems (J01DH), fluoroquinolones (J01MA), glycopeptides (J01XA), polymyxins (J01XB), daptomycin (J01XX09) and oxazolidinones: linezolid (J01XX08) and tedizolid (J01XX11) [15].

[b]For the UK, data for England, Northern Ireland, Scotland and Wales are presented separately.

The three EU/EEA counties that did not participate were Denmark, Lichtenstein and Sweden.

Agency (EMA) Joint Scientific Opinion on a list of outcome indicators for surveillance of AMR and antimicrobial consumption in humans and food producing animals [15]. The following antimicrobial groups and agents were included under broad-spectrum antimicrobials: piperacillin and beta-lactamase inhibitor (ATC J01CR05), third- and fourth-generation cephalosporins (J01DD and J01DE), monobactams (J01DF), carbapenems (J01DH), fluoroquinolones (J01MA), glycopeptides (J01XA), polymyxins (J01XB), daptomycin (J01XX09) and oxazolidinones: linezolid (J01XX08) and tedizolid (J01XX11) [15].

Statistical analysis

Adjustment for design effect due to clustering of antimicrobial use in the participating hospitals for estimation of the confidence intervals was performed with the 'survey' package (v. 3.33–2) for analysis of complex survey samples in R.

For the calculation of the EU/EEA prevalence of antimicrobial use, the participating countries' prevalence was weighted using the number of occupied beds per day as estimated by the latest available Eurostat data [16].

For countries applying the standard protocol, a multiple logistic regression model was built to predict the country prevalence of patients receiving one or more antimicrobial agents on the day of survey based on case-mix. The variables included in the model were age, sex, length of hospital stay (i.e. number of days up to the day of survey), McCabe score, intubation, presence of urinary catheter, surgery since admission, patient/consultant specialty, hospital type and hospital size [1].
For countries applying the 'light' protocol, and thus only submitting aggregated denominator data, the model included only patient/consultant specialty, hospital type and hospital size.

Ethics statement

Ethical approval was at the discretion of each national public health and government body. All data shared with ECDC on patient and institutional level were anonymous.

Results

In total, 1,753 hospitals from 29 countries participated in the PPS, of which two countries, Germany and Norway, provided aggregated denominator data on a ward level. The representativeness of the sample was optimal in 17 countries, good in 10 countries and poor in two countries (Bulgaria and the Netherlands). After adjustment for over-representation of countries contributing to the PPS with more than 20,000 patients, 325,737 patients from 1,275 hospitals remained in the dataset used for this analysis.

Pooled results were only reported for the EU/EEA corresponding to 310,755 patients from 1,209 hospitals. Of these, 357 (29.5%) were primary care hospitals, 414 (34.2%) were secondary care hospitals, 245 (20.3%) were tertiary care hospitals and 165 (13.6%) were specialised hospitals. The hospital type was unknown for 28 (2.3%) hospitals.

Prevalence of antimicrobial use

Among all patients, 102,093 (32.9%) received at least one antimicrobial agent. Among these, 72,094 (70.6%) received one antimicrobial agent, 24,091 (23.6%) received two, 4,631 (4.5%) received three, and 1,277 (1.3%) received four or more antimicrobial agents (maximum eight). In total, 139,609 prescribed antimicrobial agents were recorded. The overall weighted prevalence of antimicrobial use in EU/EEA countries was 30.5% (range 15.9–55.6%) (Table 1). Antibacterials* for systemic use (J01) accounted for 128,881 (92.3%) prescriptions, antimycotics for systemic use (J02) for 4,425 (3.2%), antimycobacterials (J04) as second-line treatment of e.g. MRSA infections (rifampicin) or for treatment of mycobacteria other than tuberculosis (MOTT) for 2,315 (1.7%), nitroimidazole-derived antiprotozoals (P01AB) for 2,113 (1.5%), intestinal antiinfectives (A07AA) for 1,857 (1.3%) and dermatological antifungals for systemic use (D01BA) for 18 (0.01%)*. Most antimicrobial agents (101,638 prescriptions, 72.8%) were administered parenterally, 37,530 (26.9%) orally, 266 (0.2%) by inhalation, and 175 (0.1%) by other routes. The reason for prescribing the antimicrobial was documented in the patient's medical records for 112,033 (80.2%) prescriptions.

Indications for antimicrobial use

Of 139,609 antimicrobial agents prescribed, 98,986 (70.9%) were for treatment of infection and of these 69.8% were prescribed for the treatment of a community-acquired infection (Figure 1). The most common site of infection was the respiratory tract (31.8%), followed by systemic infections (14.7%), the urinary tract (13.9%) and the gastrointestinal tract (13.6%). Other body sites accounted for 26.0% of the site of infection for antimicrobial treatment.

The proportion of antimicrobial agents prescribed for prophylaxis was 24.9%. More than half (10,741/19,798, 54.2%) of surgical prophylaxis courses were prescribed for more than 1 day (country range 19.8–95.0%) (Figure 2).

Most commonly used antimicrobial agents

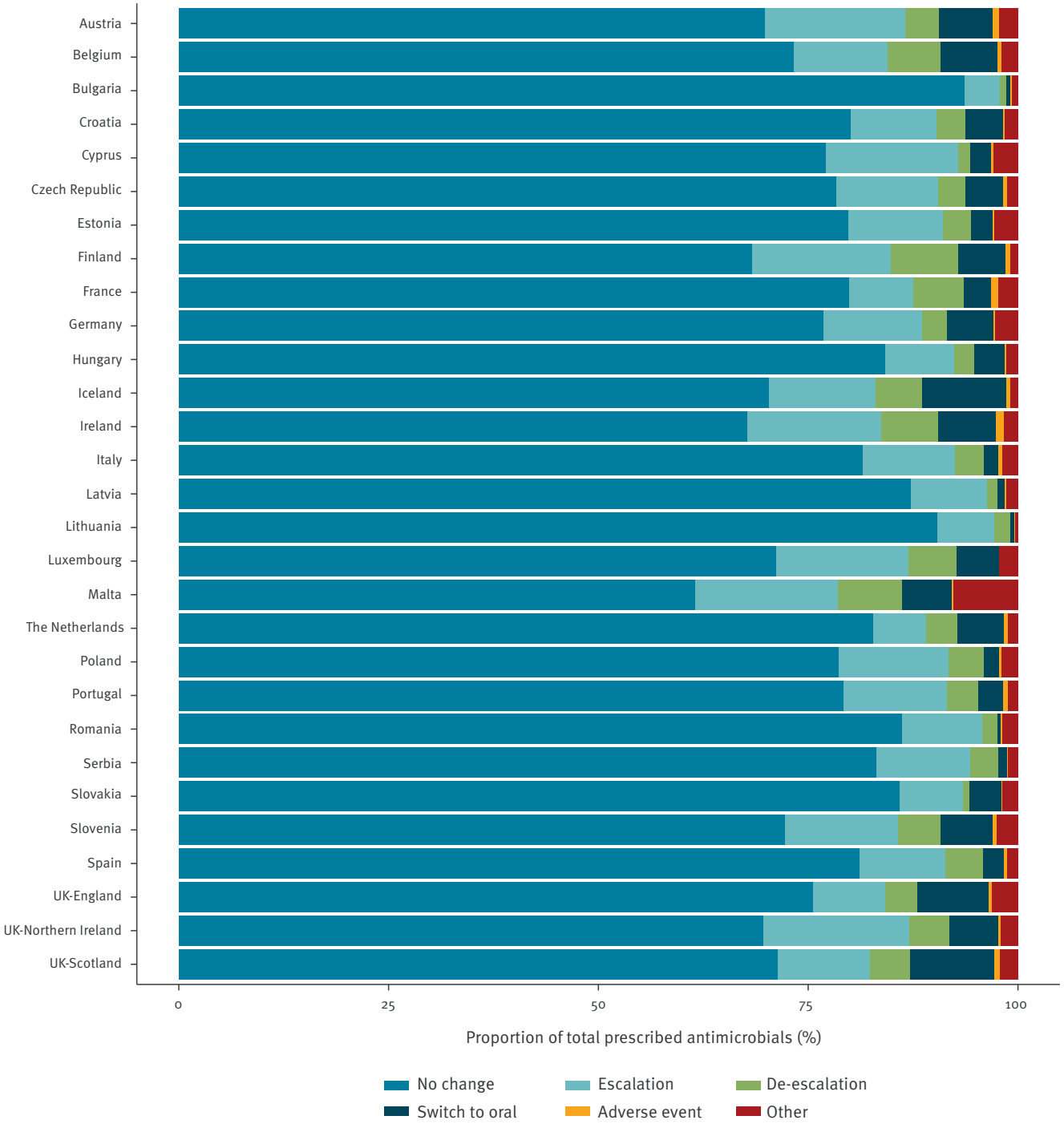
The antimicrobial agents that accounted for 75% of total antimicrobial use (DU75%) are presented in Figure 3. Antimicrobial prescription varied by indication. Of 27,324 antimicrobial prescriptions used for the treatment of HAIs, combination of penicillins with beta-lactamase inhibitors (J01CR) were the antimicrobial agents most commonly used (19.8%) followed by carbapenems (J01DH) and fluoroquinolones (J01MA) with 9.9% and 9.4%, respectively.

Of 69,067 antimicrobial prescriptions for the treatment of community-acquired infections, the three antimicrobial agents most commonly prescribed were combinations of penicillins and beta-lactamase inhibitors (J01CR: mainly amoxicillin and beta-lactamase inhibitor, J01CR02, and piperacillin and beta-lactamase inhibitor, J01CR05) followed by third-generation cephalosporins (J01DD) and fluoroquinolones (J01MA) with 23.2%, 11.7% and 11.1%, respectively.

Of 19,798 antimicrobial prescriptions for surgical prophylaxis, the three most common antimicrobial agents were first-generation cephalosporins (J01DB), second-generation cephalosporins (J01DC) and combinations of penicillins with beta-lactamase inhibitors (J01CR), with 26.6%, 17.9% and 15.1%, respectively. The proportion of broad-spectrum antibacterials among all antibacterials for systemic use (J01) is shown in Figure 4.

Figure 5

Change of antimicrobial during the infection episode and reported reason for change, 26 European Union/European Economic Area countries[a] and Serbia, 2016–2017



UK: United Kingdom.

[a]For the UK, data for England, Northern Ireland and Scotland are presented separately.

Greece, Norway and UK-Wales did not collect information on change of antimicrobials.

The three EU/EEA counties that did not participate were Denmark, Lichtenstein and Sweden.

Change of antimicrobial agent

In total, information about change of the antimicrobial during the infection episode was reported for 76.8% of antimicrobial prescriptions. For antimicrobial prescriptions where the information was reported, most (79.0%, country range: 61.5–93.6%) had not been changed since the initiation of the treatment (Figure 5). Escalation, de-escalation and switch from intravenous to oral use were reported for 10.9%, 3.9%, and 4.0% antimicrobial prescriptions, respectively. The change was due to adverse effects for 0.4% and to other reasons for 1.8% prescriptions.

Antimicrobial stewardship structure and process indicators

The median full-time equivalents for antimicrobial stewardship consultants per 250 beds was 0.08 (country range: 0–0.60), with 76.3% of the participating hospitals reporting antimicrobial use guidelines and 54.3% reporting some dedicated time for antimicrobial stewardship. Among the hospitals that submitted information on structure and process indicators for antimicrobial stewardship, the proportion of hospitals in the EU/EEA participating countries that had implemented a formal policy for post-prescription review in at least one ward was 52.5% while the proportion of hospitals participating in a national or regional hospital antimicrobial consumption surveillance network was 60.2% (Table 1).

Discussion

One in three patients hospitalised in acute care hospitals in the EU/EEA received one or more antimicrobials on the day of the PPS. The majority of the antimicrobials were prescribed for the treatment of a community-acquired infection. However, almost one in five antimicrobial prescriptions was for the treatment of a HAI. Prevention and control of HAIs reduces the need for antimicrobials and is an essential component of strategies to reduce unnecessary antimicrobial use. Antimicrobial use was similar to or lower than what was observed in other studies, such as the international PPS (range: 27.4–50.0%) [17] or the United States (US) 2011 PPS (49.9%) [18].

About one in seven antimicrobial prescriptions was for surgical prophylaxis, which represented the third most common indication. Surgical prophylaxis is recommended for the prevention of surgical site infections [19,20]. For the majority of surgical procedures, one preoperative dose is sufficient. In this PPS, however, more than half of the antimicrobial courses for surgical prophylaxis lasted more than 1 day. Although this proportion slightly decreased since the first survey in 2011–12 (54% vs 59%), it remains very high and outside the recommended duration in common with other studies where it ranged from 40.6% to 86.3% [17]. This is an important source of unnecessary use of antimicrobials and should be a priority target for future efforts on antimicrobial stewardship in many European acute care hospitals.

Overall, more than one in 10 antimicrobial prescriptions were for medical prophylaxis. This proportion is higher than the proportion of medical prophylaxis in the international PPS (7.4%) [17] and the proportion of medical prophylaxis in the US 2011 PPS (6.9%) [18]. Given the limited number of indications for medical prophylaxis and that it should only be used when indicated in relevant guidelines [9], a proportion of these prescriptions may represent antimicrobial use without clear indication and are therefore, unnecessary.

Pneumonia was by far the most common indication for antimicrobial treatment, accounting for one in four antimicrobials prescribed for therapeutic indications. Lower urinary tract infection was the second most frequent indication, accounting for almost one in 10 prescribed antimicrobials for therapeutic indications. These results are comparable with those of the 2011–12 survey (where 23.1% of prescriptions for therapeutic indications were for pneumonia and 11.1% for lower urinary tract infection) and in line with the US 2011 PPS on antimicrobial use [18], although the proportion of antimicrobials for treatment of a urinary tract infection was slightly lower in the international PPS than in our survey [17].

There was considerable variability in the prevalence of antimicrobial use among participating countries. Although part of this variability may be explained by differences in patient case-mix and the incidence of HAIs, it also reflects differences in antimicrobial prescription practices in acute care hospitals e.g. variation in the ratio between penicillins vs other beta-lactam antibiotics (including cephalosporins and carbapenems) and fluoroquinolones between participating countries (data not shown).

The most commonly prescribed antimicrobial agents were amoxicillin and beta-lactamase inhibitor, piperacillin and beta-lactamase inhibitor and ceftriaxone. Despite extensive global shortage in 2017 [21], piperacillin and beta-lactamase inhibitor was the second most commonly used antimicrobial whereas it ranked fifth in the 2011–12 survey. By contrast, ciprofloxacin, which was the second most commonly prescribed antimicrobial agent in the 2011–12 survey, ranked fourth in 2016–17. This decrease may reflect the antimicrobial stewardship efforts or focused attempts to reduce *Clostridium difficile* infections. Fluoroquinolone and glycopeptide use was lower in the EU/EEA in 2016–17 than reported in the US 2011 PPS where these antimicrobials were the first and second most commonly prescribed ones (accounting for 14.4% and 10.8% of prescriptions, respectively) [18].

Among the reasons for change of antimicrobial during the infection episode, the proportion of de-escalation and switch from intravenous to oral administration varied among participating countries. In several countries, de-escalation or switch to oral treatment was uncommon. It was not possible to assess the appropriateness

of low proportions of change, as no information was collected about the reasons for continuing or changing antimicrobial. However, both de-escalation and switch to oral treatment likely reflect the result of review of antimicrobial treatment when microbiological information is available, or when the condition of the patient improves, and are recommended measures to support prudent use of antimicrobials [9,22].

There was large variability among participating countries in the human resources available for antimicrobial stewardship as well as in the implemented antimicrobial stewardship strategies. For almost all participating countries, some hospitals had a consultant in charge of antimicrobial stewardship and while this is encouraging, considering that the majority of hospitals still have no or limited dedicated staff for antimicrobial stewardship (or access to such a consultant), promoting this must be a priority in the coming years.

In this PPS, the proportion of broad-spectrum antibacterials among all antibacterials for systemic use, as proposed by the ECDC, EFSA and EMA Joint Scientific Opinion, reflects their level of consumption in hospitals and the corresponding selection pressure [15]. These antibacterials can be found in the 'Watch' and 'Reserve' groups of antimicrobials, as defined in the WHO Model Lists of Essential Medicines [23]. In this PPS, the proportion of broad-spectrum antibacterials ranged from less than 20% to more than 50% depending on the country. This could in part be explained by the high prevalence of resistance among a number of reported microorganisms, e.g. MRSA, vancomycin-resistant enterococci or third-generation cephalosporin-resistant Enterobacteriaceae [24]. However, many of these antibacterials are also associated with both emergence and spread of healthcare-associated *Clostridium difficile* and multidrug-resistant microorganisms and in particular for third-generation cephalosporins, fluoroquinolones and carbapenems, with the emergence of multidrug-resistant Gram-negative bacteria [7], which are currently among the most important public health threats related to AMR. The wide variation and sometimes extensive use of broad-spectrum antibacterials indicates the need to review their indications in many countries and hospitals. Antimicrobial stewardship programmes must be designed to take into account both the risk of emergence of AMR and patient safety. Ensuring that broad-spectrum antibacterials are used appropriately is a key element of any strategy against AMR.

An important indicator of the quality of antimicrobial prescription is the documentation of the reason for the prescription in the patient notes. In our survey, almost one in five antimicrobial prescriptions did not include documentation of the reason for antimicrobial prescription. While this was lower than in the 2011–12 survey, it still indicates that ensuring that antimicrobial prescriptions can be reviewed effectively in all cases to assess their appropriateness remains an ongoing challenge. In the US 2011 PPS, the rationale for the antimicrobial prescription was missing only in 6.9% of prescriptions [18].

The strengths of this survey are its large size and the use of a standardised protocol across all participating hospitals in 28 EU/EEA countries and Serbia. With only two EU/EEA countries (Bulgaria and the Netherlands) having provided data on a non-representative sample of acute care hospitals and two additional EU/EEA countries (Denmark and Sweden) having declined participation, we believe that this PPS offers a representative picture of antimicrobial consumption in acute care hospitals in the EU/EEA, with meaningful benchmarks for participating countries and hospitals. The results were largely comparable to those of the 2011–12 PPS, which is both reassuring in terms of methodology but disappointing in terms of little change of antimicrobial prescription practice in European acute care hospitals in the past 5 years.

One limitation of this survey is its cross-sectional design, which evaluated antimicrobial use on 1 day only. However, this design has been shown to provide reliable results that can be used for identifying targets for intervention [2]. Moreover, the size and representativeness of the sample counterbalance this limitation. Another limitation is that we were not able to assess whether antimicrobial prescription was in line with existing international or national guidelines. However, observations such as prolonged duration of surgical prophylaxis as well as the high use of fluoroquinolones, third-generation cephalosporins and carbapenems, likely indicate inappropriate antimicrobial use that can be addressed by specific actions.

In conclusion, this second ECDC PPS of HAIs and antimicrobial use provided representative data on antimicrobial use in acute care hospitals across EU/EEA countries. These data allow for identifying targets for future antimicrobial stewardship interventions. Ultimately, these results will be helpful to promote prudent use of antimicrobials at national and European level and contribute to the efforts to ensure that European patients are receiving appropriate treatment while at the same time minimising the risk of adverse effects, and the emergence and spread of AMR.

*Author's correction:

In the Results, under the subtitle 'Prevalence of antimicrobial use,' a sentence mistakenly stated 'Antimicrobials for systemic use (J01)' instead of 'Antibacterials for systemic use (J01)'. In the same sentence, the percentage for 'dermatological antifungals for systemic use (D01BA) for 18 (1.3%)' mistakenly stated '(1.3%)' instead of '(0.01%)'. The mistakes were corrected on 21 November 2018, as requested by the authors.

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Acknowledgements

The authors would like to thank all the participating hospitals and in particular, the hospital staff that collected, validated and entered the data during the survey and the national teams that coordinated the survey in each participating country; the Belgian Antibiotic Policy Coordination Committee (BAPCOC); Martyn Nedyalkov (National Center of Infectious and Parasitic Diseases (NCIPD), Sofia, Bulgaria); Rumyana Hristova (National Center of Infectious and Parasitic Diseases (NCIPD), Sofia, Bulgaria); Violeta Voynova–Georgieva (Military Medical Academy (MMA), Sofia, Bulgaria); Alexander Hristov (National Center of Infectious and Parasitic Diseases (NCIPD), Sofia, Bulgaria); Nadezhda Vladimirova (National Center of Infectious and Parasitic Diseases (NCIPD), Sofia, Bulgaria); Vivika Adamson (Tartu University Hospital, Tartu, Estonia); Mait Altmets (North Estonia Medical Centre, Tallinn, Estonia); Mailis Hansen (West-Tallinn Central Hospital, Tallinn, Estonia); Prof Uga Dumpis (Pauls Stradins Clinical University Hospital, Riga, Latvia); Jaap ten Oever (Department of Internal Medicine and Radboud Center for Infectious Diseases, Radboud University Medical Center); Maria Goreti Silva (Direção-Geral da Saúde (DGS), Lisbon, Portugal); Carlos André Palos (Hospital Beatriz Ângelo (BHA), Loures, Portugal); Jana Námešná (Regional Public Health Authority in Banská Bystrica, Slovakia).

Conflict of interest

None declared.

Authors' contributions

Diamantis Plachouras performed the analysis and wrote the original draft; Carl Suetens managed and coordinated the survey planning and execution and performed analysis; Tommi Kärki contributed to the development of the study design and the coordination of the execution of the study; Sonja Hansen, Susan Hopkins, Outi Lyytikäinen, Maria Luisa Moro, Jacqui Reilly, Peter Zarb and Walter Zingg were members of the HAI-Net expert group that developed the methodology of the survey; Pete Kinross contributed to the coordination of the execution of the study; Dominique L. Monnet and Klaus Weist contributed to the analysis plan and the methodology of the survey; the PPS study group members contributed to the development of the study design, approved the design of the survey, contributed to the coordination of the execution of the study in their respective countries, and provided national interpretations on the analysis. All authors critically reviewed and edited the manuscript.

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Antimicrobial use in European long-term care facilities: results from the third point prevalence survey of healthcare-associated infections and antimicrobial use, 2016 to 2017

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Citation style for this article:
Ricchizzi Enrico, Latour Katrien, Kärki Tommi, Buttazzi Rossella, Jans Béatrice, Moro Maria Luisa, Nakitanda Olivia Aya, Plachouras Diamantis, Monnet Dominique L., Suetens Carl, Kinross Pete, the HALT Study Group. Antimicrobial use in European long-term care facilities: results from the third point prevalence survey of healthcare-associated infections and antimicrobial use, 2016 to 2017. Euro Surveill. 2018;23(46):pii=1800394. https://doi.org/10.2807/1560-7917.ES.2018.23.46.1800394

Article submitted on 17 Jul 2018 / accepted on 14 Oct 2018 / published on 15 Nov 2018

Antimicrobials are commonly prescribed and contribute to the development of antimicrobial resistance in long-term care facilities (LTCFs). In 2010, the European Centre for Disease Prevention and Control initiated point prevalence surveys (PPS) of healthcare-associated infections and antimicrobial use in European LTCFs, performed by external contractors as the Healthcare-Associated infections in Long-Term care facilities (HALT) projects. Here, we investigated prevalence and characteristics of antimicrobial use and antimicrobial stewardship indicators in European LTCFs in 2016–17. Twenty-four European Union/European Economic Area (EU/EEA) countries, the former Yugoslav Republic of Macedonia and Serbia participated in the third PPS in European LTCFs. Overall, 4.9% (95% confidence interval: 4.8–5.1) of LTCF residents in the EU/EEA participating countries received at least one antimicrobial. The most commonly reported Anatomical Therapeutic Chemical (ATC) groups were beta-lactam antibacterials/penicillins (J01C), other antibacterials (J01X) (e.g. glycopeptide antibacterials, polymyxins), quinolones (J01M), sulfonamides and trimethoprim (J01E), and other beta-lactams (J01D). Urinary tract infections and respiratory tract infections were the main indications for antimicrobial prescription. This PPS provides updated and detailed information on antimicrobial use in LTCFs across the EU/EEA that can be used to identify targets for future interventions, follow-up of these interventions and promote prudent use of antimicrobials in European LTCFs.

Introduction

Life expectancy is increasing steadily in the European Union/European Economic Area (EU/EEA). Population projections estimate that by 2050 the old-age dependency ratio, calculated as the number of individuals aged over 65 years per 100 people of working age, will reach 50% [1]. The ageing population is one reason for the transitions in healthcare delivery systems taking place in several EU/EEA countries. This includes reductions in hospital beds and in several countries more patient care being provided in long-term care settings [2]. Long-term care facilities (LTCFs) deliver a blend of health and social services to people who are limited in their ability to live independently, especially due to old age, and are in need of less intensive medical care than that usually provided in hospitals [3].

Despite the fact that less intensive medical care is provided in LTCFs than in hospitals, healthcare-associated infections (HAIs) are common in the vulnerable LTCF populations [4-9]. For this reason, antimicrobials are commonly prescribed in LTCFs, contributing to the development of antimicrobial resistance (AMR) and possibly leading to adverse events such as *Clostridium difficile* infection, and infections that are more difficult to treat [10,11]. As there is increasing evidence that LTCFs can serve as a reservoir for the transmission of resistant organisms to other healthcare settings, close monitoring of the situation is needed [12,13]. Furthermore, the lack of diagnostic capabilities may lead to suboptimal antimicrobial prescription in LTCFs [14,15].

Table 1

Prevalence of antimicrobial use, by country, 23 European Union/European Economic Area countries[a], the former Yugoslav Republic of Macedonia and Serbia, 2016–2017

Country	LTCFs	Eligible residents	Antimicrobial use			
			Residents with at least one antimicrobial	Observed prevalence	Mean prevalence of LTCFs	Median prevalence of LTCFs
	n	n	n	% (95% CI)	%	IQR (%)
Austria	12	2,065	67	3.2 (2.5 to 4.1)	2.9	2.4 (1.0 to 4.7)
Belgium	79	8,206	482	5.9 (5.4 to 6.4)	5.8	5.1 (2.9 to 8.1)
Croatia	8	1,607	32	2.0 (1.4 to 2.8)	3.2	3.6 (0.8 to 4.9)
Cyprus	11	312	29	9.3 (6.3 to 13.1)	10.1	7.7 (4.8 to 17.0)
Denmark	95	3,346	350	10.5 (9.4 to 11.5)	10.7	9.0 (6.3 to 15.0)
Finland	149	5,914	394	6.7 (6.0 to 7.3)	7.0	5.9 (2.3 to 10.5)
France	91	6,957	187	2.7 (2.3 to 3.1)	2.7	2.3 (0 to 4.3)
Germany	82	6,705	85	1.3 (1.0 to 1.6)	1.3	0.9 (0 to 1.9)
Greece	13	812	49	6.0 (4.5 to 7.9)	7.5	4.2 (3.0 to 11.6)
Hungary	75	7,670	71	0.9 (0.7 to 1.2)	0.9	0 (0 to 1.4)
Ireland	109	5,613	543	9.7 (8.9 to 10.5)	11.7	8.6 (5.4 to 14.7)
Italy	196	11,417	495	4.3 (4.0 to 4.7)	5.5	3.1 (0.8 to 6.6)
Lithuania	26	3,438	25	0.7 (0.5 to 1.1)	0.9	0 (0 to 1.0)
Luxembourg	16	1,616	42	2.6 (1.9 to 3.5)	2.5	1.5 (0.9 to 4.2)
Malta	11	2,485	66	2.7 (2.1 to 3.4)	1.6	1.4 (0.5 to 2.4)
The Netherlands	57	4,547	202	4.4 (3.9 to 5.1)	5.1	4.3 (1.6 to 6.7)
Norway	62	2,447	169	6.9 (5.9 to 8.0)	7.0	4.6 (2.1 to 10.3)
Poland	24	2,281	73	3.2 (2.5 to 4.0)	4.4	2.9 (0.9 to 6.5)
Portugal	132	3,633	220	6.1 (5.3 to 6.9)	6.8	4.3 (0 to 10.0)
Slovakia	59	5,091	113	2.2 (1.8 to 2.7)	2.9	1.2 (0 to 3.4)
Spain	46	6,808	717	10.5 (9.8 to 11.3)	11.7	10.8 (3.5 to 17.3)
Sweden	285	3,604	118	3.3 (2.7 to 3.9)	3.2	0 (0 to 5.6)
UK – Northern Ireland	70	2,614	270	10.3 (9.2 to 11.6)	10.4	9.8 (5.0 to 14.3)
UK – Scotland	52	2,147	138	6.4 (5.4 to 7.5)	6.2	5.1 (0 to 10.9)
UK – Wales	28	966	98	10.1 (8.3 to 12.2)	10.1	8.2 (5.5 to 11.4)
EU/EEA	**1,788**	**102,301**	**5,035**	**4.9 (4.8 to 5.1)**	**5.8**	**3.6 (0 to 8.5)**
former Yugoslav Republic of Macedonia	4	294	26	8.8 (5.9 to 12.7)	5.2	5.1 (2.5 to 7.9)
Serbia	6	1,168	57	4.9 (3.7 to 6.3)	6.0	4.0 (3.7 to 5.5)

CI: confidence interval; EU/EEA: European Union/European Economic Area; IQR: interquartile range; LTCFs: long-term care facilities; UK: United Kingdom.

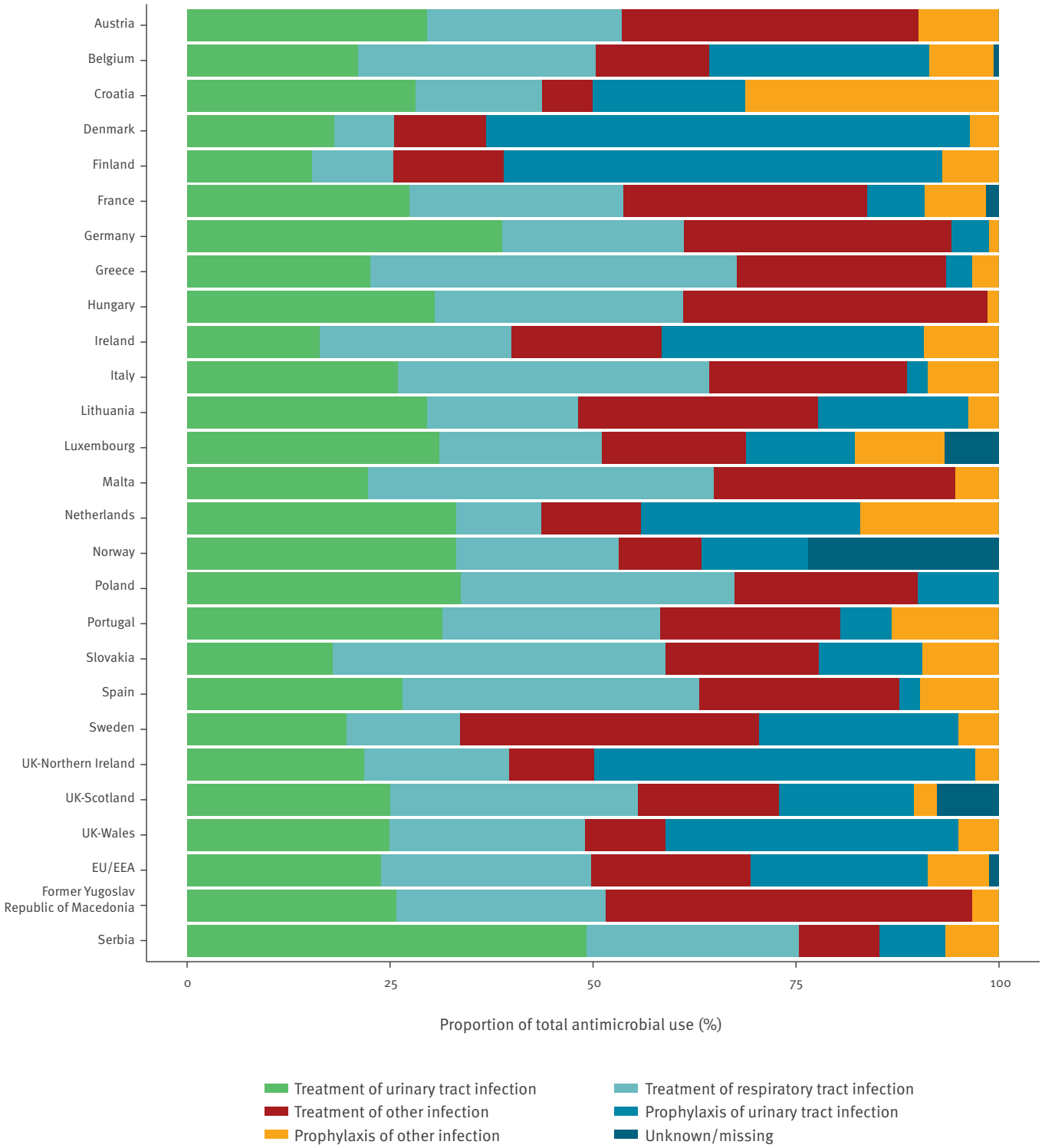
[a]For the United Kingdom, data for Northern Ireland, Scotland and Wales are presented separately. England did not participate in the survey. The Czech Republic did not provide resident-level data.

Data on antimicrobial use in LTCFs are necessary to understand the reasons, magnitude and determinants of antimicrobial prescribing and to inform public health policies on prudent use of antimicrobials. In June 2017, the European Commission published guidelines for the prudent use of antimicrobials in human medicine, recommending to establish antimicrobial stewardship programmes in all healthcare facilities, including LTCFs [16]. Although several European countries already measure antimicrobial consumption, methodologies have not been consistent precluding meaningful comparisons, furthermore they have often concentrated in the acute care settings, with little attention given to LTCFs.

For this reason, the European Centre for Disease Prevention and Control (ECDC) initiated surveillance of HAIs and antimicrobial use in European LTCFs with point prevalence surveys (PPSs) under the Healthcare-Associated infections in Long-Term Care facilities (HALT) projects in 2010, 2013 and, most recently, in 2016–17. In the present study, we investigated the prevalence and characteristics of antimicrobial use and antimicrobial stewardship indicators in European LTCFs reported in the third European PPS of HAIs and antimicrobial use in LTCFs (HALT-3) in 2016–17.

Figure 1

Indications (treatment or prophylaxis, for the most commonly sites of infection) for antimicrobial use in long-term care facilities, by country, 22 European Union/European Economic Area countries[a], the former Yugoslav Republic of Macedonia and Serbia, 2016–2017

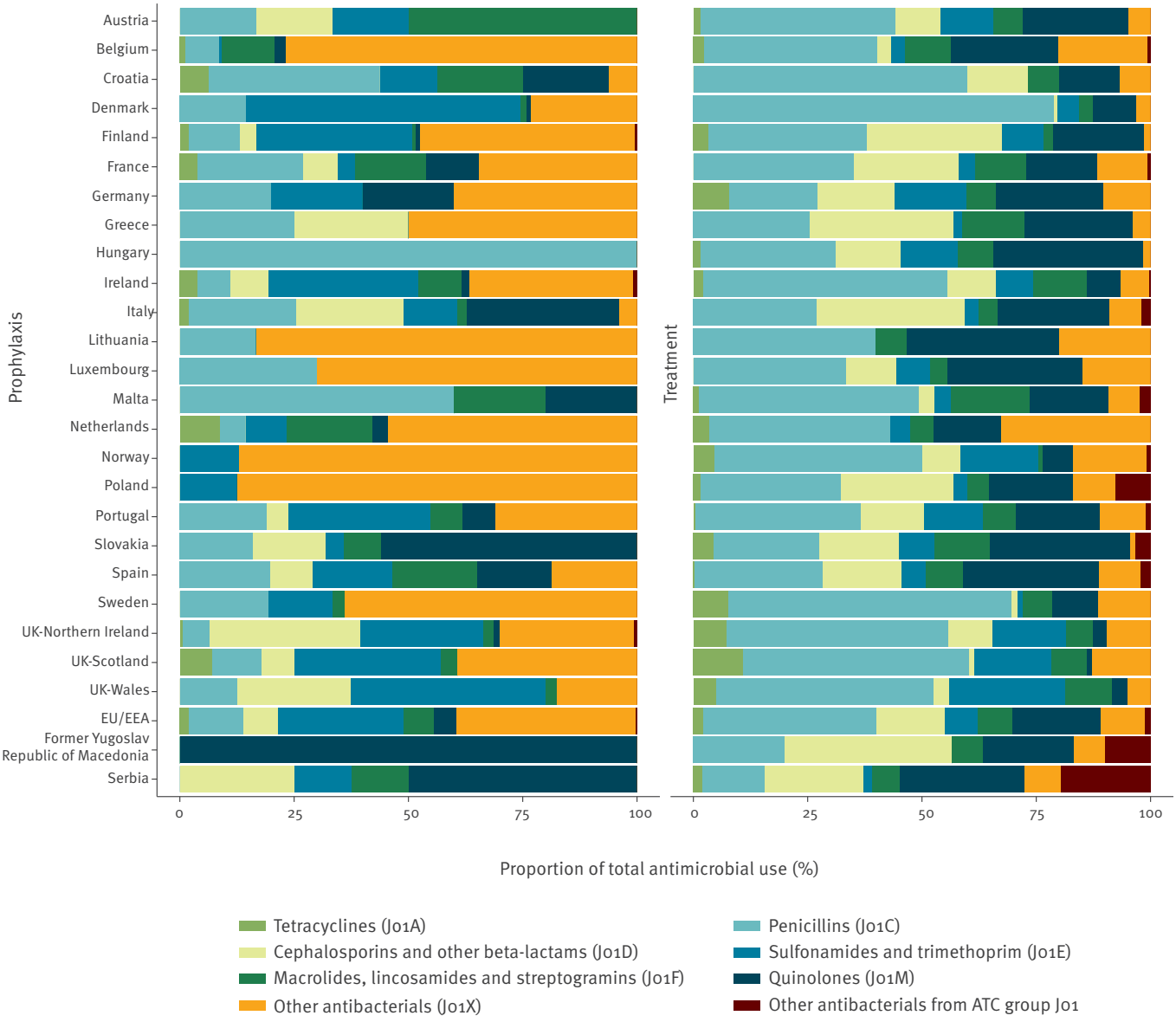


EU/EEA: European Union/European Economic Area.

[a]For the United Kingdom, data for Northern Ireland, Scotland and Wales are presented separately. England did not participate in the survey. The Czech Republic did not provide resident-level data. Cyprus did not provide detailed information on antimicrobial prescribing.

Figure 2

Distribution of antibacterials for systemic use (ATC group J01) into groups, by main indication (prophylaxis or treatment) and by country, 22 European Union/European Economic Area countries[a], the former Yugoslav Republic of Macedonia and Serbia, 2016–2017



EU/EEA: European Union/European Economic Area.

[a]For the United Kingdom, data for Northern Ireland, Scotland and Wales were reported separately. England did not participate in the survey. The Czech Republic did not provide resident-level data. Cyprus did not provide detailed information on antimicrobial prescribing.

Methods

Survey design

The survey was performed in 24 EU/EEA countries and two EU candidate countries, the former Yugoslav Republic of Macedonia and Serbia. The countries were asked to recruit LTCFs in their country for participation in the survey. According to the protocol [17], the selected LTCFs had to provide a broad range of services and assistance to people with limited abilities to function independently on a daily basis (i.e. to autonomously perform the basic activities of daily living over an extended period of time). In addition, these LTCFs could also provide basic medical services (wound dressing, pain management, medication, health monitoring, prevention, rehabilitation or palliative care), but the LTCF residents had to be medically stable, without the need for constant specialised medical care or invasive medical procedures. Resident stay in the selected

Table 2

Multivariable linear regression analysis of long-term care facility and resident characteristics in relation to the prevalence of antimicrobial use, 19 European Union/European Economic Area countries[a], the former Yugoslav Republic of Macedonia and Serbia, 2016–2017

Characteristics	Coefficient (95% CI)	p-value
Type of LTCF		
Residential home	Ref	
General nursing home	0.38 (-0.54 to 1.31)	0.418
Mixed	1.41 (0.40 to 2.42)	**0.006**
Size of LTCF		
≥ 105 beds	Ref	
65–104 beds	0.62 (-0.47 to 1.71)	0.266
37–64 beds	2.25 (1.22 to 3.29)	**< 0.001**
< 37 beds	3.27 (2.25 to 4.29)	**< 0.001**
Characteristics of LTCF residents (%)		
Aged over 85 years	0.05 (0.03 to 0.08)	**< 0.001**
Male	0.08 (0.05 to 0.11)	**< 0.001**
Using a wheelchair or bedridden	-0.04 (-0.06 to -0.02)	**< 0.001**
Disoriented in time and/or space	0.00 (-0.01 to 0.02)	0.648
Urinary and/or faecal incontinence	0.02 (-0.00 to 0.04)	0.052
Pressure sore	-0.03 (-0.09 to 0.02)	0.229
Other wound	0.10 (0.06 to 0.14)	**< 0.001**
Surgery in the previous 30 days	0.20 (0.10 to 0.30)	**< 0.001**
Urinary catheter	0.04 (0.00 to 0.08)	**0.043**
Vascular catheter	0.26 (0.18 to 0.33)	**< 0.001**

CI: confidence interval; EU/EEA: European Union/European Economic Area; LTCF: long-term care facility.

[a]For the United Kingdom, data for Northern Ireland, Scotland and Wales were reported separately. England did not participate in the survey. The Czech Republic did not provide resident-level data. France, Portugal, Norway and Sweden were excluded from the multivariable analysis (see Methods).

Significant p-values are shown in bold.

LTCFs could vary from temporary to permanent (until end of life).

To improve country representativeness, a recommended minimum number of LTCFs per country was calculated and provided to the national coordinators. For each country, the recommended sample size was calculated anticipating a national crude HAI prevalence of 4%, with a 95% confidence interval (CI) of 3–5% (1% precision). Although representative sampling was strongly recommended, purposive sampling, including convenience sampling or voluntary participation after the invitation of all LTCFs, was also accepted. Different types of LTCF could be recruited. While also specialised LTCF types (such as psychiatric facilities, rehabilitation centres and palliative care centres) were invited to participate, only data from general nursing homes (providing principally care to seniors with severe illnesses or injuries), residential homes (facilities usually providing personal care, housekeeping and three meals a day) and mixed LTCFs (providing mixed services for elderly or other resident populations) were considered for analysis. For countries contributing to the survey with more residents than in the calculated recommended sample size, a randomised sub-sample was used in the final analysis [17].

Data collection

Participating countries were asked to organise the survey during one of four proposed periods: April–June or September–November in 2016 or 2017. Ideally, data had to be collected on a single day for each LTCF. In large LTCFs, data collection could take place over 2 or more consecutive days, but all residents within one ward or unit had to be surveyed on the same day.

Data collection was conducted either by an external data collector (i.e. the national coordinator or a person trained by the national coordinator) or by a local data collector (i.e. an LTCF staff member, e.g. designated physician, infection control practitioner or nurse). To ensure standardisation of data collection, a 'train-the-trainers' workshop for the national coordinators was held in December 2015. It was recommended that national coordinators organise at least one 1-day information and training session for the LTCFs before the national survey [17].

A resident questionnaire was used to collect data for each resident receiving a systemic antimicrobial on the day of the survey. Data included resident characteristics (age, gender, length of stay in the LTCF (less or greater than 1 year)), risk factors (urinary catheter, vascular catheter, pressure sores, other wounds), care load indicators (faecal and/or urinary incontinence, disorientation in time and/or space, impaired mobility) and antimicrobial use (name of antimicrobial agent(s), indication and reasons for antimicrobial use, place of prescription, administration route, end or review date of documented prophylaxis or treatment) [17].

The 2018 version of the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) Index of the World Health Organization Collaborating Centre for Drug Statistics Methodology was used to classify the antimicrobials into different groups [18]. Antimicrobial agents for systemic use within ATC groups A07AA (intestinal antiinfectives), D01BA (dermatological antifungals for systemic use), J01 (antibacterials for systemic use), J02 (antimycotics for systemic use), J04 (antimycobacterials), when used for treatment of mycobacteria (including tuberculosis) or as reserve for multidrug-resistant bacteria and P01AB (nitroimidazole-derived antiprotozoals), were included. Antiviral agents were not included.

Two main indications for antimicrobial use were recorded, i.e. prophylaxis and treatment. The indication

Table 3

Structure and process indicators of antimicrobial stewardship reported in participating LTCFs, by country, 23 European Union/European Economic Area countries[a], the former Yugoslav Republic of Macedonia and Serbia, 2016–2017

Country[a]	Responding LTCFs	Written guidelines for appropriate antimicrobial use in the LTCF		Annual regular training on appropriate antimicrobial prescribing		Responding LTCFs	A 'restrictive list' of antimicrobials to be prescribed		Antimicrobial groups reported as being restricted ('restrictive list')(ATC code)							
									J01DD	J01MA	J01DH	J01XA	J01XA01	IAA	BSA	D06AX09, R01AX06
	n	n	%	n	%	n	n	%	n	n	n	n	n	n	n	n
Austria	12	9	75.0	2	16.7	12	2	16.7	0	0	2	1	0	0	0	0
Belgium	78	27	34.6	5	6.4	79	11	13.9	1	1	2	2	2	3	2	5
Croatia	8	1	12.5	0	0	8	1	12.5	1	0	0	0	0	0	1	0
Cyprus	11	2	18.2	1	9.1	11	1	9.1	1	1	0	0	1	0	0	0
Czech Republic	9	1	11.1	1	11.1	9	1	11.1	0	0	1	1	1	0	0	0
Denmark	95	2	2.1	0	0	95	1	1.1	0	0	0	0	0	0	0	0
Finland	147	20	13.6	7	4.8	149	4	2.7	0	0	0	0	0	4	0	0
Germany	82	1	1.2	2	2.4	82	0	0.0	0	0	0	0	0	0	0	0
Greece	13	0	0	0	0	13	5	38.5	4	4	4	4	4	4	4	4
Hungary	72	6	8.3	2	2.8	75	10	13.3	0	0	2	2	5	10	1	0
Ireland	106	41	38.7	8	7.5	109	15	13.8	6	1	7	2	5	6	1	3
Italy	193	41	21.2	19	9.8	195	110	56.4	36	19	91	60	77	45	29	16
Lithuania	26	0	0	0	0	26	1	3.8	0	0	1	1	1	0	0	1
Luxembourg	16	1	6.3	0	0	16	0	0.0	0	0	0	0	0	0	0	0
Malta	11	5	45.5	1	9.1	11	0	0.0	0	0	0	0	0	0	0	0
The Netherlands[b]	21	21	100	NA[c]	NA	22	21	95.5	0	0	0	0	0	0	0	0
Norway	51	39	76.5	9	17.6	NA[c]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Poland	24	7	29.2	2	8.3	24	8	33.3	4	2	6	4	5	2	3	0
Portugal	130	49	37.7	28	21.5	132	102	77.3	51	35	67	53	68	57	48	48
Slovakia	59	19	32.2	0	0	59	59	100.0	59	59	59	59	59	59	59	0
Spain	42	31	73.8	14	33.3	46	25	54.3	6	0	21	13	11	5	7	3
Sweden	285	285	100	236	82.8	285	0	0.0	0	0	0	0	0	0	0	0
UK – Northern Ireland	70	20	28.6	2	2.9	70	2	2.9	0	0	0	0	0	2	0	0
UK –Scotland	52	15	28.8	1	1.9	51	5	9.8	1	1	0	0	0	4	1	0
UK – Wales	26	3	11.5	0	0	28	2	7.1	0	0	0	0	0	1	1	0
EU/EEA	**1 639**	**646**	**39.4**	**340**	**20.7**	**1 607**	**386**	**24.0**	**170**	**123**	**263**	**202**	**239**	**202**	**157**	**80**
Former Yugoslav Republic of Macedonia	4	1	25.0	1	25.0	4	0	0.0	0	0	0	0	0	0	0	0
Serbia	6	2	33.3	1	16.7	6	1	16.7	1	1	0	0	0	1	1	0

BSA: Broad-spectrum antibiotics; D06AX09, R01AXA6: Mupirocin; EU/EAA: European Union/European Economic Area; IAA: Intravenously-administered antibiotics; J01DD: Third-generation cephalosporins; J01DH: Carbapenems; J01MA: Fluoroquinolones; J01XA: Glycopeptides; J01XA01: Vancomycin (parenteral); LTCF: long-term care facility; NA: not available.

[a]For the United Kingdom, data for Northern Ireland, Scotland and Wales are presented separately. England did not participate in the survey.

[b]Only a limited number of participating LTCFs in the Netherlands collected antimicrobial stewardship data.

[c]Data were not collected.

France did not provide data for the items presented in the table.

was further divided according to the anatomical site or diagnosis of prophylaxis or treatment: urinary tract, genital tract, skin or wound, respiratory tract, gastrointestinal tract, eye, ear-nose-mouth, surgical site, tuberculosis, systemic infection, unexplained fever or other site or diagnosis not previously specified.

An LTCF institutional questionnaire was used to collect data on structures and processes in place in each participating LTCF, including current infection control practices and antimicrobial policies, e.g. written guidelines for appropriate antimicrobial use in the facility, annual regular training on appropriate antimicrobial prescribing or a 'restrictive list' of antimicrobials to be prescribed. In addition, anonymised and aggregated denominator data were also collected for the entire eligible LTCF population and included information on gender distribution, as well as the proportion of residents aged over 85 years who were receiving at least one antimicrobial agent, were disoriented in time and/or space, had urinary and/or faecal incontinence, had impaired mobility, had pressure sores, had a urinary catheter, had a vascular catheter, had other wounds and/or had surgery in the previous 30 days.

Statistical analysis

All data were checked for errors, omissions and inconsistent answers on the national level and centrally before analysis.

Analyses were performed in SAS 9.3 (SAS Institute, Cary, NC, United States) and R 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria). We calculated the crude, pooled prevalence of antimicrobial use as the number of residents receiving at least one antimicrobial agent divided by the total number of eligible residents on the day of the survey. We also calculated the mean, median and interquartile range (IQR) for the prevalence of antimicrobial use for the included LTCFs overall and within each country.

Multivariable linear regression was used to assess the association between antimicrobial use on the day of the survey and the type and size of LTCFs, as well as characteristics of the LTCF resident population, including care load indicators. Countries reporting data by LTCF ward without indication of the corresponding LTCF (Portugal and Sweden), or data from LTCFs with missing population data on the LTCF questionnaire (France and Norway), as well as LTCFs which reported a prevalence of antimicrobial use of more than 60%, were excluded from this analysis. The latter were considered outliers and represented less than 0.2% of all participating LTCFs.

Ethical considerations and confidentiality

Each participating country had different requirements for ethical approval for the survey, with some requiring approval from an ethics committee as well as written informed consent of the residents (or their proxies). Confidentiality of the data was ensured by the use of a unique, coded survey identification number for each LTCF and for each resident.

Results

Participation

In total, 3,052 LTCFs with 181,462 eligible residents from 24 EU/EEA countries participated in the survey. After adjustment for over-representation of countries contributing to the survey with more than the recommended number of residents, 102,301 eligible residents from 1,788 LTCFs remained in the dataset used for this analysis (Table 1). Data from the United Kingdom (UK) were reported separately for three administrations: UK-Northern Ireland, UK-Scotland and UK-Wales. UK-England did not participate in the survey. The Czech Republic only provided institutional-level data for nine LTCFs and was therefore excluded in the antimicrobial use and resident data analysis.

Antimicrobial use and resident data

On the day of the survey, 5,035 residents received at least one antimicrobial agent, resulting in a crude, pooled prevalence of antimicrobial use of 4.9% (95% CI: 4.8 to 5.1). The mean antimicrobial use prevalence of LTCFs was 5.8% and the median was 3.6% (interquartile range (IQR): 0.0–8.5) (Table 1).

Detailed information on antimicrobial prescribing was provided for 5,006 residents (i.e. all participating countries except Cyprus and the Czech Republic). The median age of residents was 85 years; 65.7% were female and 93.8% received one antimicrobial agent, while 5.8% received two and 0.4% received more than two. In total, 5,344 antimicrobial agents were reported to have been given on the day of the survey, an average of 1.07 antimicrobial agents per resident. Antimicrobials were mainly administered orally (88.1%) The parenteral route (intramuscular or intravenous) was used for 10.9% of prescribed antimicrobials and nasal or rectal administration route was reported for only 0.7% of prescribed antimicrobials.

Antimicrobials were most frequently prescribed within the same LTCF (77.9%), followed by an acute care hospital (12.9%) or another location (5.1%), with no data provided for the remaining 4.2%. The indication was reported as treatment for 69.5% and prophylaxis for 29.4% of prescribed antimicrobials, and indication was missing for the remaining 1.1%. An end or review date for the prescription was documented for 64.6% of prescribed antimicrobials and was higher for treatment (81.6%) than for prophylaxis (26.2%). Figure 1 shows the distribution of antimicrobial use by indication and common site of infection for the EU/EEA overall and for each country.

Overall, the urinary tract was the most common body site for which antimicrobials were prescribed (46.1%), followed by respiratory tract (29.4%) and skin or wound (12.6%). Combined, these sites accounted for 88.0% of

all antimicrobial prescriptions. When stratified by indication, the most common sites for antimicrobial treatment were the respiratory tract (37.2%), urinary tract (34.4%), skin or wound (15.8%) and gastrointestinal tract (2.8%). For prophylaxis, the urinary tract was the most common body site (74.0%), followed by respiratory tract (11.3%), skin or wound (4.8%), another non-specified body site (3.4%) and gastrointestinal tract (2.4%).

Antibacterials for systemic use (ATC J01) accounted for 95.4% of all antimicrobial prescriptions. Other antimicrobial groups accounted for the remaining 4.6%, i.e. nitroimidazole derivatives (P01AB, 1.5%), intestinal anti-infectives–antibiotics (A07AA, 1.3%), antimycotics for systemic use (J02, 1.2%), antimycobacterials for treatment of tuberculosis (J04A, 0.5%) and antifungals for systemic use (D01B, 0.2%).

In total, 5,098 prescriptions of antibacterials for systemic use (ATC J01) were reported. Within this group, the most frequently reported subgroups were: beta-lactam antibacterials, penicillins (J01C: 30.2%), other antibacterials (J01X: 18.6%), quinolones (J01M: 14.9%), sulfonamides and trimethoprim (J01E: 13.3%) and other beta-lactams (J01D: 12.6%). Other groups accounted for the remaining 10.4% of antibacterials for systemic use. Figure 2 shows the distribution of antibacterials for systemic use by indication (prophylaxis or treatment) and by country.

For prophylaxis of urinary tract infection (UTI), the most frequently used antimicrobial agents were trimethoprim (J01EA01: 29.7%), nitrofurantoin (J01XE01: 27.0%), methenamine (J01XX05: 11.6%), cefalexin (J01DB01: 6.1%) and fosfomycin (J01XX01: 5.9%); these accounted for 81.8% of all antimicrobials used for prophylaxis of UTI.

The LTCF and LTCF population characteristics associated with prevalence of antimicrobial use, as identified in the multivariable linear regression analysis, are presented in Table 2. The regression model indicated that LTCF and LTCF population characteristics only explained 19% of the variance in the prevalence of antimicrobial use (R^2 = 0.1889). Prevalence of antimicrobial use was significantly higher in mixed LTCFs, as well as in LTCFs with less than 65 beds. For the demographic characteristics, for one percent increase in the proportion of male residents the prevalence of antimicrobial use increased by 7%. For one percent increase in the proportion of residents over 85 years of age, the prevalence of antimicrobial use increased by 5%. For the care load indicators and risk factors, the most significant increases in antimicrobial use prevalence were associated with the proportion of residents with a vascular catheter and with surgery in the previous 30 days; for one percent increase in the proportion of these risk factors, the prevalence increased by 26% and 20%, respectively.

Antimicrobial stewardship indicators

Of the antimicrobial stewardship indicators reported at LTCF level, the most common was 'written guidelines for appropriate antimicrobial use in the LTCF' (39.4%). Annual regular training on appropriate antimicrobial prescribing was reported by 20.7% of LTCFs included in the sample. Having a 'restrictive list' of antimicrobials was reported by 24.0% of LTCFs; the antimicrobials most commonly restricted were carbapenems (J01DH, 70.1%), parenteral vancomycin (J01XA01, 63.7%), all intravenously administered antibiotics (53.9%), glycopeptides (J01XA, 53.9%), third-generation cephalosporins (J01DD, 45.3%), 'broad-spectrum antibiotics' (41.9%), fluoroquinolones (J01MA, 32.8%) and mupirocin (D06AX09 and R01AX06, 21.3%) (Table 3).

Discussion

This study examined antimicrobial prescribing in LTCFs in 24 EU/EEA countries. The crude prevalence of residents receiving at least one antimicrobial agent was 4.9%; the majority of antimicrobials being administered orally. Antimicrobials were more frequently prescribed for the treatment of an infection, while almost one third were given as prophylaxis. The crude prevalence of antimicrobial use in this survey in 2016–17 was similar to that reported in previous similar HALT surveys from 2010 (4.3%) and 2013 (4.4%) [19,20]. UTIs and respiratory tract infections were the main indications for antimicrobial use, both for treatment or as prophylaxis. This and previous similar surveys in the EU/EEA consistently show large variations of antimicrobial prescribing practices in LTCFs, across and within participating countries [19-21]. The prevalence of residents receiving antimicrobials for prophylaxis also varied largely across countries. In Denmark and Finland, prophylaxis was reported more frequently than treatment, confirming the high proportion of prophylaxis reported in previous surveys from these countries [19,20].

The most commonly prescribed antimicrobials were: penicillins, other antibacterials, quinolones, sulfonamides and trimethoprim, and other beta-lactams. Penicillins, other antibacterials and quinolones were also the most frequently prescribed antimicrobials in both the 2010 and 2013 HALT surveys. For UTI prophylaxis, other antibacterials, sulfonamides and trimethoprim, and penicillins were the most commonly prescribed antimicrobials, as in both the 2010 and 2013 surveys [19,20].

There is variation within the EU/EEA in what is considered long-term care with regard to sheltered housing, length of stay and range of beneficiaries, as well as an absence of a clear division between medical and social services [22]. To enhance comparability, we only included nursing homes, residential homes and mixed LTCFs in this analysis. Despite this, we noted differences in the case-mix of resident populations. For example, Spain reported that post-acute care residents were commonly included to the surveyed population. In

the Netherlands, the level of care provided in the LTCFs covers residents that previously would have often been admitted to a hospital. Therefore, such differences in the definition of long-term care might partially explain a high prevalence of antimicrobial use in some EU/EEA countries. The large variation between LTCFs in the prevalence of residents with a vascular catheter or with previous surgery is an indication that some of the participating LTCFs could, in fact, be step-down facilities with a very different resident case-mix than an average nursing home.

Large differences were observed in the prevalence of care load indicators and risk factors between countries, as well as within each country (unpublished data). Our multivariable analysis showed that several of these indicators and risk factors were independently and positively associated with prevalence of antimicrobial use. However, our model that took into account LTCF characteristics and resident characteristics, including care load and risk factors, only explained 19% of the variation in the prevalence of antimicrobial use in LTCFs in EU/EEA countries. This suggests that other factors, such as national or regional regulations on antimicrobial use, as well as local habits and prescriber preferences and practices, have a larger impact than characteristics of the residents' population [23]. In this survey, prophylaxis of UTI was a frequent indication for antimicrobial use in LTCFs, remaining the most common indication in several countries and showing no significant decline since the HALT surveys performed in 2010 or 2013 [19,20]. Although evidence suggests that long-term antimicrobials for prophylaxis may reduce the risk of recurrence of UTIs in women [24], this benefit diminishes immediately on cessation of antimicrobial use and, more importantly, is associated with a large increase in the proportion of antibiotic-resistant bacteria isolated from urine and faeces. Therefore, the practice of prescribing antimicrobials for prophylaxis of UTI should be carefully evaluated, and more studies about the effectiveness of prophylaxis of UTIs in the LTCF populations may be needed, depending also on the chosen antimicrobial. For example, the characteristics of methenamine (ATC J01XX05) are very different from that of other antimicrobials commonly prescribed for prophylaxis of UTI [25,26].

Information on antimicrobial stewardship indicators was collected to describe the resources available in LTCFs to support rational use of antimicrobials. Documentation of the end or review date for the prescription in the residents' notes is an indicator of the quality of antimicrobial prescription, and this end or review date was documented for almost two out of three prescriptions overall; however, end or review dates were only reported in one out of four prescriptions for prophylaxis. Other antimicrobial stewardship indicators, such as guidelines for appropriate use, were reported by a small proportion of LTCFs in the EU/EEA. Some countries, such as France, Germany, the Netherlands and Norway, reported the dissemination of national guidelines and Norway and the Netherlands reported that the guidelines were specific for the elderly patient population. The antimicrobial stewardship indicator data in this survey were comparable with that from previous similar surveys, which indicate that improvements in antimicrobial stewardship are urgently needed in LTCFs in the EU/EEA [16,27].

The strengths of this survey include the use of a standardised protocol across all participating LTCFs, the collection of detailed data on the LTCF characteristics and antimicrobial stewardship practices and the inclusion of a wide variety of LTCF residents and data on their antimicrobial use. The survey is characterised by broad participation and a very large sample size, providing a good overall picture of antimicrobial use in LTCFs in the EU/EEA, with meaningful benchmarks for participating countries and LTCFs. Considering the participation and representativeness of the current survey, it is important to note that the overall number of participating countries increased from the previous HALT survey in 2013; in addition, the number of participating LTCFs increased progressively between the first survey in 2010 and this iteration in 2016–17. Increasing participation remains important, as repeating the survey at European level with regular time intervals can encourage countries to develop their own national surveillance network for LTCFs, as has been the case in the Netherlands, Norway and Sweden, for example [28-30].

One limitation of this survey was its cross-sectional design, as a survey conducted on one single day can be prone to variation. Nevertheless, this methodology was chosen because of its feasibility when applied in settings with limited resources for surveillance and for infection prevention and control, such as LTCFs. Another limitation was that country representativeness was not optimal in all countries and convenience sampling was often used; both of these factors add to the limitations for inter-country comparisons. An additional limitation of our analysis was the large number of LTCFs that did not report any resident with at least one antimicrobial agent on the day of the survey, which may be another consequence of the differences between participating LTCFs and might warrant more sophisticated statistical methods to take this into account in future analyses.

In conclusion, this third PPS provided overall representative data on antimicrobial use in LTCFs across the EU/EEA countries, and demonstrated that continued surveillance for antibiotic use and stewardship practices in LTCFs remains critical. The survey data allow for identifying targets for future antimicrobial stewardship interventions, specifically in LTCFs; for example focusing on prophylaxis for UTIs, following up on the impact of interventions and, ultimately, contributing to the promotion of prudent use of antimicrobials in LTCFs.

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Acknowledgements

The authors would like to thank all the participating LTCFs and, in particular, all LTCF staff who collected, validated and entered the data during the survey and the national teams that coordinated the survey in each participating country.

The authors would also like to acknowledge the contribution of the following persons in particular: Vivika Adamson (Tartu University Hospital, Tartu, Estonia); Mait Altmets (North Estonia Medical Centre, Tallinn, Estonia); Mailis Hansen (West-Tallinn Central Hospital, Tallinn, Estonia); Saija Toura (National Institute for Health and Welfare, Helsinki, Finland); Dinah Arifulla, (National Institute for Health and Welfare, Helsinki, Finland); Anaïs Machut (CPias Auvergne-Rhône-Alpes, University hospital (HCL), Lyon, France); Gaëtan Gavazzi (University Hospital, Grenoble, France); Konstantinos Papanikolaou (Heraklion University Hospital (PAGNH), Heraklion, Greece) Andreas Panoskaltsis (Heraklion University Hospital (PAGNH), Heraklion, Greece); Ria Benkő and Mária Matuz (Operational Contact Points for Epidemiology – Antimicrobial Consumption (AMC), University of Szeged, Hungary); Henny Lugten (Accoladezorg, Bosch en Duin, the Netherlands); Barbara Gryglewska (Department of Internal Medicine and Gerontology, Faculty of Medicine, Jagiellonian University Medical College, Kraków, Poland); Małgorzata Bulanda (Chair of Microbiology, Faculty of Medicine Jagiellonian University Medical School, Krakow, Poland); Waleria Hryniewicz (National Medicines Institute (NMI), Warsaw, Poland); the National Programme for Protection of Antibiotics (NPOA) funded by the Ministry of Health; Maria Goreti Silva (Direção-Geral da Saúde (DGS), Lisbon, Portugal); Elena Noriega (Direção-Geral da Saúde (DGS), Lisbon, Portugal); Ana Paula Cruz (Direção-Geral da Saúde (DGS), Lisbon, Portugal).

Conflict of interest

None declared.

Authors' contributions

Enrico Ricchizzi (ER) wrote the original draft; Katrien Latour, Pete Kinross and ER managed and coordinated planning and execution of the survey, and performed the data analysis; Tommi Kärki contributed to the design of the survey and co-ordination of its execution, contributed to the data analysis and wrote the advanced draft; Rossella Buttazzi contributed to the data analysis; Béatrice Jans, Maria Luisa Moro, Dominique L. Monnet and Carl Suetens contributed to the design of the survey; Olivia Aya Nakitanda and Diamantis Plachouras contributed to coordination of the execution of the survey; the HALT Study Group members contributed to design of the survey, coordinated its execution in their respective countries and provided national interpretations on the results of the analysis. All authors critically reviewed and edited the manuscript.

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Prevalence of healthcare-associated infections, estimated incidence and composite antimicrobial resistance index in acute care hospitals and long-term care facilities: results from two European point prevalence surveys, 2016 to 2017

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Citation style for this article:
Suetens Carl, Latour Katrien, Kärki Tommi, Ricchizzi Enrico, Kinross Pete, Moro Maria Luisa, Jans Béatrice, Hopkins Susan, Hansen Sonja, Lyytikäinen Outi, Reilly Jacqui, Deptula Aleksander, Zingg Walter, Plachouras Diamantis, Monnet Dominique L, the Healthcare-Associated Infections Prevalence Study Group, Members of the Healthcare-Associated Infections Prevalence Study Group. Prevalence of healthcare-associated infections, estimated incidence and composite antimicrobial resistance index in acute care hospitals and long-term care facilities: results from two European point prevalence surveys, 2016 to 2017. Euro Surveill. 2018;23(46):pii=1800516. https://doi.org/10.2807/1560-7917.ES.2018.23.46.1800516

Article submitted on 20 Sep 2018 / accepted on 07 Nov 2018 / published on 15 Nov 2018

Point prevalence surveys of healthcare-associated infections (HAI) and antimicrobial use in the European Union and European Economic Area (EU/EEA) from 2016 to 2017 included 310,755 patients from 1,209 acute care hospitals (ACH) in 28 countries and 117,138 residents from 2,221 long-term care facilities (LTCF) in 23 countries. After national validation, we estimated that 6.5% (cumulative 95% confidence interval (cCI): 5.4–7.8%) patients in ACH and 3.9% (95% cCI: 2.4–6.0%) residents in LTCF had at least one HAI (country-weighted prevalence). On any given day, 98,166 patients (95% cCI: 81,022–117,484) in ACH and 129,940 (95% cCI: 79,570–197,625) residents in LTCF had an HAI. HAI episodes per year were estimated at 8.9 million (95% cCI: 4.6–15.6 million), including 4.5 million (95% cCI: 2.6–7.6 million) in ACH and 4.4 million (95% cCI: 2.0–8.0 million) in LTCF; 3.8 million (95% cCI: 3.1–4.5 million) patients acquired an HAI each year in ACH. Antimicrobial resistance (AMR) to selected AMR markers was 31.6% in ACH and 28.0% in LTCF. Our study confirmed a high annual number of HAI in healthcare facilities in the EU/EEA and indicated that AMR in HAI in LTCF may have reached the same level as in ACH.

Introduction

In 2016, the European Centre for Disease Prevention and Control (ECDC) estimated that the burden of six main types of healthcare-associated infection (healthcare-associated pneumonia, urinary tract infection, surgical site infection, *Clostridium difficile* infection, neonatal sepsis and primary bloodstream infection) expressed in disability-adjusted life years (DALYs) in the European Union and European Economic Area (EU/EEA) was higher than the combined burden of 31 other infectious diseases under surveillance by ECDC [1,2]. The estimated number of healthcare-associated infections (HAI) used in the study was based on the data of the first ECDC point prevalence survey (PPS) of HAI and antimicrobial use in acute care hospitals (ACH) from 2011 to 2012 [3] and did not take into account HAI occurring in other healthcare facilities. In particular, ECDC had previously estimated that the number of residents with an HAI on any given day in European long-term care facilities (LTCF) was of the same order

Table 1a

Key characteristics of healthcare facilities, patients and residents included in the point prevalence survey (PPS) samples, PPS in acute care hospitals (n = 1,275) and long-term care facilities (n = 2,242), 30 EU/EEA countries, Serbia and the former Yugoslav Republic of Macedonia, 2016–2017

Country	ACH								LTCF								
	Number of hospitals		Type of ACH					Intensive care patients	Number of LTCF		Type of LTCF				Residents in (a) + (b) + (c)		
	Country total	In PPS sample	Primary	Secondary	Tertiary	Specialised	Unknown	(%)	Country total	In PPS sample	General nursing home (a)	Residential home (b)	Mixed LTCF (c)	Other LTCF types	>85 years-old (%)	Urinary catheter (%)	Recent surgery (%) (past 30 days)
Austria	162	49	25	11	2	11	0	4.0	817	14	0	7	5	2	35.8	10.8	1.0
Belgium	197	43	27	9	7	0	0	4.9	1,559	86	79	0	0	7	56.5	3.1	0.9
Bulgaria	241	12	1	4	7	0	0	6.9	33	NP	NA	NA	NA	NA	NA	NA	NA
Croatia	32	34	6	15	9	4	0	6.0	325	8	0	0	8	0	40.9	3.1	1.1
Cyprus	83	8	2	4	2	0	0	9.6	90	13	7	0	4	2	54.8	8.0	4.8
Czech Republic	144	45	2	30	11	2	0	8.1	73	11	0	4	5	2	NA	NA	NA
Denmark	52	NP	NA	NA	NA	NA	NA	NA	827	95	0	0	95	0	51.8	9.0	1.7
Estonia	27	23	10	7	1	4	1	3.3	59	NP	NA	NA	NA	NA	NA	NA	NA
Finland	59	51	18	16	14	2	1	3.8	1,928	157	148	0	1	8	51.4	4.2	0.6
France	1,237	50	32	10	6	2	0	3.8	9,744	91	91	0	0	0	61.6	1.6	0.8
Germany	1,857	49	25	7	4	13	0	5.0	10,389	84	55	15	12	2	49.6	8.6	1.3
Greece	123	42	1	23	16	2	0	7.6	263	13	0	0	13	0	48.8	12.1	0.7
Hungary	94	38	14	10	6	7	1	2.8	1,177	111	65	9	1	36	25.3	1.9	0.7
Iceland	8	2	0	1	1	0	0	5.2	43	NP	NA	NA	NA	NA	NA	NA	NA
Ireland	60	60	9	17	7	27	0	3.0	578	185	75	0	34	76	47.7	7.0	1.5

ACH: acute care hospital; EU/EEA: European Union/European Economic Area; LTCF: long-term care facility; NA: not applicable; ND: no data collected in national protocol; NP: did not participate; PPS: point prevalence survey; UK: United Kingdom.

Country data representativeness was poor in Bulgaria and the Netherlands for the PPS in ACH and poor in Austria, Croatia, Cyprus, Greece, Luxembourg, Malta and Poland for the PPS in LTCF. The Czech Republic only submitted data on institutional indicators.

Table 1b

Key characteristics of healthcare facilities, patients and residents included in the point prevalence survey (PPS) samples, PPS in acute care hospitals (n = 1,275) and long-term care facilities (n = 2,242), 30 EU/EEA countries, Serbia and the former Yugoslav Republic of Macedonia, 2016–2017

Country	ACH								LTCF								
	Number of hospitals		Type of ACH					Intensive care patients	Number of LTCF		Type of LTCF				Residents in (a)+(b)+(c)		
	Country total	In PPS sample	Primary	Secondary	Tertiary	Specialised	Unknown	(%)	Country total	In PPS sample	General nursing home (a)	Residential home (b)	Mixed LTCF (c)	Other LTCF types	>85 years-old (%)	Urinary catheter (%)	Recent surgery (%) (past 30 days)
Italy	1,134	56	13	14	25	4	0	6.0	3219	215	61	85	50	19	54.0	12.1	1.3
Latvia	24	14	0	9	3	2	0	3.5	82	NP	NA	NA	NA	NA	NA	NA	NA
Lithuania	64	62	25	26	8	3	0	2.8	154	26	0	0	26	0	12.4	0.8	0.3
Luxembourg	12	12	2	5	1	3	1	5.9	62	16	15	1	0	0	58.4	5.3	1.5
Malta	4	4	1	1	1	1	0	4.8	41	11	0	8	3	0	51.1	5.0	0.6
The Netherlands	79	19	10	8	1	0	0	6.0	700	57	0	0	57	0	43.0	6.6	3.5
Norway	53	43	11	9	4	0	19	6.3	907	62	62	0	0	0	NA	10.0	3.4
Poland	936	80	22	20	23	15	0	3.8	373	25	12	12	0	1	30.5	19.4	0.9
Portugal	225	93	24	40	18	9	2	4.2	360	268	0	0	132	136	29.6	15.1	0.9
Romania	311	40	16	10	3	11	0	6.4	628	NP	NA	NA	NA	NA	NA	NA	NA
Slovakia	107	50	20	11	7	12	0	5.2	677	69	27	0	32	10	28.3	3.1	1.1
Slovenia	21	20	0	11	3	6	0	5.8	90	NP	NA	NA	NA	NA	NA	NA	NA
Spain	576	96	17	39	32	5	3	5.0	5,387	46	0	0	46	0	48.1	5.1	5.1
Sweden	144	NP	NA	NA	NA	NA	NA	NA	2,300	417	285	0	0	132	57.9	9.9	2.1
UK–England	158	32	0	19	10	3	0	3.4	17,473	NP	NA	NA	NA	NA	NA	NA	NA
UK–Northern Ireland	16	16	6	4	2	4	0	3.2	445	70	0	15	55	0	44.8	5.0	0.6
UK–Scotland	46	45	12	14	7	12	0	2.8	873	52	34	17	1	0	43.9	8.5	0.3
UK–Wales	21	21	6	10	4	1	0	3.7	795	30	9	7	12	2	49.7	7.8	1.7
EU/EEA	8,307	1,209	357	414	245	165	28	4.6%	62,471	2,232	1025	180	592	435	45.6%	6.7%	1.5%
EU/EEA (n, %, mean of countries)	252	100%	29.5%	34.2%	20.3%	13.6%	2.3%	4.9%	1,893	100%	45.9%	12.3%	22.3%	19.5%	44.8%	7.3%	1.5%
Former Yugoslav Republic of Macedonia	ND	NP	NA	NA	NA	NA	NA	NA	21	4	3	0	1	0	15.3	8.8	0.7
Serbia	66	66	1	45	14	6	0	6.5	90	6	0	0	6	0	28.1	6.1	0.6

ACH: acute care hospital; EU/EEA: European Union/European Economic Area; LTCF: long-term care facility; NA: not applicable; ND: no data collected in national protocol; NP: did not participate; PPS: point prevalence survey; UK: United Kingdom.

Country data representativeness was poor in Bulgaria and the Netherlands for the PPS in ACH and poor in Austria, Croatia, Cyprus, Greece, Luxembourg, Malta and Poland for the PPS in LTCF. The Czech Republic only submitted data on institutional indicators.

of magnitude as the number of patients with an HAI on any given day in ACH [4-6].

In the period from 2016 to 2017, ECDC organised two PPS of HAI and antimicrobial use: the second PPS in ACH and the third PPS in LTCF in the EU/EEA. The objective of the current study was to report on the HAI and antimicrobial resistance results of both surveys and to estimate the combined total number of HAI on any given day and the number of HAI per year in 2016 and 2017 in the EU/EEA.

Methods

Participation of countries

All EU/EEA countries and EU candidate and potential candidate countries were invited to organise a national PPS in ACH and LTCF in their country in any of four periods (April to June or September to November of 2016 or 2017). For reasons of feasibility at national level, the PPS in ACH and LTCF could be organised during different periods. Data were collected according to two specific standardised ECDC protocols [7,8]. All countries used the ECDC protocols and included all HAI types except for one country (Norway) for ACH and four countries (France, the Netherlands, Norway and Sweden) for LTCF Norway used national protocols with the same case definitions as in the ECDC protocols, but provided fewer details and did not require the inclusion of all types of HAI. LTCF data from France and the Netherlands were also collected using national protocols not including all types of HAI. LTCF protocols in France, the Netherlands and Norway all included urinary tract infections, lower respiratory tract infections and skin infections, in addition to other HAI types varying by country. Surveys in separate healthcare administrations in the United Kingdom (UK), i.e. England, Northern Ireland, Scotland and Wales, were organised independently and results were reported separately.

Selection of participating facilities and patients

It was recommended that countries selected the participating ACH and LTCF by systematic random sampling from national lists ranked by type and size to ensure optimal country representativeness. For each country, the required sample size was calculated for an estimated prevalence of 6% for ACH and 4% for LTCF, based on the results of the previous PPS [3,6], with an absolute precision of 1%. Representativeness was categorised as optimal, good, poor or very poor, depending on the sampling method of the facilities, the number of included patients/residents and the number of included facilities [7,8]. For example, 'optimal representativeness' meant that the country performed systematic sampling of at least 25 healthcare facilities or included at least 75% of all facilities or beds at national level, and achieved the recommended sample size.

For ACH, the protocol recommended that data from a single ward should be collected on one single day and that the time frame for data collection for all wards of a single hospital would not exceed 3 weeks. For LTCF, it was recommended to collect data on a single day, except for larger LTCF.

We included all patients/residents present on the hospital ward or LTCF at 8:00 on the day of the PPS and still present at the time of day when the PPS was performed. In addition, LTCF residents needed to be full-time residents (i.e. living 24 hours a day in the LTCF). Patients/residents who were temporarily absent from their room, e.g. for diagnostic procedures, had to be included.

Case definitions

Case definitions for HAI differed for ACH and for LTCF, reflecting differences in access to diagnostic methods between the two settings, as well as the specific signs and symptoms of infection in elderly LTCF residents [7,8]. For both PPS, an HAI was defined as active on the day of the PPS when signs and symptoms were present on the date of the PPS, or when signs and symptoms were no longer present but the patient/resident was still receiving treatment for that infection on the date of the PPS. HAI present on admission were included in both protocols. In the LTCF protocol, HAI associated with a stay in any other healthcare facility – another LTCF or a hospital – were included. In the ACH protocol, however, only HAI imported from other ACH were included, excluding HAI present on admission associated with a previous LTCF stay. LTCF data in France and Sweden did not include HAI imported from other healthcare facilities.

Data analysis

Data were analysed with Stata, version 14.1 (StataCorp, Texas, United States). The prevalence of HAI was expressed as the percentage of patients/residents with at least one HAI on the day of the PPS. To account for clustering within ACH or LTCF, 95% confidence intervals (CI) were calculated using the svy proportion command in Stata. Overall weighted prevalence percentages were calculated by applying the country-specific prevalence on the number of occupied beds in each country and summing up the total number of patients with at least one HAI for EU/EEA countries. National denominator data were obtained by questionnaire from national survey coordinators, from Eurostat data if national denominator data were not submitted [9-11] or from the previous PPS if Eurostat data were missing or incomplete [3,4,6]. To estimate the total number of HAI or patients with at least one HAI for the whole EU/EEA, the average results from participating EU/EEA countries were applied to the national denominator data from non-participating EU/EEA countries. For data collected using national protocols which did not include all types of HAI, imputation of non-included types of HAI was done based on EU/EEA averages to make prevalence percentages comparable. In ACH, imputation resulted in adding 7.3% (36/495) of patients with HAI in Norway. In LTCF, imputation resulted in adding 5.8% (12/206) of residents with HAI in France, 6.9% (11/160)

Table 2a

Prevalence and estimated incidence of healthcare-associated infections in European acute care hospitals, 28 EU/EEA countries and Serbia, 2016–2017 (n = 325,737 patients)

Country	Patients in PPS sample	Patients with at least one HAI in PPS sample (HAI prevalence)[a]			Validation-corrected HAI prevalence[b]	Occupied beds in the country (average per day)	Patients with at least one HAI on a given day, estimated		Hospital discharges annually in the country	HAI incidence, estimated		Patients with at least one HAI, annually, estimated	
	n	n	%	95% CI	%	n	n	95% CI	n	%	95% CI	n	95% CI
Austria	13,461	541	4.0	3.4–4.7	NR	36,351	1,461	1,243–1,716	2,707,753	2.3	1.5–3.3	62,306	40,978–89,762
Belgium	11,800	856	7.3	6.4–8.3	NR	37,651	2,731	2,397–3,109	1,858,726	5.4	3.7–7.6	101,110	68,186–141,713
Bulgaria[c]	2,200	76	3.5	1.7–6.8	NR	25,324	875	434–1,733	1,632,089	1.8	0.9–3.8	29,572	13,909–61,597
Croatia	10,466	551	5.3	4.5–6.2	NR	11,047	581	495–683	667,849	4.1	2.8–5.6	27,129	18,937–37,561
Cyprus	1,036	85	8.2	5.4–12.4	ND	1,437	118	77–178	166,295	4.8	2.5–8.7	8,010	4,158–14,541
Czech Republic	15,117	1,015	6.7	5.9–7.6	NR	40,691	2,732	2,413–3,090	2,260,239	5.4	3.9–7.3	122,313	87,039–165,208
Estonia	4,220	178	4.2	2.4–7.3	NR	4,582	193	111–332	222,363	3.3	1.6–6.6	7,393	3,558–14,761
Finland	9,079	803	8.8	7.5–10.4	NR	15,894	1,406	1,187–1,660	915,892	5.1	3.3–7.5	46,735	30,053–68,350
France	16,522	965	5.8	4.9–7.0	NR	159,810	9,334	7,823–11,116	11,330, 996	4.1	2.7–5.9	467,961	311,830–671,498
Germany	11,324	409	3.6	2.8–4.7	NR	400,132	14,452	11,087–18,789	19,480,504	3.1	1.9–4.8	604,495	373,766–938,383
Greece	9,401	938	10.0	8.5–11.6	NR	18,252	1,821	1,559–2,121	1,562,761	4.3	3.1–5.7	66,487	48,386–89,068
Hungary	20,588	818	4.0	3.3–4.8	NR	46,134	1,833	1,516–2,212	2,226,485	3.5	2.1–5.4	78,095	46,906–120,082
Iceland	633	40	6.3	0.8–36.8	5.7	642	41	5–237	39,198	6.7	0.6–48.6	2,609	239–19,038
Ireland	10,333	633	6.1	5.0–7.5	NR	10,932	670	546–820	705,000	4.2	2.7–6.3	29,671	18,846–44,323
Italy	14,773	1,186	8.0	6.8–9.5	NR	167,619	13,457	11,362–15,899	8,930,979	6.0	4.2–8.3	534,709	373,705–740,544

CI: confidence interval; EU/EEA: European Union/European Economic Area; HAI: healthcare-associated infection; NA: not applicable; ND: validation study not done NR: validation study not representative of country PPS sample; PPS: point prevalence survey; UK: United Kingdom.

[a] Country-weighted HAI prevalence for the EU/EEA= estimated number of patients with at least one HAI a single day / occupied beds.

[b] Validation-corrected prevalence of patients with at least one HAI: only given for countries that reached national representativeness for their national validation study (at least 75% of recommended sample size of 750 validated patients and/or validation of at least 75% of included hospitals).

[c] Poor country representativeness in Bulgaria and the Netherlands.

Table 2b

Prevalence and estimated incidence of healthcare-associated infections in European acute care hospitals, 28 EU/EEA countries and Serbia, 2016–2017 (n = 325,737 patients)

Country	Patients in PPS sample	Patients with at least one HAI in PPS sample (HAI prevalence)[a]			Validation-corrected HAI prevalence[b]	Occupied beds in the country (average per day)	Patients with at least one HAI on a given day, estimated		Hospital discharges annually in the country	HAI incidence, estimated		Patients with at least one HAI, annually, estimated	
	n	n	%	95% CI	%	n	n	95% CI	n	%	95% CI	n	95% CI
Latvia	3,807	140	3.7	2.6–5.2	4.9	5,127	189	132–268	300,575	2.5	1.4–4.1	7,447	4,322–12,399
Lithuania	12,415	359	2.9	2.1–4.0	3.2	14,613	423	301–590	705,224	2.6	1.3–4.6	18,046	9,322–32,167
Luxembourg	2,018	103	5.1	4.0–6.5	8.5	1,860	95	75–120	74,782	3.4	2.1–5.3	2,569	1,560–3,995
Malta	961	60	6.2	5.2–7.4	7.9	972	61	51–72	72,909	2.6	1.9–3.4	1,877	1,380–2,507
The Netherlands[c]	4,441	170	3.8	3.4–4.3	NR	24,167	925	826–1,036	1,700,000	2.3	1.6–3.2	39,585	27,525–54,115
Norway[d]	9,628	495	5.1	4.1–6.4	ND	10,505	540	430–677	776,203	2.4	1.5–3.6	18,767	11,873–28,340
Poland	21,712	1,249	5.8	4.8–6.9	4.7	120,492	6,931	5,764–8,317	8,254,611	3.5	2.3–5.0	289,602	193,881–415,274
Portugal	16,982	1,544	9.1	8.1–10.2	7.8	27,907	2,537	2,236–2,841	1,128,245	5.9	4.4–7.8	66,860	49,568–87,500
Romania	11,443	417	3.6	2.8–4.7	5.9	57,091	2,080	1,610–2,682	3,674,275	2.6	1.7–4.0	97,257	62,340–146,893
Slovakia	9,145	370	4.1	3.1–5.3	NR	20,279	820	630–1,066	1,005,003	3.1	2.1–4.6	31,519	20,848–46,607
Slovenia	5,720	373	6.5	5.8–7.3	ND	5,581	363	322–409	380,077	4.4	3.3–5.6	16,635	12,630–21,441
Spain	19,546	1,516	7.8	7.1–8.5	NR	84,908	6,586	5,983–7,243	5,247,215	4.9	3.6–6.4	255,169	186,398–335,644
UK–England	20,148	1,297	6.4	5.4–7.6	NR	96,774	6,230	5,264–7,358	9,450,142	2.2	1.4–3.2	205,722	130,191–303,990
UK–Northern Ireland	3,813	234	6.1	4.8–7.9	5.8	4,965	305	236–392	302,008	3.5	1.8–5.9	10,527	5,559–17,841
UK–Scotland	11,623	504	4.3	3.5–5.3	NR	11,448	496	406–606	1,156,473	2.2	1.5–3.2	25,539	16,992–36,977
UK–Wales	6,400	362	5.7	4.7–6.7	6.0	6,715	380	318–453	827,634	2.2	1.3–3.3	17,880	10,595–27,545
Participating EU/EEA countries[a,e]	**310,755**	**18,287**	**5.5**	**4.5–6.7**	**6.5**	**1,469,903**	**80,665**	**66,864–97,824**	**89,762,505**	**3.7**	**2.4–5.3**	**3,293,595**	**2,185,484–4,789,661**
Serbia	14,982	650	4.3	3.5–5.4	NR	18,920	821	656–1,024	988,383	3.3	2.3–4.6	32,337	22,714–45
EU/EEA, corrected[e,f]	NA	NA	5.5	4.5–6.7	6.5	1,503,881	82,713	67,674–99,256	91,885,503	3.7	2.4–5.3	3,372,146	2,220,554–4,854,535
EU/EEA, corrected after validation	**NA**	**NA**	**6.5**	**5.4–7.8**	**NA**	**1,503,881**	**98,166**	**81,022–117,484**	**91,885,503**	**4.1**	**3.4–4.9**	**3,758,014**	**3,122,024–4,509,617**

CI: confidence interval; EU/EEA: European Union/European Economic Area; HAI: healthcare-associated infection; NA: not applicable; ND: validation study not done NR: validation study not representative of country PPS sample; PPS: point prevalence survey; UK: United Kingdom.

[a] Country-weighted HAI prevalence for the EU/EEA= estimated number of patients with at least one HAI a single day / occupied beds.

[b] Validation-corrected prevalence of patients with at least one HAI: only given for countries that reached national representativeness for their national validation study (at least 75% of recommended sample size of 750 validated patients and/or validation of at least 75% of included hospitals).

[c] Poor country representativeness in Bulgaria and the Netherlands.

[d] Norway used a national PPS protocol requiring imputation of non-included types of HAI for 24 hospitals.

[e] Cumulative 95% CI for the EU/EEA. Cumulative sums are rounded and may differ from the sum of the individual rounded country estimates.

[f] Corrected for non-participating EU countries with estimation for Denmark and Sweden combined.

Table 3

Country-weighted prevalence and estimated incidence of healthcare-associated infections (HAI) by type of HAI in European acute care hospitals (n = 19,626) and long-term care facilities (n = 3,858), 30 EU/EEA countries, 2016–2017

Type of HAI	Acute care hospitals								Long-term care facilities							
	HAI in PPS sample		Country-weighted HAI prevalence		Estimated HAI on a given day, EU/EEA[a]		Estimated annual HAI, EU/EEA[a]		HAI in PPS sample		Country-weighted HAI prevalence		Estimated HAI on a given day, EU/EEA[a]		Estimated annual HAI, EU/EEA[a]	
	N	% total	n	95% cCI	N	95% cCI	n	95% cCI	n	% total	%	95% cCI	n	95% cCI	n	95% cCI
Pneumonia	4,200	21.4	1.26	0.96–1.68	18,935	14,398–25,265	862,084	567,728–1 283,203	143	3.7	0.15	0.06–0.32	4,948	1,946–10 658	112,868	44,390–243,134
Other lower respiratory tract infection[b]	838	4.3	0.24	0.15–0.41	3,568	2,208–6,192	183,232	91,731–376,990	847	22.0	0.88	0.59–1.14	29,010	19,412–37,826	1,058,853	708,542–1 380,653
Common cold/ influenza	NI	NA	NA	NA	NA	NA	NA	NA	290	7.5	0.29	0.13–0.51	9,678	4,368–16,782	441,543	199,312–765,693
Urinary tract infection	3,710	18.9	1.10	0.85–1.43	16,491	12,822–21,455	869,941	572,105–1,278,951	1,233	32.0	1.29	0.87–1.66	42,687	28,898–54,825	1,298,388	878,983–1,667,596
Surgical site infection	3,601	18.3	1.08	0.81–1.44	16,130	12,185–21,715	518,182	293,036–858,222	66	1.7	0.09	0.03–0.20	2,829	944–6,500	57,366	19,133–131,803
Bloodstream infection	2,116	10.8	0.69	0.48–1.00	10,294	7,241–15,097	375,050	227,552–613,624	19	0.5	0.04	0.01–0.07	1,168	193–2,389	23,692	3,908–48,442
Clostridium difficile infection	951	4.8	0.32	0.21–0.51	4,786	3,105–7,721	189,526	105,154–340,978	37	1.0	0.05	0.01–0.14	1,787	424–4,755	18,118	4,296–48,206
Other gastrointestinal infection	792	4.0	0.24	0.14–0.41)	3,549	2,108–6,166	144,926	64,880–312,212	75	1.9	0.1	0.03–0.20	3,187	1,012–6,473	145,409	46,184–295,333
Skin and soft tissue infection	823	4.2	0.21	0.13–0.36	3,146	1,900–5,451	108,269	45,149–242,816	828	21.5	0.83	0.51–1.19	27,459	17,021–39,307	626,415	388,293–896,687
Eye, ear, nose or mouth infection	557	2.8	0.16	0.09–0.35	2,400	1,278–5 194	123,091	54,155–303,206	183	4.7	0.17	0.08–0.31	5,712	2,707–10,369	173,733	82,323–315,390
Systemic infection	1,069	5.4	0.29	0.17–0.52	4,388	2,586–7,799	251,237	110,732–549,877	35	0.9	0.04	0.01–0.08	1,223	286–2,534	37,201	8,691–77,061
Other infection	969	4.9	0.30	0.19–0.50	4,518	2,867–7,574	154,138	65,647–332,357	102	2.6	0.12	0.04–0.24	3,878	1,366–8,077	117,958	41,556–245,683
All types of HAI, EU/EEA[a]	19,626	100	NA	NA	88,204	62,697–129,630	3,779,677	2,197,869–6,492,437	3,858	100	NA	NA	133,565	78,576–200,494	4,111,544	2,425,610–6,115,682
All types of HAI, EU/EEA, corrected after validation	**NA**	**NA**	**NA**	**NA**	**104,177**	**74,743–152,575**	**4,464,159**	**2,620,139–7,641,606**	**NA**	**NA**	**NA**	**NA**	**143,565**	**64,736–260,655**	**4,422,629**	**1,998,384–7,950,784**

cCI: cumulative 95% confidence interval (sum of country-specific lower respectively upper country interval limits); EU/EEA: European Union/European Economic Area; HAI: healthcare-associated infection; NA: not applicable; NI: not included in protocol; PPS: point prevalence survey.

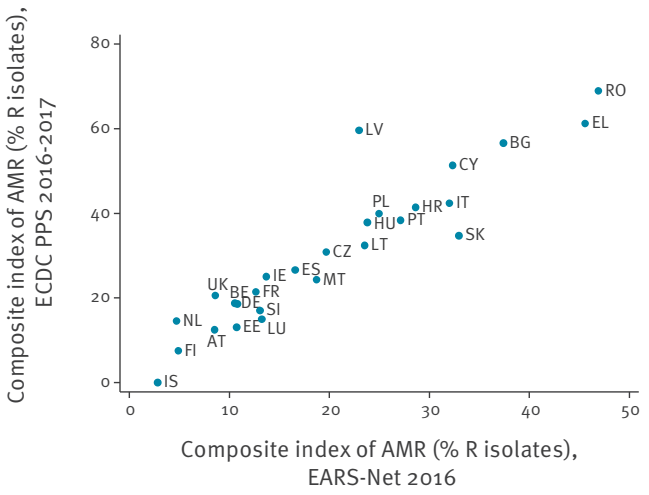
[a] After correction for non-participating countries. Cumulative sums are rounded and may differ from the sum of the individual rounded country estimates.

[b] Other lower respiratory tract infections included bronchitis, tracheobronchitis, bronchiolitis, tracheitis, lung abcess or empyema, without evidence of pneumonia.

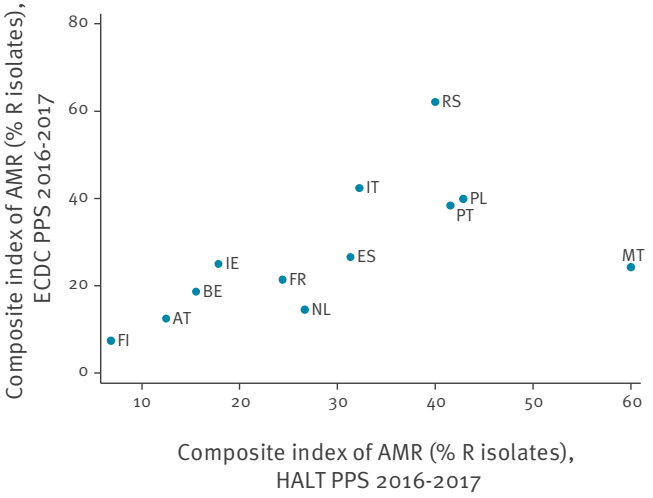
Figure

Correlations of composite index of antimicrobial resistance, EU/EEA countries and Serbia, 2016–2017

A. Correlation between the composite indices of AMR from the PPS in acute care hospitals, 2016-2017 and EARS-Net, 2016 (n = 27 countries)



B. Correlation between the composite indices of AMR from the PPS in acute care hospitals, 2016-2017 and the PPS in long-term care facilities, 2016-2017 (n = 12 countries)



ACH: acute care hospital; AMR: antimicrobial resistance; AT: Austria; BE: Belgium; BG: Bulgaria; CY: Cyprus; CZ: Czech Republic; DE: Germany; EARS-Net: European Antimicrobial Resistance Surveillance Network; ECDC: European Centre for Disease Prevention and Control; EE: Estonia; EL: Greece; ES: Spain; FI: Finland; FR: France; HALT: Healthcare-associated infections in LTCF project; HR: Croatia; HU: Hungary; IE: Ireland; IS: Iceland; IT: Italy; LT: Lithuania; LTCF: long-term care facility; LU: Luxembourg; LV: Latvia; MT: Malta; NL: the Netherlands; NO: Norway; PL: Poland; PPS: point prevalence survey; PT: Portugal; RO: Romania; RS: Serbia; SI: Slovenia; SK: Slovakia; UK: United Kingdom.

Composite index of AMR: *Staphylococcus aureus* resistant to meticillin, *Enterococcus faecium* and *Enterococcus faecalis* resistant to vancomycin, Enterobacteriaceae resistant to third-generation cephalosporins, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* resistant to carbapenems; EARS-Net: Enterobacteriaceae other than *Escherichia coli* and *Klebsiella pneumoniae* not included. Other species represented 32.5% of tested Enterobacteriaceae in ACH. France: percentage non-susceptible (resistant + intermediate) isolates instead of percentage resistant isolates. In addition to poor representativeness of participating LTCF in Malta, specimens in these LTCF were known to be taken predominantly in cases of treatment failure (panel B).

in the Netherlands and 7.6% (9/119) in Norway, or 0.8% (32/3,780) overall. As these imputations were done for the aggregated national results, correction of CI for clustering within LTCF could not be applied for these countries and binomial exact CI were used instead.

Antimicrobial resistance

Antimicrobial resistance (AMR) in HAI was evaluated using two indicators: a composite index of AMR and the percentage of carbapenem-resistant Enterobacteriaceae. The composite index of AMR was calculated as the percentage of resistant isolates for the 'first level' AMR markers in the PPS protocols divided by the sum of the isolates for which results from antimicrobial susceptibility testing (AST) were reported. These first level markers were *Staphylococcus aureus* resistant to meticillin (MRSA), *Enterococcus faecium* and *Enterococcus faecalis* resistant to vancomycin, Enterobacteriaceae resistant to third-generation cephalosporins, and *Pseudomonas aeruginosa* and *Acinetobacter baumannii* resistant to carbapenems. The percentage of resistant isolates was not calculated when less than 10 isolates with known AST results were reported. The composite index of AMR at country level was validated by examining the correlation with the composite AMR index calculated from EARS-Net data from 2016, including all components of the index except AST results for Enterobacteriaceae other than *Escherichia coli* and *Klebsiella pneumoniae* because they are not included in EARS-Net [12,13]. Correlations were analysed using the Spearman correlation coefficient rho and the R-squared (R^2) and regression coefficient from linear regression.

Prevalence to incidence conversion

Estimates of the total number of HAI and patients acquiring at least one HAI per year in ACH were based on prevalence to incidence conversion using the Rhame and Sudderth formula [14]. Details of the method are reported in the ECDC PPS report for 2011 and 2012 [3]. In addition, sensitivity analyses of the conversion were carried out using a method developed by Willrich et al. (personal communication: Niklas Willrich, 24 May 2018), in which the estimates of the length of stay were based on a Grenander estimator for discrete monotonously decreasing distributions [15].

Table 4a

Composite index of antimicrobial resistance in bacteria from healthcare-associated infections in acute care hospitals (n = 8,413) and long-term care facilities (n = 565), 30 EU/EEA countries, Serbia and the former Yugoslav Republic of Macedonia[a], 2016–2017

Country	Acute care hospitals[a]								Long-term care facilities[a]			
	Composite index of AMR				Carbapenem-resistant Enterobacteriaceae				Composite index of AMR		Carbapenem-resistant Enterobacteriaceae	
	Tested isolates	Resistant isolates	Estimated annual HAI		Tested isolates	Resistant isolates	Estimated annual HAI		Tested isolates	Resistant isolates	Tested isolates	Resistant isolates
	n	%	n	95% CI	n	%	n	95% CI	n	%	n	%
Austria[b]	217	12.4	1,759	713–3,984	124	0.8	55	8–387	16	12.5	12	0.0
Belgium	495	18.6	8,458	4,422–14,621	318	1.3	261	104–654	45	15.6	34	0.0
Bulgaria[b]	53	56.6	8,687	3,189–23,328	30	10.0	2,014	479–8,291	NP	NA	NA	NA
Croatia[b]	280	41.4	3,823	2,491–5,808	114	5.3	300	80–1,053	6	NA	4	NA
Cyprus[a,b]	37	51.4	1,070	431–2,380	15	6.7	19	3–119	0	NA	NA	NA
Czech Republic[a]	627	30.8	16,348	9,726–25,665	393	0.8	87	30–261	NP[a]	NA	NA	NA
Denmark[a]	NP	NA	UNK	NA	NA	NA	UNK	NA	0	NA	0	NA
Estonia	107	13.1	462	138–1,398	58	0.0	0	NA	NP	NA	NA	NA
Finland	188	7.4	298	139–619	92	0.0	0	NA	44	6.8	36	0.0
France[a]	738	21.4	44,953	21,316–86,180	413	0.5	785	129–4,943	41	24.4	35	14.3
Germany	197	18.8	27,228	13,378–52,651	95	2.1	1,769	420–7,444	2	NA	1	NA
Greece[b]	456	61.2	10,605	7,809–14,193	197	43.7	4,157	2,467–6,831	2	NA	1	NA
Hungary	256	37.9	5,383	2,578–9,837	126	0.8	41	6–289	7	NA	6	NA
Iceland	15	0.0	0	NA	10	0.0	0	NA	NP	NA	NA	NA
Ireland	192	25.0	1,206	454–2,704	107	0.9	45	6–306	28	17.9	12	8.3
Italy	555	42.3	63,930	39,969–98,909	306	16.7	11,660	6,489–20,554	93	32.3	67	5.6
Latvia	47	59.6	804	309–2,043	19	5.3	38	4–356	NP	NA	NA	NA
Lithuania	108	32.4	1,509	680–3,224	35	0.0	0	NA	2	.	3	NA
Luxembourg[b]	67	14.9	79	26–228	38	2.6	4	0–46	3	.	2	NA

AMR: antimicrobial resistance; CI: confidence interval; EU/EEA: European Union/European Economic Area; HAI: healthcare-associated infection; NA: not applicable; ND: no data collected in national PPS; NP: did not participate; PPS: point prevalence survey; UNK: unknown; UK: United Kingdom.

[a]Antimicrobial resistance data were not reported by Norway and UK–Scotland in the PPS in acute care hospitals and by Denmark, Norway and UK–Scotland in the PPS in long-term care facilities. Cyprus did not submit case-based HAI data for long-term care facilities. The Czech Republic only collected institutional indicators for the PPS in long-term care facilities. For France, the percentage of non-susceptible (resistant+intermediate) isolates is given instead of the percentage resistant isolates.

[b]Country data representativeness was poor in Bulgaria and the Netherlands for the PPS in acute care hospitals and poor in Austria, Croatia, Cyprus, Greece, Luxembourg, Malta and Poland for the PPS in long-term care facilities.

[c]Cumulative 95% confidence intervals for the EU/EEA. Cumulative sums are rounded and may differ from the sum of the individual rounded country estimates.

Composite index of AMR: *Staphylococcus aureus* resistant to meticillin, *Enterococcus faecium* and *Enterococcus faecalis* resistant to vancomycin, *Enterobacteriaceae* resistant to third-generation cephalosporins, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* resistant to carbapenems. Enterobacteriaceae selected for the AMR markers: *Escherichia coli, Klebsiella* spp., *Enterobacter* spp., *Proteus* spp., *Citrobacter* spp., *Serratia* spp. and *Morganella* spp. The percentage of resistance was not calculated if less than 10 isolates were reported.

Table 4B

Composite index of antimicrobial resistance in bacteria from healthcare-associated infections in acute care hospitals (n = 8,413) and long-term care facilities (n = 565), 30 EU/EEA countries, Serbia and the former Yugoslav Republic of Macedoniaa, 2016–2017

Country	Acute care hospitals[a]								Long-term care facilities[a]			
	Composite index of AMR				Carbapenem-resistant Enterobacteriaceae				Composite index of AMR		Carbapenem-resistant Enterobacteriaceae	
	Tested isolates	Resistant isolates	Estimated annual HAI		Tested isolates	Resistant isolates	Estimated annual HAI		Tested isolates	Resistant isolates	Tested isolates	Resistant isolates
	n	%	n	95% CI	n	%	n	95% CI	n	%	n	%
Malta[b]	33	24.2	195	69–544	25	4.0	23	0–2,216	15	60.0	7	NA
The Netherlands[b]	110	14.5	2,755	1,201–6,052	73	2.7	167	40–688	15	26.7	13	0.0
Norway[a]	ND	NA	UNK	NA	ND	NA	UNK	NA	ND	NA	ND	NA
Poland[b]	531	39.9	30,356	18,445–47,719	262	6.9	2,535	976–6,569	21	42.9	13	0.0
Portugal	829	38.4	9,177	5,431–14,287	462	6.9	1,062	347–2,643	65	41.5	47	10.6
Romania	164	68.9	13,913	7,377–25,458	80	33.8	3,475	1,726–6,923	NP	NA	NA	NA
Slovakia	164	34.8	3,061	1,543–5,848	101	2.0	247	60–1,022	8	NA	4	NA
Slovenia	194	17.0	969	397–2,087	117	1.0	3	1–17	NP	NA	NA	NA
Spain	926	26.6	25,722	15,842–38,973	512	4.1	2,632	1,136–5,609	134	31.3	82	0.0
Sweden	NP	NA	UNK	NA	NA	NA	UNK	NA	3	NA	1	NA
UK–England	370	20.5	7,634	3,950–13,560	205	1.5	316	101–986	NP	NA	NA	NA
UK–Northern Ireland	40	25.0	333	145–758	17	0.0	0	NA	2	NA	0	NA
UK–Scotland[a]	ND	NA	UNK	NA	ND	NA	UNK	NA	ND	NA	ND	NA
UK–Wales	35	37.1	351	67–1,213	8	NA	0	NA	1	NA	0	NA
EU/EEA[c]	8,031	31.6	291,067	162,417–504,270	4,352	6.2	31,696	14,611–78,205	553	28.0	380	4.2
Former Yugoslav Republic of Macedonia	NP	NA	UNK	NA	ND	NA	UNK	NA	2	NA	1	NA
Serbia	382	62.0	7,555	4,516–12,230	201	25.4	1,435	801–2,481	10	40.0	8	NA

AMR: antimicrobial resistance; CI: confidence interval; EU/EEA: European Union/European Economic Area; HAI: healthcare-associated infection; NA: not applicable; ND: no data collected in national PPS; NP: did not participate; PPS: point prevalence survey; UNK: unknown; UK: United Kingdom.

[a]Antimicrobial resistance data were not reported by Norway and UK–Scotland in the PPS in acute care hospitals and by Denmark, Norway and UK–Scotland in the PPS in long-term care facilities. Cyprus did not submit case-based HAI data for long-term care facilities. The Czech Republic only collected institutional indicators for the PPS in long-term care facilities. For France, the percentage of non-susceptible (resistant + intermediate) isolates is given instead of the percentage resistant isolates.

[b]Country data representativeness was poor in Bulgaria and the Netherlands for the PPS in acute care hospitals and poor in Austria, Croatia, Cyprus, Greece, Luxembourg, Malta and Poland for the PPS in long-term care facilities.

[c]Cumulative 95% confidence intervals for the EU/EEA. Cumulative sums are rounded and may differ from the sum of the individual rounded country estimates.

Composite index of AMR: *Staphylococcus aureus* resistant to meticillin, *Enterococcus faecium* and *Enterococcus faecalis* resistant to vancomycin, *Enterobacteriaceae* resistant to third-generation cephalosporins, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* resistant to carbapenems. Enterobacteriaceae selected for the AMR markers: *Escherichia coli, Klebsiella* spp., *Enterobacter* spp., *Proteus* spp., *Citrobacter* spp., *Serratia* spp. and *Morganella* spp. The percentage of resistance was not calculated if less than 10 isolates were reported.

Table 5

Prevalence of healthcare-associated infections in long-term care facilities, 23 EU/EEA countriesa, Serbia and the former Yugoslav Republic of Macedonia, 2016–2017 (n = 103,763 residents)

Country	LTCF included in analysis	Residents included in analysis	Residents with at least one HAI in PPS sample (HAI prevalence)[b]			HAI from other facility[c]	HAI prevalence origin own LTCF[d]	LTCF beds in the country	Residents with at least one HAI on a given day, estimated	
	n	n	n	%	95%CI	%	n	n	n	(95% CI)
Austria[e]	12	2,065	105	5.1	2.8–8.9	6.5	4.6	72,602	3,504	1,966–6,145
Belgium	79	8,206	354	4.3	3.6–5.1	4.9	3.6	146,462	5,997	5,037–7,152
Croatia[e]	8	1,607	15	0.9	0.4–1.9	13.3	0.7	37,249	329	159–679
Cyprus[e]	11	312	15	4.8	2.7–7.8	ND	ND	3,436	157	89–255
Denmark	95	3,346	175	5.2	4.5–6.1	5.0	4.8	42,668	2,120	1,808–2,481
Finland	149	5,914	208	3.5	3.0–4.1	5.1	3.2	50,373	1,685	1,436–1,967
France[f]	91	6,957	206	3.0	2.6–3.4	ND	3.0	687,936	19,352	16,831–22,134
Germany	82	6,705	115	1.7	1.3–2.3	13.0	1.3	852,849	13,936	10,209–18,878
Greece[e]	13	812	51	6.3	3.7–10.5	3.8	5.9	10,849	647	381–1,079
Hungary	75	7,670	73	1.0	0.7–1.4	4.1	0.9	57,929	523	369–743
Ireland	109	5,613	276	4.9	4.2–5.8	6.0	4.5	30,531	1,427	1,207–1,682
Italy	196	11,417	442	3.9	3.3–4.6	13.6	3.1	186,872	6,870	5,787–8,149
Lithuania	26	3,438	32	0.9	0.4–1.9	15.6	0.6	11,722	104	50–212
Luxembourg[e]	16	1,616	30	1.9	1.1–3.0	0.0	1.8	6,966	123	75–199
Malta[e]	11	2,485	76	3.1	1.6–5.9	12.3	2.3	5,035	146	75–281
The Netherlands[f]	57	4,547	160	3.5	3.0–4.1	5.0	3.2	92,000	3,075	2,624–3,580
Norway[f]	62	2,447	119	4.9	4.0–5.8	2.5	4.6	39,583	1,829	1,521–2,178
Poland[e]	24	2,281	90	3.9	2.1–7.3	7.6	3.5	17,291	649	345–1,198
Portugal	132	3,633	214	5.9	4.5–7.6	15.9	4.3	8,400	470	362–608
Slovakia	59	5,091	108	2.1	1.5–3.0	4.5	2.0	27,497	554	392–778
Spain	46	6,808	579	8.5	7.0–10.3	18.9	6.2	372,306	30,064	24,688–36,501
Sweden	285	3,604	57	1.6	1.2–2.1	ND	1.6	93,000	1,396	1,051–1,864
UK–Northern Ireland	70	2,614	97	3.7	2.9–4.7	7.1	3.4	15,924	561	443–710
UK–Scotland	52	2,147	125	5.8	4.5–7.5	2.4	5.3	37,746	2,087	1,610–2,697
UK–Wales	28	966	58	6.0	4.4–8.2	0.0	6.0	24,646	1,405	1,026–1,915
Participating EU/EEA countries[b,g]	**1,788**	**102,301**	**3,780**	**3.6**	**2.9–4.5**	**8.9**	**3.1**	**2,931,872**	**99,008**	**79,539–124,064**
Former Yugoslav Republic of Macedonia	4	294	10	3.4	2.3–4.9	0.0	2.7	1,166	38	26–55
Serbia	6	1,168	37	3.2	1.9–5.1	7.3	2.8	19,654	592	362–960
EU/EEA, corrected[g,h]	NA	NA	NA	3.6	2.9–4.5	NA	NA	3,486,999	117,754	94,599–147,553
EU/EEA, corrected after validation	**NA**	**NA**	**NA**	**3.9**	**2.4–6.0**	**NA**	**NA**	**3,486,999**	**129,940**	**79,570–197,625**

EU/EEA: European Union/European Economic Area; HAI: healthcare-associated infection; LTCF: long-term care facility; PPS: point prevalence survey; ND: no data collected in national protocol; UK: United Kingdom.

[a] The Czech Republic only submitted data on institutional indicators from 11 LTCF and was not included in the current analysis.

[b] Country-weighted HAI prevalence for the EU/EEA= estimated number of residents with at least one HAI on a single day / occupied beds; occupied beds = number of LTCF beds × average occupancy of 0.95.

[c] Percentage of HAI imported from a hospital or another LTCF; not included in France and Sweden, and unknown for Cyprus (aggregated data).

[d] HAI prevalence for HAI with the own LTCF as origin, i.e. excluding HAI imported from other healthcare facilities and HAI with unknown origin (Supplement).

[e] Country data representativeness was poor in Austria, Croatia, Cyprus, Greece, Luxembourg, Malta and Poland.

[f] France, the Netherlands and Norway used a national protocol which required imputation of non-included types of HAI.

[g] Cumulative 95% confidence intervals for the EU/EEA.

[h] Corrected for non-participating EU/EAA countries with estimation for Bulgaria, Czech Republic, Estonia, Iceland, Latvia, Romania, Slovenia and UK–England combined.

In LTCF, only the number of HAI could be estimated. As LTCF usually are permanent residences, HAI do not prolong the length of stay of a resident as they do in ACH. Therefore, the incidence of HAI in LTCF per year was estimated by multiplying the prevalence by 365 days and dividing it by the duration of infection (in days), with a correction for an average occupancy of LTCF beds of 95%, calculated from institutional denominator data. The duration of infection was estimated, by type of HAI, from the date of onset to the date of the PPS, using the median duration of HAI until the day of the PPS multiplied by 2.

Validation studies

It was strongly recommended that all participating EU/EEA countries perform validation studies of their national PPSs. For the PPS in ACH, ECDC also offered financial support to national institutions coordinating PPS so that they could organise validation studies with a minimum requirement to re-examine 250 patient charts in five ACH. For both the PPS in ACH and that in LTCF, the objective was to estimate representative validity parameters at the EU/EEA level rather than at country level ([16]; ACH validation protocol available from the authors on request). Validation studies were performed by national validation teams composed of members of the national coordination teams, using the ECDC HAI case definitions as gold standard. Validation results were calculated for each country, by matching patients included in the validation sample with their corresponding data collected in the primary PPS. The percentage of false positives (FP) and false negatives (FN) was calculated from the matched analysis and applied to the total national database to calculate the sensitivity and specificity for each country, as several countries selected high prevalence wards for validation to improve precision as recommended by the validation study protocol. For correction of the EU/EEA prevalence of HAI, the EU/EEA mean FN and FP were applied to the total number of patients. The validation-corrected HAI prevalence was converted using the Rhame and Sudderth formula to estimate the corrected HAI incidence and total number of patients in ACH with at least one HAI per year in the period 2016 to 2017.

To calculate CI around EU/EEA estimates, the number of patients with at least one HAI obtained from the lower and upper limits of the country-specific 95% CIs were summed up and divided by the total number of occupied beds (for prevalence) or the total number of discharges (for estimated incidence) in the EU/EEA. These 'cumulative 95% CI' (95% cCI) therefore reflect a larger, more conservative uncertainty than would be obtained by calculating 95% CI on the EU/EEA totals, which is in accordance with the limitations of the prevalence measurement and the uncertainty inherent to the conversion of prevalence to incidence.

Results

Point prevalence survey in acute care hospitals

Participation

In total, 1,735 hospitals from 28 EU/EEA countries and one EU candidate country (Serbia) participated in the second PPS of HAI and antimicrobial use in European ACH in the period 2016 to 2017. Counting UK administrations separately, the country representativeness of the sample was optimal in 20 countries, good in 10, and poor in two countries. After adjustment for over-representation of countries contributing more than 20,000 patients to the PPS, 325,737 patients from 1,275 ACH remained in the final sample. Aggregated results were only reported for the EU/EEA, corresponding to 310,755 patients from 1,209 ACH. The distribution of the type of ACH and the percentage of patients requiring intensive care by country is shown in Table 1.

Prevalence and estimated incidence of healthcare-associated infections

A total of 19,626 HAI were reported in 18,287 patients with HAI (1.07 HAI per infected patient). The prevalence of patients with at least one HAI in the EU/EEA sample was 5.9% (country range: 2.9–10.0%; Table 2). The prevalence varied between 4.4% (2,177/49,381 patients) in primary care hospitals (n = 333) to 7.1% (7,591/104,562 patients) in tertiary care hospitals (n = 222) and was highest in patients admitted to intensive care units, where 19.2% (2,751/14,258) patients had at least one HAI compared with 5.2% (15,536/296,397) on average for all other specialties combined (Supplement).

When extrapolated to the average daily number of occupied beds per country, the weighted HAI prevalence was 5.5% (95% cCI: 4.5–6.6%). The weighted annual incidence of patients acquiring at least one HAI per year in the period 2016 to 2017, estimated using prevalence to incidence conversion, was 3.7 (95% cCI: 2.4–5.3) patients per 100 admissions. National PPS validation studies were carried out by 28 countries (UK administrations counted separately) in a total of 236 ACH in the EU/EEA. National validation teams re-examined 12,228 patient charts independently from the primary PPS surveyors. These studies showed that on average, 2.3% (country range: 0.3–5.6%) of patients who were reported as not having a HAI actually had an HAI (false negatives) while one in five (mean: 20.3%, country range: 0–46.2%) patients reported as having an HAI did not have an HAI (false positives), resulting in a mean sensitivity of HAI detection of 69.4% (country range: 40.1–94.4%) and a mean specificity of 98.8% (country range: 96.1–100%). When correcting for these results, the adjusted prevalence of patients with at least one HAI was estimated at 6.5% (95% cCI: 5.4–7.8%). Using the Rhame and Sudderth formula to convert the latter percentage, the corrected annual incidence was estimated at 4.1 (95% cCI: 3.4–4.9) patients per 100 admissions. Applying the EU/EEA averages to denominator data from non-participating EU/EEA

countries (Denmark and Sweden), this resulted in an estimated total of 98,166 (95% cCI: 81,022–117,484) patients with at least one HAI on any given day and 3,758,014 (95% cCI: 3,122,024–4,509,617) patients with at least one HAI per year in the period 2016 to 2017 in ACH in the EU/EEA.

Types of HAI and isolated microorganisms

The most frequently reported types of HAI were respiratory tract infections (21.4% pneumonia and 4.3% other lower respiratory tract infections), urinary tract infections (18.9%), surgical site infections (18.4%), bloodstream infections (10.8%) and gastro-intestinal infections (8.9%), with *C. difficile* infections accounting for 44.6% of the latter or 4.9% of all HAI. Twenty-three per cent of HAI were present on admission. One third of HAI on admission were surgical site infections. Country-weighted prevalence percentages and estimated numbers of HAI per year are shown in Table 3. After correction for non-participating countries and validation, a total of 4.5 million (95% cCI: 2.6–7.6 million) HAI were estimated to occur per year in the period 2016 to 2017 in ACH in the EU/EEA.

A total of 13,085 microorganisms were reported in 10,340 (52.7%) HAI. The 10 most frequently isolated microorganisms were *E. coli* (16.1%), *S. aureus* (11.6%), *Klebsiella* spp. (10.4%), *Enterococcus* spp. (9.7%), *P. aeruginosa* (8.0%), *C. difficile* (7.3%), coagulase-negative staphylococci (7.1%), *Candida* spp. (5.2%), *Enterobacter* spp. (4.4%) and *Proteus* spp. (3.8%).

Antimicrobial resistance in healthcare-associated infections and correlation with EARS-Net data

AST data were available for 8,031 (88.9%) of 9,034 microorganisms included in the composite index of AMR. The index was 31.6% overall (mean of countries: 30.8%) and varied from 0% in Iceland to 68.9% in Romania. The index by country was strongly correlated with the index calculated from 2016 EARS-Net data on invasive isolates (Spearman's correlation coefficient *rho*: 0.93; $p<0.001$; R^2: 0.86. Figure) and was on average 36% higher for HAI in ACH from the PPS than in the EARS-Net data (mean of countries in EARS-Net: 20.3%). Carbapenem resistance in Enterobacteriaceae was 6.2% overall (mean of countries: 5.9%) and ranged from 0% in Estonia, Finland, Iceland, Lithuania and UK–Northern Ireland to 43.7% in Greece (Table 4). This indicator also correlated well with carbapenem resistance in *E. coli*and *K. pneumoniae* in EARS-Net data (Spearman's *rho*: 0.76; $p<0.001$) and was on average 45% higher in HAI in ACH from the PPS than in EARS-Net data (mean of countries in EARS-Net: 2.6%). The total number of patients acquiring an HAI with at least one resistant microorganism was estimated at 291,067 (95% cCI: 162,417–504,270) patients for the composite index of AMR and 31,696 (95% cCI: 14,611–78,205) patients for carbapenem-resistant Enterobacteriaceae.

Point prevalence survey in long-term care facilities

Participation

In total, 3,062 LTCF from 24 EU/EEA countries and two EU candidate countries (Serbia and the former Yugoslav Republic of Macedonia) participated in the third PPS of HAI and antimicrobial use in European LTCF in the period 2016 to 2017. Counting UK administrations separately, good or optimal representativeness of the national sample was obtained in 18 of 24 EU/EEA countries. After adjustment for over-representation, 117,138 residents from 2,221 LTCF were included for analysis. The main aggregated results were reported for 80.5% of participating LTCF, i.e. general nursing homes (n = 1,025), residential homes (n = 176) and mixed LTCF (n = 587), corresponding to 102,301 residents and 1,788 LTCF in EU/EEA countries. The characteristics of LTCF and residents by country are shown in Table 1.

Prevalence of healthcare-associated infections

A total of 3,858 HAI were reported in 3,780 residents with HAI (1.02 HAI per infected resident). The prevalence of residents with at least one HAI was 3.7% (country range: 0.9–8.5%). When extrapolated to the average number of occupied LTCF beds per country, the weighted HAI prevalence in LTCF was 3.6% (95% cCI: 2.9–4.5%). Validation of the PPS in LTCF was performed for 953 residents in 17 LTCF in 10 countries. National validation teams found 1.1% (95% CI: 0.5–2.0%) false-negative residents and 19.6% (95% CI: 9.4–33.9%) false-positive residents, yielding a sensitivity of 73.7% and a specificity of 99.2% when applied on the total EU/EEA database. The country-weighted, validation-corrected HAI prevalence was 3.9% (95% cCI: 2.4–6.0%). Applying the EU/EEA prevalence to denominator data from non-participating EU/EEA countries, the total number of residents with at least one HAI on any given day in EU/EEA LTCF was estimated at 129,940 (95% cCI: 79,570–197,625) residents (Table 5).

Types of healthcare-associated infections and isolated microorganisms

The most frequently reported types of HAI in LTCF were respiratory tract infections (33.2% overall, 3.7% pneumonia, 22.0% other lower respiratory tract infections, 7.2% common cold/pharyngitis, 0.3% influenza), urinary tract infections (32.0%) and skin infections (21.5%). The majority of the reported HAI (84.7%) were associated with the LTCF where the PPS was performed, while 7.5% and 1.4% were associated with a hospital or another LTCF, respectively. The origin was unknown for 6.4% of HAI in LTCF. Country-weighted prevalence percentages and estimated number of infections per year are given by type of HAI in Table 3. The total number of HAI in LTCF in the EU/EEA, after applying EU averages for non-participating EU/EEA countries and correcting for validation, was estimated at 4.4 million (95% cCI: 2.0–8.0 million). Microbiological data in LTCF were available for 742 (19.2%) HAI. The 10 most frequently isolated bacteria were *E. coli* (30.7%), *S.*

aureus (12.3%), *Klebsiella* spp. (11.4%), *Proteus* spp. (10.6%), *P. aeruginosa* (7.1%), *Enterococcus* spp. (4.8%), *C. difficile* (4.4%), *Streptococcus* spp. (2.8%) *Enterobacter* spp. (2.1%) and coagulase-negative staphylococci (1.9%).

Antimicrobial resistance in healthcare-associated infections and correlation with data from the hospital point prevalence survey

AST results were available for 553 (77.6%) of 713 microorganisms included in the composite index of AMR. The index could be calculated for 11 countries with at least 10 isolates, and was 28.0% overall, ranging from 6.8% in Finland to 60.0% in Malta (Table 4). The composite index of AMR correlated well between ACH and LTCF, although Malta was an outlier (Figure, Spearman's *rho* excluding Malta: 0.86; $p<0.001$; $R^2 = 0.69$). On average, the percentage of resistant microorganisms was similar in both settings (regression coefficient excluding Malta: 1.08). Carbapenem resistance in Enterobacteriaceae in LTCF was 4.2% overall and did not correlate significantly with the percentage in ACH (Table 4).

Discussion

Because both the PPS in ACH and that in LTCF were performed during 2016 and 2017, this provided the first opportunity to estimate the prevalence, incidence and annual number of HAI for ACH and for LTCF in the EU/EEA for the same time period. As expected, the overall prevalence of HAI was higher in ACH than in LTCF, also after correction based on validation study results. However, when estimating the total number of HAI, both settings were shown to have similarly high numbers of HAI annually. In total, 8.9 million distinct HAI episodes were estimated to occur annually in ACH and LTCF in the EU/EEA. In ACH, where the incidence per patient could be calculated, the number of patients with at least one HAI was estimated at 3.8 (95% cCI: 3.1–4.6) million patients per year in the period 2016 to 2017.

The country-weighted HAI prevalence before validation correction in ACH of 5.5% (95% cCI: 4.5–6.7%) was similar to the HAI prevalence of 5.7% (95% cCI: 4.5–7.4%) in the ECDC PPS in ACH in the period 2011 to 2012 [3]. The unweighted HAI prevalence in LTCF of 3.7% before correction was only slightly higher than the prevalence of 3.4% found in the ECDC PPS in LTCF in 2013 [6], although imported HAI were included in the period 2016 to 2017. The final corrected country-weighted HAI prevalence estimates of 6.5% in ACH and 3.9% in LTCF were higher because they were corrected for the results of the validation studies, which made the current estimates more robust than the previous estimates. Similarly, the estimated incidence and number of HAI in ACH presented in this study were higher than the number estimated in the ECDC PPS from 2011 to 2012 [3] because of the correction for the results of the validation study and should therefore not be interpreted as an increase for ACH compared with the period 2011 to 2012.

The strong correlation of the composite index of AMR in the ECDC PPS in ACH with the EARS-Net data supports the validity of AMR data collected in the PPSs. The 36% higher percentage of resistant isolates in HAI in the ECDC PPS was expected given that EARS-Net only includes data from invasive isolates, i.e. from bloodstream infections and meningitides, and that a large proportion of isolates reported to EARS-Net are from community-associated bloodstream infections, especially for MRSA and *E. coli* resistant to third-generation cephalosporins. However, the fact that the composite index of AMR in LTCF was at the same level as in ACH, at least in countries where both indicators could be calculated, is of concern. Even though the low testing frequency in LTCF is probably biased towards HAI which are non-responsive to empiric treatment, this finding emphasises the urgent need to reinforce measures to improve infection prevention and control, antimicrobial stewardship as well as microbiological laboratory support for LTCF.

Our study has several limitations. Firstly, the small number of countries and LTCF that performed validation studies in the PPS in LTCF resulted in less robust prevalence estimates for LTCF than for ACH, even though the LTCF validation results could be used at the EU/EEA level. Secondly, the conversion from prevalence to incidence using the Rhame and Sudderth formula has been shown to have several limitations in itself, especially for smaller samples [17,18]. The estimates depend on the estimators used, as not all data can be acquired from a cross-sectional prevalence study. Nevertheless, sensitivity analyses that we performed with more recent estimator methodology (personal communication: Niklas Willrich, 24 May 2018) [15] yielded EU/EEA estimates which were close to those reported here, with few exceptions at individual country level. Especially considering the wide CI, this gave more weight to our estimates (Supplement). Thirdly, the estimates also strongly depended on the quality of the national denominator data of the number of beds, and, for ACH, discharges and patient days. Providing reliable national denominator data has been shown to be difficult for many countries that sometimes provided estimates rather than precise numbers, especially for LTCF. In addition, as national denominator data for specialised LTCF were only available in two countries, a specific incidence for these types of LTCF could not be estimated. In several countries, however, the number of beds for these LTCF are included in the total number of LTCF beds for the country. We only reported results for the main types of LTCF, as these types were consistently included in all countries. Fourthly, the number of residents with at least one HAI each year could not be estimated for LTCF in the EU/EEA. Longitudinal HAI incidence data would be required to produce such estimates. Fifthly, three countries preferred using their national PPS protocols for LTCF and one country for

ACH, resulting in less robust estimates. Sixthly, the total number of HAI with resistant pathogens could only be estimated for ACH because of the poor availability of microbiological results in LTCF Moreover, the annual incidence estimates of HAI with resistant pathogens in ACH are underestimated because: (i) in almost half of the HAI in ACH, a microorganism was not reported, (ii) for 11% of the reported microorganisms, AST results were not yet available on the day of the PPS and (iii) correction for countries without data and correction for validation was not performed. Despite these limitations, the estimated number of HAI with carbapenem-resistant Enterobacteriaceae using Rhame and Sudderth conversion in our study (31,696 infections, of which 27,393 were HAI with carbapenem-resistant *E. coli* or *K. pneumoniae*) was close to the number of 33,172 infections with carbapenem-resistant *E. coli* or *K. pneumoniae* recently estimated by Cassini et al. using a different methodology [19].

The main strengths of this study are its large sample size and the use of standardised protocols for data collection and validation across participating ACH and LTCF. Despite some countries providing less representative samples, these PPSs as a whole offer a representative picture of HAI in the EU/EEA, with benchmarks to help direct future action in ACH and LTCF in participating countries.

Conclusion

This study reports, to our knowledge, the most accurate and robust estimates of the total number of HAI in healthcare facilities in the EU/EEA to date, and confirms that HAI, and AMR in bacteria responsible for HAI, represent a significant healthcare issue and public health challenge for the EU/EEA. Considering that previous studies have shown that HAI in ACH alone are responsible for more deaths in the EU/EEA than all other infectious diseases under surveillance at European level [1,2], and that our study showed that there are as many HAI in LTCF as there are in ACH, more focus needs to be dedicated to the prevention of HAI and AMR, through the application of available recommendations and guidelines [20-25], in both ACH and LTCF.

*Erratum

The list of members of the Healthcare-Associated Infections Prevalence Study Group was left out in the original publication and was added on 16 November 2018.

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Acknowledgements

The authors would like to thank all the participating hospitals and long-term care facilities in particular, the staff that collected, validated and entered the data during the survey and the national teams that coordinated the surveys in each participating country and that performed the validation studies.

Conflict of interest

None declared.

Authors' contributions

Carl Suetens performed the analysis and wrote the original draft; Katrien Latour, Tommi Kärki, Enrico Ricchizi and Pete Kinross performed analyses, contributed to the development of the study design and the coordination of the execution of the study; Katrien Latour, Enrico Ricchizi, Béatrice Jans and Maria Luisa Moro were the contractor team that supported ECDC for the coordination of the third PPS in long-term care facilities (ECDC-funded HALT-3 project). Sonja Hansen, Susan Hopkins, Outi Lyytikäinen, Jacqui Reilly, Alexander Deptula and Walter Zingg were members of the HAI-Net PPS expert group that developed the methodology of the survey in acute care hospitals; Pete Kinross contributed to the coordination of the execution of the study; Diamantis Plachouras and Dominique L Monnet contributed to the analysis plan and the methodology of the survey; the members of the Healthcare-Associated Infections study group members contributed to the development of the study design, approved the design of the survey, contributed to the coordination of the execution of the study in their respective countries, and provided national interpretations on the analysis. All authors critically reviewed and edited the manuscript.

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Antimicrobial prescribing in long-term care facilities: a nationwide point-prevalence study, Slovenia, 2016

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Citation style for this article:
Stepan Dora, Ušaj Lea, Petek Šter Marija, Smolinger Galun Marjetka, Smole Hermina, Beović Bojana. Antimicrobial prescribing in long-term care facilities: a nationwide point-prevalence study, Slovenia, 2016. Euro Surveill. 2018;23(46):pii=1800100. https://doi.org/10.2807/1560-7917.ES.2018.23.46.1800100

Article submitted on 05 Mar 2018 / accepted on 14 Jul 2018 / published on 15 Nov 2018

Residents in long-term care are at high risk of infections because of their old age and many related health problems that lead to frequent antibiotic prescribing. The aim of the study was to assess antibiotic use in Slovenian long-term care facilities (LTCFs). The point-prevalence study was conducted between April and June 2016. Online questionnaires were sent to all Slovenian LTCFs. Eighty (68.4%) of the 117 LTCFs contacted, caring for 13,032 residents (70.6% of all Slovenian LTCF residents), responded to the survey. On the day of the study, the mean antibiotic prevalence per LTCF was 2.4% (95% confidence interval: 1.94–2.66). Most (70.2%) of the residents taking antibiotics were female. Most residents were being treated for respiratory tract (42.7%) or urinary tract (33.3%) infections. Co-amoxiclav and fluoroquinolones were the most frequently prescribed antibiotics (41.0% and 22.3% respectively). Microbiological tests were performed for 5.2% of residents receiving antibiotics. Forty nine (19.8%) residents receiving antibiotics were colonised with multidrug-resistant bacteria (MDR). Antibiotic use in Slovenian LTCFs is not very high, but most prescribed antibiotics are broad-spectrum. Together with low use of microbiological testing and high prevalence of colonisation with MDR bacteria the situation is worrisome and warrants the introduction of antimicrobial stewardship interventions.

Introduction

All European Union countries have seen an increase in the population aged 65 years and over in the past 10 years. In many countries, including Slovenia, elderly people represent one fifth or more of the population [1]. In Organisation for Economic Co-operation and Development member countries in 2011, the number of long-term care beds ranged from 17.5 to 81.7 per 1,000 inhabitants 65 years and older [2]. Residents in long-term care are at high risk of infections because of their old age and age-related health problems that lead to frequent antibiotic prescribing. A systematic literature review showed that 47% to 79% of long-term care facility (LTCF) residents receive antibiotics each year [3]. In addition, LTCFs may represent foci for multidrug-resistant bacteria [4].

Antimicrobial stewardship interventions in nursing homes are needed to provide effective treatment for patients with infection and avoid excessive and inappropriate use that may aggravate antimicrobial resistance in the facilities and beyond [5]. The first step towards improved antimicrobial prescribing is to analyse the current patterns of antimicrobial use. Several studies on antimicrobial use in LTCFs have been published in the past few years, but with some exceptions [6-10], the studies included relatively few LTCFs from one country. Slovenia was included in the Healthcare-Associated Infections in Long-Term Care Facilities Project (HALT) in 2010 with six LTCFs and in the 2013 HALT-2 study with four LTCFs; in the latter study the Slovenian LTCF sample was not representative [11,12]. The aim of this study was to provide a deeper insight into antibiotic prescribing patterns in Slovenian LTCFs.

Material and methods

Study population

In Slovenia, there are 129 LTCFs, 12 of which are specialised nursing homes for adults; all other LTCFs serve mixed populations [13]. After excluding specialised institutions, we invited 117 Slovenian LTCFs, comprising 18,457 residents, to take part in our study. The contact information for all LTCFs in the country was obtained from the website of the Association of Social Institutions in Slovenia [13]. Data on age and sex of residents were obtained from the Association's 2016 report [14]. All residents who were receiving systemic antibiotic treatment and who gave consent to the study were included in the analysis.

Table 1

Characteristics of the facilities and residents included in the study on antimicrobial prescribing in long-term care facilities, Slovenia 2016 (n = 80 facilities)

Variable	n	%
Number of residents in participating LTCFs	13,032	100
Mean number of residents per facility	163 (range 21–608)	NA
Number of wheelchair users	3,693	28.3
Number of bedridden residents	3,511	26.9
Number of residents with dementia	5,467	42.0

LTCF: long-term care facility; NA: not applicable.

Study design and time schedule

For our point-prevalence study, we used an adapted version of the HALT protocol [12]. The study was conducted in each facility in the time window between 1 April and 30 June 2016. On the day of the study, data on patients on antimicrobial treatment and the facility were collected simultaneously. The directors, chief nurses and medical doctors of each LTCH were informed about the survey in advance, but the exact day of the survey was communicated to the LTCF only 1 or 2 days before the survey day.

Data collection

Data were collected either by an LTCF employee (most often a (head) nurse) or, in the case of larger facilities, a local researcher supported by the survey coordinators. On the day of the study, the study coordinators were in contact by phone or in person with all local researchers, who collected the data themselves to ensure the correct execution of the survey. All facilities were asked to fill in two online questionnaires. The first was an institutional questionnaire on LTCF characteristics and population (numbers of residents, wheelchair users, bedridden residents, residents with dementia, residents taking antimicrobial treatment and characteristics of the physician working in the facility). The second was a questionnaire for each resident receiving systemic antibiotic treatment on the day of the study. It explored the resident's characteristics (age, sex), antimicrobial use (compound name, indication for therapy, prescribed doses, route of administration), risk factors (presence of urinary catheter, vascular catheter and wounds), care-load indicators (faecal and/or urinary incontinence, dementia, impaired mobility). We asked who prescribed the antibiotic treatment and which diagnostic tests were performed to diagnose infection. Colonisation with multidrug-resistant bacteria (meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), extended-spectrum beta-lactamase (ESBL) producing enterobacteria, carbapenem-resistant Enterobacteriaceae (CRE)) in patients receiving antibiotics was recorded from the residents' documents. We included all oral, intramuscular and intravenous systemic antibiotic treatments. Topical antibiotics, antivirals, antifungals and antiseptics were excluded, as well as mupirocin nasal ointment for MRSA decolonisation.

Data analysis

Numeric variables were presented with arithmetic mean (x), median, range (highest and lowest value) and standard deviation (sd). Descriptive variables were presented as rates and percentages. Statistical significance was assessed with the chi-squared test and odds ratios were calculated with R 3.3.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Ethical considerations and confidentiality

The study was approved by National Medical Ethics Committee of the Republic of Slovenia (n. 0120–568/2015–4, KME 32/12/15). Informed consent to collect relevant data was obtained from residents or, when residents were considered by nursing staff to lack the capacity to consent, their next of kin. To ensure confidentiality, the residents' data were anonymised and unique LTCF and resident numbers were recorded in the questionnaires. The link between the labels given to the LTCF and the patients was discarded after data analysis.

Results

Eighty out of 117 Slovenian LTCFs (68.4%) responded to our invitation, and 13,032 (70.6%) residents participated in our survey. On the day the survey was conducted, 317 of 13,032 residents received antibiotics (2.4%; median: 1.9%; range: 0–7.6%; 95% confidence intervals (CI): 1.94–2.66%). Further analysis of the per-patient data was performed on the population of 255 patients (2.0% of residents in the LTCFs included in the study) who gave informed consent. Some responses were missing for up to 3% (8/255) of residents in the study. The characteristics of the participating LTCFs are presented in detail in Table 1.

The majority of the physicians (80%; 80/100) who prescribed the antibiotic treatment worked in other institutions beside the LTCF (health centre, hospital), the remaining 20% (20/100) worked only in the facility. The antibiotic treatment for 208 of 247 residents (84.2%) was prescribed by general practitioners working in the LTCF; for 17 cases (6.9%) the treatment was started in hospital, for 11 cases (4.5%) the antibiotics were prescribed in specialist clinics, and four antibiotic therapies (1.6%) were prescribed by a doctor on duty.

The mean age of the residents with an antimicrobial treatment was 83.4 years (median: 85 years; range: 46–100 years), 179 (70.2%) were female. Other characteristics of the residents included in the study are presented in Table 2.

Detailed data on antibiotics were available for 251 residents, seven residents (2.8%) received two antibiotic agents simultaneously. 241 residents (96.0%) received

Table 2

Characteristics of the residents receiving antibiotics and included in the analysis, study on antimicrobial prescribing in long-term care facilities, Slovenia 2016 (n = 255)

Characteristic	Total		Male		Female	
	n	%	n	%	n	%
Indication for antibiotic treatment	**255[a]**	**100[a]**	**76[a]**	**100[a]**	**179[a]**	**100[a]**
Respiratory tract infection	109	42.7	31	40.8	78	43.6
Urinary tract infection	85	33.3	24	31.6	61	34.1
Skin and skin structure infections	50	19.6	17	22.4	33	18.4
Gastrointestinal infections	3	1.2	1	1.3	2	1.1
Prophylaxis	3	1.2	1	1.3	2	1.1
Other	12	4.7	4	5.3	8	4.5
Associated diseases and risk factors for various infections	**247[a,b]**	**100[a]**	**73[a]**	**100[a]**	**174[a]**	**100[a]**
Urinary catheter	34	13.8	18	24.7	16	9.2
Vascular catheter	2	0.8	0	0	2	1.1
Urinary incontinence	189	76.5	46	63.0	143	82.2
Faecal incontinence	148	60.0	44	60.3	104	59.8
Wounds, ulcers	53	21.5	21	28.8	32	13.4
Dementia	99	40.1	28	38.4	71	40.8
Wheelchair-users	77	31.2	22	30.1	55	31.6
Bedridden residents	95	38.5	28	38.4	67	38.5
Other (post cerebrovascular insult, nasogastric tube etc.)	23	9.3	10	13.7	13	7.5
No risk factor	18	7.3	6	8.2	12	7.0

[a] More than one category possible in one individual.

[b] Information available for 247 residents.

antimicrobial treatment per os, only two residents received parenteral antibiotic treatment (co-amoxiclav intravenously or gentamicin intramuscularly), seven residents (2.8%) received treatment per nasogastric tube (co-amoxiclav, cefixime, ciprofloxacin, moxifloxacin) and one per percutaneous gastric tube (co-amoxiclav). Co-amoxiclav was the most frequently prescribed antibiotic overall, used in 14.1% of urinary tract infections (UTI), 61.7% of respiratory tract infections (RTI) and 48.7.0% of skin and skin structure infections. Fluoroquinolones were the second most commonly prescribed antibiotics, with ciprofloxacin being the most common in this group; ciprofloxacin was prescribed in 31.8. % of UTI cases (Supplementf1). Detailed information on the antibiotic treatments by indication is presented in the Supplement.

The commonest diagnostic tests used in RTI were C-reactive protein (66/105, 62.9%) and blood cell count (in 60/105, 57.1% of RTI), the urine dipstick test was performed in 71/83 (85.5%) of UTI cases, whereas for most skin infections (28/48, 58.3%) no diagnostic tests were done. Microbiological testing was performed in 13/245 (5.3%) of cases.

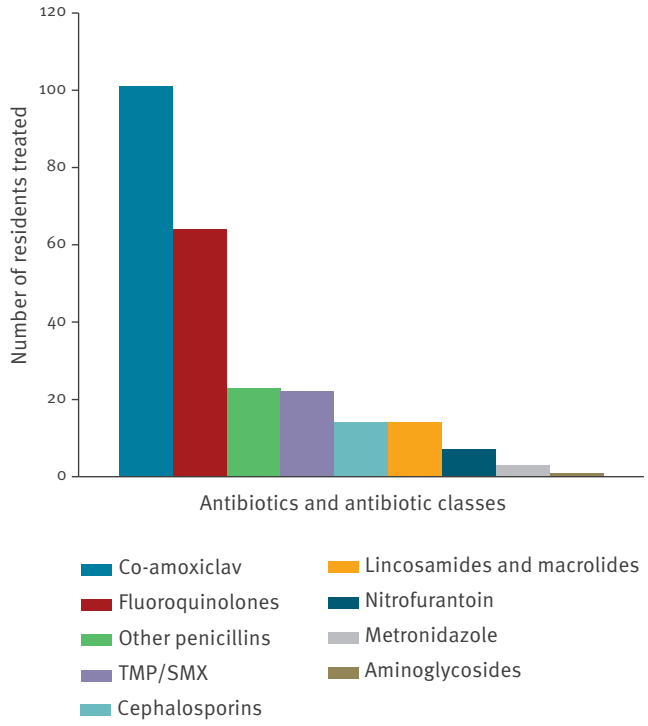
Forty nine (19.8%) of 247 residents receiving antibiotics were colonised with multidrug-resistant bacteria. Specifically, 39/247 (15.8%) of residents receiving antibiotics were colonised with ESBL-producing bacteria, 11/247 (4.5%) with MRSA and there were two cases of CRE. No cases of VRE colonisation were found. Three residents were colonised with multiple multi-drug resistant micro-organisms (MDRO), of whom two had MRSA and ESBL and one was colonised with ESBL and CRE. Of the 36 residents colonised only with ESBL-producing bacteria, most received co-amoxiclav (n = 9), followed by fluoroquinolones (n = 6) and TMP/SMX (n = 5). Of 11 residents colonised with MRSA, four residents received co-amoxiclav.

Risk factors for antimicrobial use

According to the Slovenian statistics office, 63% of LTCF residents in 2016 were 80 years old and older [14]. In our study, the share of residents receiving antibiotics who were ≥ 80 years old was 72.9%, the difference was statistically significant ($p < 0.01$, chi-squared test, OR = 0.626). Our study had 9,005 female residents who participated (69.1%) and 4,027 male residents (30.9%). Of these, 179 women and 76 men received antibiotic treatment. Sex was not significantly correlated with antibiotic prescribing ($p = 0.702$, chi-squared test, OR = 1.054). Dementia and being wheelchair-user were not significantly correlated with antibiotic prescribing ($p = 0.307$, chi-squared test, OR = 0.876, and $p = 0.506$, chi-squared test, OR = 1.096 respectively), however antibiotics were prescribed more often for bedridden residents ($p < 0.01$, chi-squared test, OR = 1.627) (Tables 1 and 2).

Figure

Distribution of prescribed antibiotics and antibiotic classes, study on antimicrobial prescribing in long-term care facilities, Slovenia, 2016 (n = 251)



Discussion

This is the first nationwide study to investigate antibiotic prescribing in LTCFs in Slovenia. Of the 13,032 residents included in the study, 317 residents (2.4%) received antimicrobial treatment on the day of our survey. Several other studies have investigated the prevalence of antibiotic use in LTCFs with similar methodology. European Surveillance of Antimicrobial Consumption (ESAC) conducted research in 21 European countries in April 2009 that included 323 LTCFs; the mean prevalence of antimicrobial treatment was 6.3% with a range from 1% to 17.3%. Slovenia was also included in the survey, with six LTCFs, and the antibiotic prevalence was 3.59% [15]. Another report from the same ESAC project included 85 LTCFs from 15 countries in April and in November 2009; the mean antibiotic prevalence was 6.5% and 5.0% respectively [16]. Two point-prevalence surveys supported by the European Centre for Disease Prevention and Control (ECDC) were performed in 2010 and 2013 [11,12]. Both surveys reported on the varying usage of antimicrobials in different European countries, including Slovenia. In HALT, the mean prevalence of antimicrobial treatment was 4.3% (range: 0.0–13.3%). Slovenia was represented with six LTCFs, and the prevalence of antibiotic treatment was 2.3% [11]. In the HALT-2 study, the mean European prevalence of antimicrobial treatment was 4.4% (range: 1–12.1%) [12]. Slovenia was also included in HALT-2, but because there were only two participating LTCFs, the results were poorly representative. A point-prevalence study was also carried out in 44 Norwegian nursing homes in spring 2006. Of the 1,473 nursing home residents, 224 (15%) were prescribed antibiotics [17]. Our survey showed lower antimicrobial use in Slovenian LTCFs than in several other European countries. The results are in line with the data on the consumption of antimicrobials for systemic use in the community (primary care sector) in Europe from 2016. Slovenia was the country with the sixth lowest prevalence of antimicrobial prescriptions (13.9 defined daily doses (DDD)/1,000 inhabitants/day) [14].

However, the prevalence of antibiotic use in LTCFs may not be comparable because of the different types of LTCFs included in the studies [18]. In our study we included mixed LTCFs, which were also the main types of LTCFs included in the HALT studies [11,12]. The mean age of residents on antimicrobial treatment in our study was 83.4 years, which is only slightly higher than the mean age in the HALT (82.5 years) and in HALT-2 (81.8 years) studies and comparable to the two ESAC reports (83 years). The population in the Norwegian study was older than in Slovenian LTCFs (76% vs 66.8% of residents aged 80 years or older) and some of the residents lived in facilities which specialised in dementia care [17,19,20].

When comparing surveys, we must also consider differences in the data collection time [18]. Our study was conducted between April and June 2016 when the influenza season was over. The differences in the time period of evaluation and the particular meteorological details of the years studied also might explain the differences between the percentages of antibiotic use in our study and the above-mentioned surveys.

In our study we found that residents receiving antibiotic treatment were older than the LTCF population in general. A Finnish study which analysed antibiotic treatments in LTCFs over a 1-month period found age below 85 years to be a risk factor for antibiotic therapy [19]. Most residents receiving antibiotics in our study were female (70%), which is similar to the findings of all previously mentioned studies [11,12,15-17]. Surprisingly, in a Canadian study which analysed antibiotic prescribing in LTCFs during a 1-year period, 74% of residents receiving antibiotics were men (74%) [20]. The prevalence of antibiotic treatments in female residents in our study reflects the predominance of female population among the LTCF residents. No influence of sex on the prevalence of antibiotic use was found in the HALT study, and there were slightly fewer female residents receiving antibiotics in comparison with the general LTCF population in HALT-2 [12]. The Finnish study found female sex to be a risk factor for antibiotic therapy [19].

Prophylaxis was given to only 1.2% of residents in our study, which that is much less than other European studies: in the HALT and HALT-2 studies, prophylaxis was given to 27.7% and 27.2% of residents receiving antibiotics, and in the Norwegian study, prophylactic use

was even more frequent than therapeutic use [11,12,17]. Low prophylactic use seems to be a Slovenian speciality, since it has already been reported in the HALT and HALT-2 studies, but the difference may be partly explained by our questionnaire where prophylaxis was not specified by anatomical site, and antibiotics given as prophylaxis for UTIs were could possibly be marked under the 'UTI' box and not the 'prophylaxis' box.

In our study antibiotics were most commonly prescribed for RTIs followed by UTI use. In the Finnish, Norwegian and Swedish studies, UTI use outnumber the RTI use, and in the European international studies, the relative frequency of indication varied from country to country with the predominance of RTIs or UTIs [11,12,17,19,21]. We may assume that the differences do not only reflect different incidence of infections but also the diagnostic approach of physicians.

Penicillins were the most commonly prescribed antibiotic class in our survey, and also in the two European studies [11,12]. More worrying is the high use of co-amoxiclav, which was prescribed far more often than other penicillins (Figure). Another problematic finding is the high prevalence of fluoroquinolones. Co-amoxiclav and fluoroquinolones are broad-spectrum antibiotics which have been linked to side-effects including *Clostridium difficile* infections and antimicrobial resistance [22-24]. The same pattern of co-amoxiclav followed by fluoroquinolones as the most commonly prescribed antibiotics was found in a French study [10]. In the HALT and HALT-2 studies, most patients received penicillins variously co-prescribed with co-amoxiclav, other antibacterials (J01X, mostly nitrofurantoin) and fluoroquinolones. In the contrast, in Norway most residents received therapy with pivmecillinam or penicillin V [11,12,17]. In our survey most residents received oral treatment. In the HALT and HALT-2 study oral administration of antibiotics was most common, but in some countries such as Italy, Bulgaria and Spain, a large proportion of antibiotics were given parenterally [11,12]. Most antibiotics in our survey and in several other studies including the two European surveys [11,12] were prescribed by primary care physicians or doctors working in the facilities, which gives an opportunity for efficient educational and other antimicrobial stewardship interventions.

Our study has several limitations. We were not able to include all LTCFs in the country, and we chose a simplified approach compared to the ECDC HALT protocols due to limited resources [12]. We did not collect microbiology results, we only collected the number of tests done. We did not classify the facilities, but excluded specialised facilities as described above. There was no strict case definition, diagnosis of the infections was obtained from patient records. Since we required informed consent from every patient (or their family) on antibiotics if we wanted to collect patient-related data, we were unable to collect detailed data on residents receiving antibiotics who did not sign informed consent, or to perform detailed analysis of patient data for the whole cohort of patients on antibiotics. In addition, we did not check the appropriateness of antibiotic therapy. Colonisation was only recorded in residents receiving antibiotics and not in other LTCF residents, and it was only derived from the medical records, not microbiological testing. Consequently, we were not able to draw any additional conclusions important for the potential interventions. We were only able to compare the sex and the age of the residents receiving antibiotics with the data from the literature that limits the relevance of statistical comparison. However, the study gives the first complete insight into antibiotic prescribing in LTCFs in Slovenia, which is needed for any further antimicrobial stewardship activity in the country.

Dementia was diagnosed in 40% of patients receiving antibiotics in our study, but in contrast with some other studies [25,26] a dementia diagnosis among residents receiving antibiotics was not more common than in other residents. In the Finnish study, antibiotic therapy was more common in patients with reported confusion [19]. Immobility was not associated with higher antibiotic use in wheelchair users, significant association was only found for bedridden residents. Being bedridden was identified as risk factor for antibiotics also by the Finnish authors [19].

Almost one fifth (19.2%) of residents receiving antibiotics in our study were colonised with multidrug-resistant microorganisms, and most of them harboured ESBL-producing bacteria. High colonisation rates were found in other studies [27,28], but different methodologies prevent the comparison of our data. We have not investigated the causative agents of infections in the residents receiving antibiotics, but the mismatch between the susceptibility of the colonising bacteria and prescribed antibiotics points to potentially ineffective antibiotic therapy in at least some cases. The use of microbiology tests in the study population (in only 5.2% of cases), is much lower than reported in the HALT studies, and increases the possibility of under-treatment, despite the fact that patients receiving treatment are generally prescribed broad-spectrum antibiotics such as co-amoxiclav and fluoroquinolones [11,12].

In conclusion we may say that the use of antibiotics in Slovenian LTCFs is not high. More problematic is the frequent use of co-amoxiclav and fluoroquinolones, broad-spectrum antibiotics known as drivers of resistance, and the cause of several important side effects. Almost exclusive empirical antibiotic use and an already-high colonisation rate with multidrug-resistant bacteria give an impression of potentially inappropriate and ineffective antibiotic treatment. Introduction of antimicrobial stewardship including guidelines for diagnostics and therapy of infections in fragile elderly population in Slovenian LTCFs should be a priority. Special attention should be paid to the most vulnerable bedridden residents.

Acknowledgements

We are grateful to all directors, head nurses and doctors working in Slovenian long-term care facilities for their help with the survey.

Conflict of interest

None declared.

Authors' contributions

Dora Stepan drafted the study protocol and the questionnaire, performed the survey and the analysis of the results, and drafted the manuscript.

Lea Ušaj drafted the study protocol and the questionnaire, performed the survey and the analysis of the results, and drafted the manuscript.

Marija Petek Šter helped to organise the study and reviewed the manuscript.

Marjetka Smolinger helped with the organisation of the study and maintained contact with the directors and head nurses in the long-term care facilities.

Hermina Smole helped with the organisation of the study and maintained contact with the directors and head nurses in the long-term care facilities.

Bojana Beović had the original idea for the study, supervised the development of the study protocol and the questionnaire, supervised the survey and the analysis of the results, and reviewed all drafts of the manuscript.

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Research article

Antimicrobial prescribing and infections in long-term care facilities (LTCF): a multilevel analysis of the HALT 2016 study, Ireland, 2017

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Citation style for this article:
Tandan M, Burns K, Murphy H, Hennessy S, Cormican M, Vellinga A. Antimicrobial prescribing and infections in long-term care facilities (LTCF): a multilevel analysis of the HALT 2016 study, Ireland, 2017. Euro Surveill. 2018;23(46):pii=1800278. https://doi.org/10.2807/1560-7917.ES.2018.23.46.1800278

Article submitted on 24 May 2018 / accepted on 05 Nov 2018 / published on 15 Nov 2018

Background: The 2016 point prevalence survey (PPS) of healthcare-associated infections (HAI) and antimicrobial use (AMU) in Irish long-term care facilities (LTCF) (HALT) showed a 9.8% AMU and 4.4% HAI prevalence, based on aggregated data analysis. **Aim:** Our aim was to identify institutional and resident risk factors of AMU and HAI. **Methods:** HALT 2016 gathered information using institutional and resident questionnaires, for residents who met the surveillance definition of active HAI and/or AMU, limiting analysis to the aggregated institutional level. In January 2017, we requested additional data on age, sex, urinary catheter use and disorientation of current residents from HALT 2016 LTCF and matched to 2016 HALT data. **Results:** Of 224 HALT 2016 LTCF, 80 provided additional information on 3,816 residents; prevalence of AMU was 10.6% and HAI was 4.7%. Presence of a coordinating physician (Odds ratio (OR): 0.3; 95% confidence interval (CI): 0.2–0.6), antimicrobial stewardship committee (OR: 0.2; 95%; CI: 0.1–0.6), healthcare assistants (OR: 0.9; 95% CI: 0.9–1.0), antimicrobial consumption feedback (OR: 0.3; 95% CI: 0.1–0.6) and medical care by personal general practitioner (OR: 0.6; 95% CI: 0.7–1.0) were associated with less AMU and feedback on surveillance of infection prevention and control (IPC) practices (OR: 0.6; 95% CI: 0.3–1.0) with less HAI. AMU and HAI varied significantly between LTCF. **Conclusions:** Multilevel modelling identified significant inter-facility variation, as well as institutional factors associated with AMU and HAI. An antimicrobial stewardship committee linked with feedback on IPC and prescribing was associated with reduced AMU and HAI.

Introduction

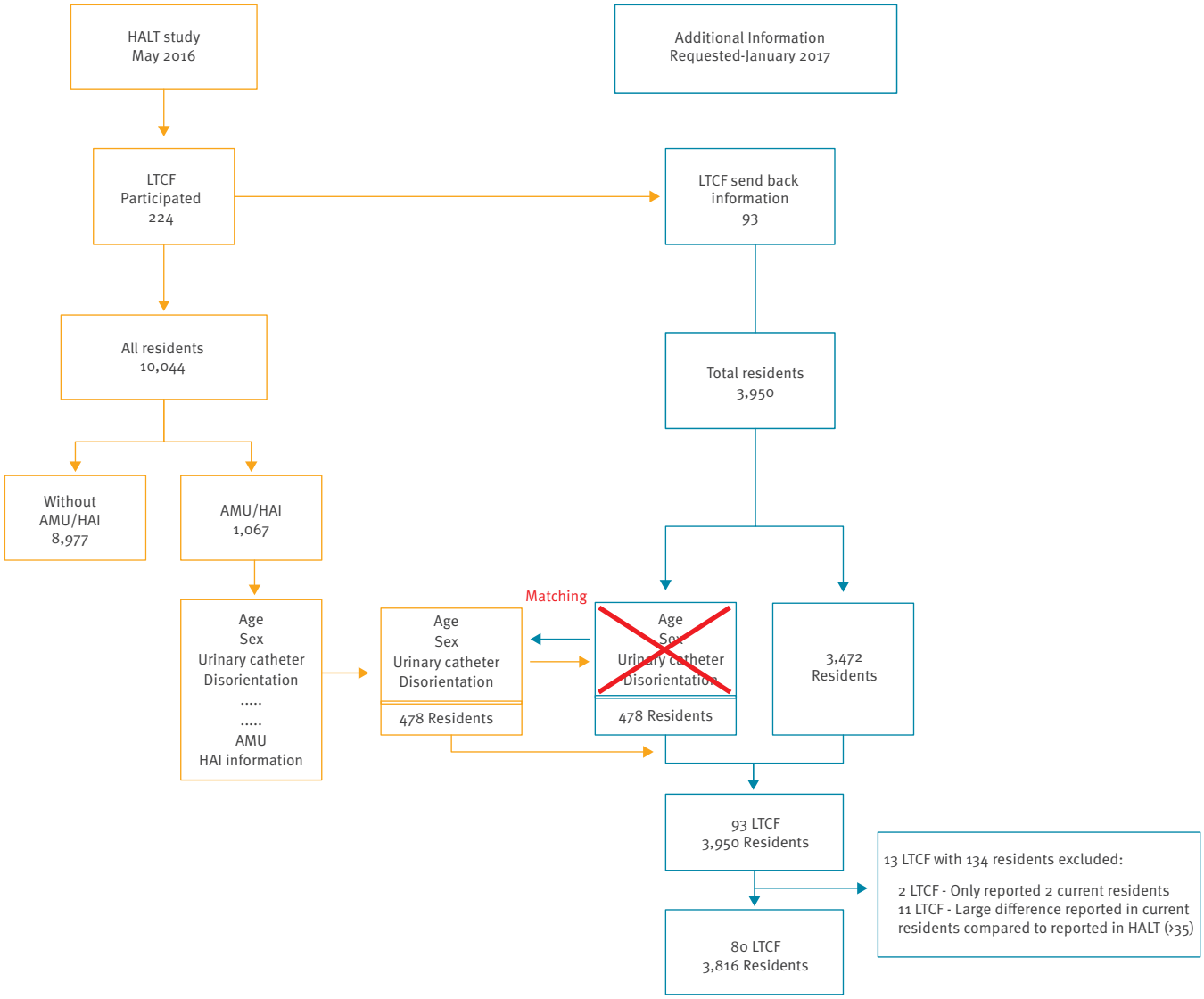
Residents in long-term care facilities (LTCF) are prone to healthcare-associated infections (HAI) due to co-morbidities with invasive procedures and exposure to indwelling devices [1]. The term LTCF may encompass a diverse range of resident care types, such as general nursing homes, intellectual disability care, psychiatric care, care for physical disability, rehabilitation and mixed-care types [2]. Due to residents' characteristics, such as co-morbid conditions, physical and functional weaknesses, and living environment, LTCF are a common setting for infections. Infection prevention and control (IPC) is challenging in LTCF because of high antimicrobial use [3,4], with urinary tract infection (UTI), respiratory tract infection (RTI) and skin and soft tissue infection (SSTI) being the most common infections for which antimicrobials are prescribed [5,6]. Prior studies have reported that nearly half of the antimicrobial use (AMU) in LTCF is unnecessary [7,8]. Inappropriate prescribing can be due to the wrong antimicrobial, indication, treatment duration or dosage. Antimicrobials account for 20% of adverse drug events in nursing homes [8]. Long-term AMU, particularly in LTCF, has been linked to *Clostridium difficile* infection (CDI), mucosal candidiasis, pulmonary and liver damage, and increased risk of colorectal adenoma [9,10].

There is substantial variation in AMU and healthcare-associated infections (HAI) between LTCF and between countries [11,12]. In the HALT 2013, the crude AMU prevalence was 4.4% (range: 1% in Hungary to 12.1% in Greece), with a HAI prevalence of 3.4% (range: 0.4% in Croatia to 7.1% in Portugal) [13]. Compared with the EU/EEA overall, the AMU prevalence in Ireland was double (9.8% in 2013 and 2016), even though the HAI prevalence was similar (5.3% in 2013 and 4.4% in 2016) [5,14].

Judicious AMU through active antimicrobial stewardship programmes is essential to slow the emergence

Figure 1

Flow diagram matching HALT 2016 data with additional database, Ireland, 2017



AMU: antimicrobial use; HAI: healthcare-associated infection; HALT: healthcare-associated infections in long-term care facilities; LTCF: long-term care facility.

of multidrug-resistant organisms (MDRO) [15]. While hospital antimicrobial stewardship programmes reduce the incidence of HAI, MDRO colonisation and CDI, their implementation in LTCF is more challenging [8,16]. The United States (US) Centers for Disease Control and Prevention (CDC) published an antimicrobial stewardship guideline specific to LTCF [17], but no such guidelines exist at the EU level, even though some European countries have specific guidelines for antimicrobial prescribing in LTCF [18]. The decision to prescribe an antimicrobial depends on a number of factors, including clinical situation, advance care plans, utilisation of diagnostic resources, perceived risk by treating physicians, resident demand, the influence of family and nursing staff, and the availability of guidelines [19].

HAI risk factors in LTCF can be related to the individual resident, the environment/institution or the treatments given [20,21]. Resident risk factors include age; length of stay; disability, such as impaired mobility or disorientation; the presence of indwelling devices; multiple comorbidities or chronic skin breaks such as pressure sores [22,23].

The healthcare-associated infections in long-term care facilities (HALT) PPS have been conducted in the

EU/EEA on three occasions since 2010, most recently in 2016–17 [5,14,24,]. We evaluated the association between institutional and resident factors and AMU and HAI in Ireland, using a combination of HALT 2016 data and additional resident risk-factor data sought retrospectively.

Methods

Study design and settings

HALT is coordinated by the European Centre for Disease Prevention and Control (ECDC), according to a standardised protocol, with the aim of evaluating AMU and HAI in LTCF [2]. In Ireland, HALT is a voluntary project coordinated by the Health Protection Surveillance Centre (HPSC), with four national PPS performed to date and increased numbers of participating LTCF each survey (2010: n = 69; 2011: n = 108; 2013: n = 190; 2016: n = 224) [5,14,24,25]. The presented analysis is based on data from the most recent HALT survey conducted in Ireland in May 2016, the full report of which was published in March 2017 [5].

Study participants

Eligible residents from participating LTCF were included in the study, with demographic information, risk factors, AMU and the presence of active HAI recorded. Residents were considered eligible if they met the surveillance case definition of active HAI and/or were prescribed systemic antimicrobials on the PPS date. HAI was defined using the updated standardised definitions (McGeer criteria [26]) of infection for surveillance in LTCF, published by the Society for Healthcare Epidemiology of America (SHEA) and the US CDC [27].

Data collection and management

Two paper questionnaires (institutional and resident) were used to collect information [5]. Institutional questionnaires recorded aggregated resident denominator and risk factor data, such as age›85 years, indwelling device use, etc., along with LTCF bed occupancy, medical care coordination, and IPC and antimicrobial stewardship activities and resources. Resident questionnaires recorded demographic and risk factor information (hospitalisation in the past 3 months, surgery in the past 30 days or the presence of vascular/urethral catheters, incontinence, disorientation or impaired mobility) for residents with active HAI and/or systemic AMU on the PPS date. Completed questionnaires were entered into the HALT software.

The first analysis was based on Ireland's HALT 2016 results, looking at aggregated data and the variation between 224 participating LTCF. However, to explore the effects of LTCF characteristics on individuals and to analyse the variation within LTCF or between individuals, more detailed information on all residents is required. Each HALT 2016 participating LTCF was subsequently contacted by the HPSC in January 2017, requesting additional anonymised data on all current residents (age, sex, presence of a urinary catheter and disorientation), with the rationale of limiting the workload associated with additional data collection. The assumption was that each LTCF's overall resident population would be unlikely to have changed significantly between May 2016 and January 2017. The additional information from each LTCF was matched to the original database, retaining the information of the eligible residents with AMU and/or with HAI to form the 'additional database'. HALT 2016 residents were matched with those on the additional database by sex and age (closest in age, in some instances), as well as urinary catheter use and disorientation; the case in the additional database was then replaced with the matched case from the original HALT 2016 database (Figure 1).

Outcome variables

The outcome variable for the HALT 2016 LTCF was the prevalence of AMU and HAI calculated per 1,000 residents. Mathematically expressed as:

$$\text{Prevalence of AMU} = \frac{\text{Total number of residents on antimicrobials on the day of survey}}{\text{Total number of residents in LTCF on the day of survey}} X\ 1{,}000$$

$$\text{Prevalence of HAI} = \frac{\text{Total number of residents with active HAI on the day of survey}}{\text{Total number of residents in LTCF on the day of survey}} X\ 1{,}000$$

The outcome variables for the additional database LTCF were 'resident with AMU (yes/no)' and 'resident with HAI (yes/no)'.

Predictor variables

In the additional database, age, sex and the presence of a urinary catheter (yes/no) or disorientation (yes/no) were available for each resident. Institutional variables in the multilevel analysis for AMU include those collected as part of antimicrobial stewardship activities; for HAI, these include IPC activities in the LTCF (Table 1).

Two databases were prepared for analysis: (i) the original HALT 2016 database with institutional data and aggregated resident information and (ii) the additional database with institutional data and individual resident information.

Statistical analysis

The aggregated analysis of the original HALT 2016 database used a negative binomial regression analysis (a conventional approach) to compare the AMU and HAI prevalence in LTCF. A negative binomial regression was used to model count data when the outcome was overdispersed [28]. This analysis reflects the skewed shape of the outcome variables, such as a high number of zeros or close to zero prevalence. The coefficients were presented as prevalence rate ratios (PRR).

The multi-level logistic regression analysis used the hierarchical structure of the data (residents nested within LTCF) and estimated the chance of a resident having AMU or HAI. The suitability of a multi-level model was checked by introducing LTCF-level variables (random parameters) to the empty model. The empty model (without explaining variables) was compared

Table 1

Variables available for antimicrobial use and healthcare-associated infection at long-term care facilities, HALT 2016 (n = 224) and additional database (n = 80), Ireland, 2017

Outcome	Variable
Antimicrobial use	• Percentage of residents › 85 years • Percentage of male residents • Percentage of residents with urinary catheter • LTCF type • LTCF size • Number of whole-time equivalent healthcare assistants • Presence of internal coordinating physician for medical care • Physician in charge of medical coordination can consult medical records of residents • Presence of antimicrobial stewardship committee • System to provide feedback to prescribers on antimicrobial consumption • Microbiological sample taken before antimicrobial started • Permission required for prescribing restricted antimicrobials • Presence of at least one antimicrobial prescribing guideline (UTI or RTI or SSTI) • Medical care provided by personal GP or others • Use of a restrictive list of antimicrobials
Healthcare- associated infections	• Percentage of residents › 85 years • Percentage of male residents • Percentage of residents with a urinary catheter • Percentage of residents with pressure sores • Percentage of single rooms • Development of a care protocol • Feedback of surveillance results to staff on IPC practices • Decision on isolation and precautions of residents colonised with resistant microorganisms • Presence of an IPC committee

HALT: healthcare-associated infections in long-term care facilities; IPC: infection prevention and control; LTCF: long-term care facility; RTI: respiratory tract infection; SSTI: skin and soft tissue infection; UTI: urinary tract infection.

with models with explaining variables and was considered an improvement if the increase in explained variance is statistically significant (log-likelihood ratio test statistic with p value‹ 0.05) [29]. Caterpillar plots were generated to compare the variance within and between LTCF. The model-building process used a forward stepwise selection process and individual (resident)-level variables were first introduced followed by group (LTCF)-level variables. Due to high colinearity between explaining variables, each variable was introduced separately and variables with a p value‹0.25 were retained in the model [30].

An adjusted odds ratio (aOR) with 95% confidence interval (CI) for AMU and HAI was calculated for the fixed effects. The Larsen's median OR (mOR) was calculated for each model to compare the differences in the outcome between LTCF [31,32]. The mOR for each LTCF is the median value of the distribution of the OR when randomly picking two residents from different LTCF, one from a higher risk LTCF and the other from a lower risk one. It confers the theoretical situation of the difference in OR if an identical individual moved from an LTCF with high prevalence of AMU or HAI to one with low prevalence [33,34]. A mOR of 1 signifies no difference between the LTCF in the probability of AMU or the occurrence of HAI [31-33]. For each mOR, a

Table 2

Univariate comparison of general characteristics between the HALT 2016 and additional database, Ireland, 2017

Resident characteristics	HALT 2016 (n = 10,044 residents)		Additional database (n = 3,816 residents)		p value
	N	%	n	%	
Residents with AMU	1,029	10.3	404	10.6	Ns
Residents with HAI	638	6.4	179	4.7	0.002[b]
Residents aged > 85 years	3,895	38.8	1,457	38.2	Ns
Male residents	3,836	38.2	1,500	39.3	Ns
Residents with a urinary catheter	661	6.6	287	7.5	Ns
Residents with pressure sores	324	3.2	146	3.8	Ns
LTCF characteristics	**n**	**%**	**n**	**%**	**p value**
Single room[a]	5,634	73.6	1,514	75.8	0.043[b]
	Median (SD)	**Range**	**Median (SD)**	**Range**	**p value**
LTCF size	41.5 (34.3)	5–176	72.0 (45.5)	10–176	Ns
WTE HCA	20.0 (23.5)	0–198	31.1 (43.5)	0–198	Ns

AMU: antimicrobial use; HAI: healthcare-associated infection; HALT: healthcare-associated infections in long-term care facilities; HCA: healthcare assistant; LTCF: long-term care facility; Ns: not significant; SD: standard deviation; WTE: whole time equivalent.

[a]Percentage of single rooms calculated from the total rooms in the LTCF.

[b]Significant at p value < 0.05.

Bayesian credible interval (CrI) was calculated based on the distribution of mOR, comparable to the CI of a fixed-effect OR. The empty model and final model were compared using the Bayesian deviance information criteria (DIC), and a lower DIC value suggests a better model fit [35,36].

Both binomial and multi-level regression analysis was performed in STATA (version 13.0). The CrI for the mOR was calculated in MLwiN (version2.35). A p value of < 0.05 was considered significant. A chi-squared test was used to test the difference between HALT 2016 and additional database information for categorical variables and t-test for numeric variables.

Results

Long-term care facilities and residents

In the HALT 2016, 224 LTCF participated. Of those, there were 102 (45.5%) nursing homes (NH), 46 (20.5%) mixed-care facilities and 31 (13.8%) intellectual disability facilities (not shown in Table 2). Of 10,044 residents, 38.2% were male, 38.8% were > 85 years, 6.6% had urinary catheterisation and 3.2% had a pressure sore (Table 2).

Subsequently, in January 2017, 93 LTCF provided additional information. After matching for age, sex, urinary catheter use and disorientation, 13 were excluded from the analysis; two LTCF reported only two current residents each and 11 LTCF reported a large discrepancy in the number of current residents compared with the number reported in HALT 2016 (> 35). Therefore, for 80 LTCF, additional information was reported on 3,816 current residents (Figure 1). Of the 80 LTCF, 404 residents had AMU (10.6%) and 179 had HAI (4.7%) (Table 2). The median age of the residents was 82 and 60.7% were female. Of residents with a urinary catheter, 14.1% had AMU and 17.3% had HAI (not shown in Table 2).

Five of the 224 HALT 2016 LTCF and three of the 80 LTCF reporting additional information had an antimicrobial stewardship committee; 137 and 45 LTCF, respectively, had an IPC committee (Table 3).

Of the 80 LTCF that provided additional information, 46 (57.5%) had participated in both HALT 2013 and 2016 (not shown in Table 2). The characteristics of the 80 LTCF that provided additional information did not differ significantly from the 224 LTCF participating in HALT 2016, apart from the occurrence of HAI, which was lower in the additional database, while the percentage of single rooms was slightly higher in the additional database (Tables 2 and 3).

Negative binomial regression analysis

The result of the negative binomial regression analysis showed that LTCF with more catheterised (urinary) residents had higher AMU (by 4%) and HAI (by 10%). None of the other LTCF-related risk factors were found to be associated with AMU or HAI (Table 4).

Multilevel logistic regression analysis

The likelihood ratio test, as well as the caterpillar plots, showed substantial variation between LTCF in AMU and HAI (Figures 2A and 2B).

For both AMU and HAI, significant resident- and LTCF-level variables are presented in the final model (Table 4). AMU was double in residents with a urinary catheter

Table 3

Overview of long-term care facility-level variables, HALT 2016 (n = 224) and additional database (n = 80), Ireland, 2017

Long-term care facility characteristics	HALT 2016 (n = 224)		Additional database (n = 80)					
			AMU			HAI		
	n	%	n	%	p value[a]	n	%	p value[a]
Internal coordinating physician for medical care	60	26.8	23	28.7	Ns	NA	NA	NA
Physician in charge of medical coordination may consult medical records of residents	168	75.0	57	71.3	Ns	NA	NA	NA
Antimicrobial stewardship committee	5	2.2	3	3.7	Ns	NA	NA	NA
Feedback to prescriber on antimicrobial consumption	32	14.3	9	11.3	Ns	NA	NA	NA
Microbiological sample taken before antimicrobials started	43	19.2	16	20.0	Ns	NA	NA	NA
Permission required for prescribing restricted antimicrobials	22	9.8	8	10.0	Ns	NA	NA	NA
Antimicrobial treatment guidelines (at least one: UTI, RTI, SSTI)	116	51.8	36	45.0	Ns	NA	NA	NA
Medical care provided by personal GP only	111	49.5	40	50.0	Ns	NA	NA	NA
Use of a restrictive list of antimicrobial in LTCF	31	13.8	13	16.3	Ns	NA	NA	NA
Development of IPC care protocol	163	72.8	NA	NA	NA	56	70.0	Ns
Feedback of surveillance results to staff on IPC practices	146	65.8	NA	NA	NA	49	61.3	Ns
Decision on isolation and precautions of residents colonised with resistant microorganisms	189	84.4	NA	NA	NA	67	83.7	Ns
IPC committee	137	61.2	NA	NA	NA	45	56.3	Ns

AMU: antimicrobial use; GP: general practitioner; HAI: healthcare-associated infection; HALT: healthcare-associated infections and antimicrobial use in long-term care facilities; IPC: infection prevention and control; LTCF: long-term care facilities; NA: not applicable; Ns: not significant; RTI: respiratory tract infections; SSTI: skin/soft tissue infection; UTI: urinary tract infections.

[a]p values calculated for HALT 2016 vs additional database.

(OR: 2.2; 95% CI: 1.5–3.1) regardless of LTCF type. HAI in residents with a urinary catheter was also double compared with residents without a catheter (OR: 2.6; 95% CI: 1.7–4.1), particularly in residents of intellectual disability facilities, as compared with nursing homes or mixed-care facilities (Figures 3A and 3B).

The presence of an internal coordinating physician for medical care (OR: 0.3; 95% CI: 0.2–0.6), an antimicrobial stewardship committee (OR: 0.2; 95% CI: 0.1–0.6), a system to provide feedback to GP on antimicrobial consumption (OR: 0.3; 95% CI: 0.1–0.6) and medical care provided by personal GP (OR: 0.6; 95% CI: 0.7–1.0) were all significantly associated with reduced prevalence of AMU. An increase in whole-time equivalent (WTE) healthcare assistants (HCA) was associated with reduced AMU prevalence (0.9 for every WTE). Taking a microbiological sample before starting antimicrobials increased the likelihood of AMU by 2.5 (95% CI: 1.3–4.6). The odds of AMU was much higher for nursing home residents (OR: 2.4; 95% CI: 1.1–5.2) and intellectual disability facility residents (OR: 6.0; 95% CI: 2.0–18.4), compared with other LTCF types (Table 4).

Staff feedback on surveillance results of IPC practices was associated with a reduction in HAI (OR: 0.6; 95%: CI 0.3–1.0).

Nursing home residents were nearly three times more likely to have HAI (OR = 2.895% CI: 1.0–7.5) than residents of other LTCF (Table 4).

For both AMU and HAI, large inter-facility differences were observed; the mOR for AMU was 2.2 (95% CrI: 1.8 –2.8) and for HAI was 2.1 (95% CrI: 1.5–3.1), indicating a doubling of the odds for both conditions if an imaginary median resident moved from a lower risk LTCF to a higher risk one (Table 4).

Discussion

To our knowledge, this is the first multi-level regression analysis of information from the HALT 2016 study. The results showed that with limited additional information, a much more detailed analysis can be performed to reveal associations between institutional, i.e. LTCF, characteristics on AMU and HAI. This approach could therefore be considered to improve antimicrobial stewardship interventions. For future HALT PPS methodology, the collection of age, sex, urinary catheterisation and disorientation status on all residents within each participating LTCF, rather than just residents with AMU and/or HAI, would add to the analysis of data and is recommended.

The aggregated-level HALT 2016 analysis showed urinary catheter use to be the only significant risk factor for both AMU and HAI, while the additional database analysis identified a number of institutional-level variables significantly associated with reduced AMU. These were the presence of an internal coordinating physician, an antimicrobial stewardship committee, feedback to GP on antimicrobial consumption, medical care provided by personal GP and higher numbers of

Table 4

Comparison of negative binomial regression and multi-level logistic regression analysis for antimicrobial use and healthcare-associated infections, HALT 2016 and additional database, Ireland, 2017

	Negative binomial regression analysis[a]				Multi-level logistic regression analysis[b]			
	AMU		HAI		AMU		HAI	
	IRR	95% CI	IRR	95% CI	OR	95% CI	OR	95% CI
Resident-level variables								
Age	NA	NA	NA	NA	1.01	1.0–1.02	1.0	1.0–1.01
Sex (reference male)	NA	NA	NA	NA	1.1	0.9–1.4	1.0	0.7–1.4
Presence of a urinary catheter	NA	NA	NA	NA	2.2	1.5–3.1[c]	2.6	1.7–4.1[c]
LTCF-level variables								
% resident›85 years	1.0	1.0–1.01	1.0	1.0–1.02	NA	NA	NA	NA
% male residents	1.0	1.0–1.02	1.0	1.0–1.01	NA	NA	NA	NA
% resident with a urinary catheter	1.04	1.0–1.05[c]	1.1	1.0–1.2[c]	NA	NA	NA	NA
Internal coordinating physician for medical care	0.9	0.6–1.5	NA	NA	0.3	0.2–0.6[c]	NA	NA
Physician in charge of medical coordination may consult medical records of residents	1.4	0.8–2.6	NA	NA	1.8	1.0–3.5	NA	NA
Antimicrobial stewardship committee	0.7	0.2–1.8	NA	NA	0.2	0.1–0.6[c]	NA	NA
Feedback to prescriber on antimicrobial consumption	1.4	0.9–2.2	NA	NA	0.3	0.1–0.6[c]	NA	NA
Microbiological sample taken before antimicrobials started	0.7	0.4–1.0	NA	NA	2.5	1.3–4.6[c]	NA	NA
Permission required for prescribing restricted antimicrobials	1.1	0.6–1.9	NA	NA	1.4	0.7–3.1	NA	NA
Antimicrobial treatment guideline (at least one: UTI, RTI, SSTI)	0.9	0.7–1.3	NA	NA	0.8	0.5–1.2	NA	NA
Medical care provided by personal GP only	1.3	0.9–1.9	NA	NA	0.6	0.7–1.0[c]	NA	NA
Use of a restrictive list of antimicrobials in LTCF	1.2	0.9–1.9	NA	NA	1.7	1.0–3.1	NA	NA
LTCF size	1.0	0.9–1.0	NA	NA	1.0	1.0–1.01	NA	NA
WTE HCA	1.0	1.0–1.01	NA	NA	0.9	0.98–1.0[c]	NA	NA
% single room in LTCF	NA	NA	1.0	0.9–1.0	NA	NA	NA	NA
% residents with pressure sores	NA	NA	1.0	1.0–1.05	NA	NA	NA	NA
Number of single rooms	NA	NA	NA	NA	NA	A	0.9	0.9–1.0
Number of residents with pressure sores	NA	NA	NA	NA	NA	NA	1.0	0.8–1.1
Development of IPC care protocol	NA	NA	0.7	0.4–1.2	NA	NA	1.5	0.8–2.6
Feedback of surveillance results to staff on IPC practices	NA	NA	0.7	0.4–1.2	NA	NA	0.6	0.3–1.0[c]
Decision on isolation and precautions of residents colonised with resistant microorganisms	NA	NA	1.4	0.7–2.8	NA	NA	1.7	0.8–3.7
IPC committee	NA	NA	0.8	0.5–1.3	NA	NA	1.3	0.8–2.1
LTCF types (reference. others)								
Nursing homes	1.1	0.7–1.9	0.7	0.3–1.6	2.4	1.1–5.2[c]	2.8	1.0–7.5[c]
Intellectual disability facilities	0.6	0.5–1.7	0.6	0.3–1.3	6.1	2.0–18.4[c]	1.5	0.4–5.4
Mixed-care facility	1.0	0.6–1.7	0.6	0.3–1.4	2.2	0.9–5.1	2.5	0.9–7.1
Measures of variation					**σ²**	**SD**	**σ2**	**SD**
Empty Model	NA	NA	NA	NA	0.5	0.2	0.4	0.2
Final Model	NA	NA	NA	NA	0.2	0.1	0.3	0.2
					mOR	95% CrL	mOR	95% CrL
Median OR in Final Model	NA	NA	NA	NA	2.2	1.8–2.8	2.1	1.5–3.1
Bayesian DIC								
Empty Model	NA	NA	NA	NA	2,472.5		1,430.4	
Final Model	NA	NA	NA	NA	2,398.2		1,392.6	

σ2: variance; CI: confidence interval; CrI: credibile interval; DIC: deviance information criteria; GP: general practitioners; HALT: healthcare-associated infections and antimicrobial use in long-term care facilities; HCA: healthcare assistant; IPC: infection prevention and control; IRR: incidence rate ratio; LTCF: long-term care facility; OR: odds ratio; RTI: respiratory tract infections; SD: standard deviation; SSTI: skin/soft tissue infection; UTI: urinary tract infections; WTE: whole time equivalent.

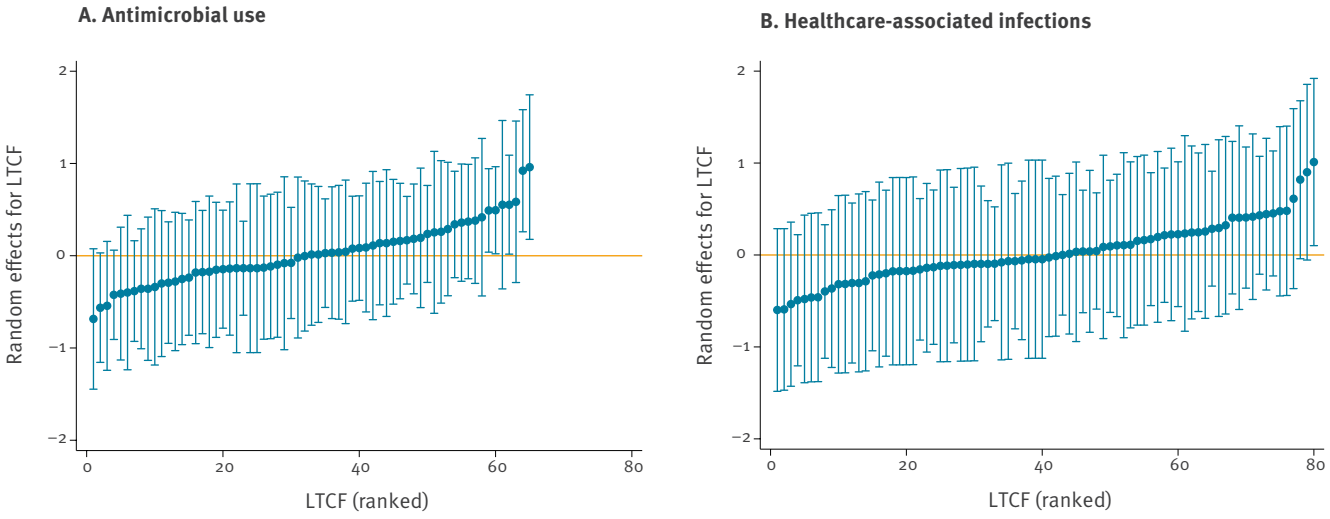
[a]Binomial regression analysis was performed on all 224 LTCF from HALT 2016.

[b]Multilevel regression analysis on 80 LTCF from additional database, 2017.

[c]Significant p value at‹0.05.

Figure 2

Caterpillar plot showing variance in (A) antimicrobial use and (B) healthcare-associated infections in long-term care facilities[a], HALT 2016 and additional database, Ireland, 2017



HALT: healthcare-associated infections and antimicrobial use in long-term care facilities; LTCF: long-term care facilities.

[a]After correcting for LTCF characteristics.

WTE HCA. Staff feedback on surveillance of IPC practices was also directly associated with a reduced HAI prevalence.

The median OR showed high variation between LTCF, with an estimated doubling of the chance of both AMU and HAI for an imaginary median resident if they moved from a low-risk LTCF to a high-risk one. Conversely, the median OR also showed that addressing institutional risk factors could theoretically halve HAI and AMU prevalence.

Formation of a local antimicrobial stewardship committee, linked with feedback on prescribing and/or IPC practices, could positively influence stewardship practices and in turn lead to reduced AMU and HAI. Other institutional changes may require more structural adjustments and resource investments, such as the appointment of internal coordinating physicians or increasing the number of WTE HCA.

Strength and limitations

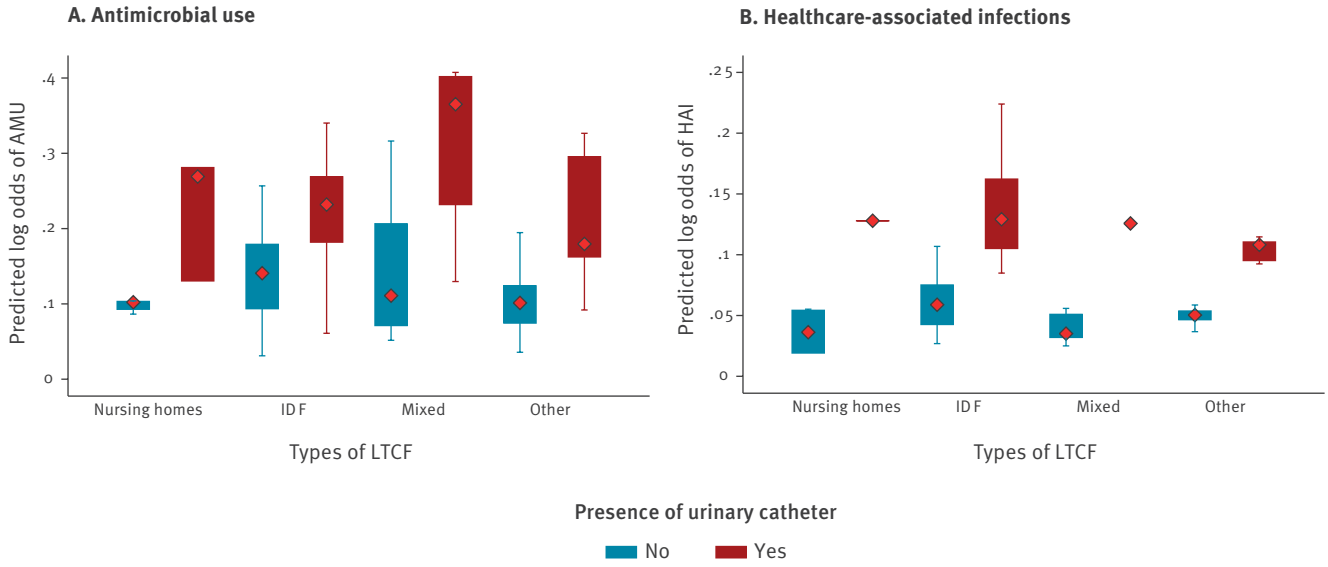
The multi-level regression analysis was not specified in advance of the HALT 2016 survey and the additional data collection may have introduced a bias. The additional data on age, sex, urinary catheter use and disorientation may only explain part of the case-mix variability with other factors captured in the 'unexplained' variation in the model. However, the comparison of the HALT 2016 database with the additional database did not show any important differences for any of the variables, although only 35% of the participating LTCF responded to the subsequent request for additional information. Most importantly, if larger LTCF contributed more, this would impact analysis and conclusions, as such LTCF may be more likely to have committees or feedback systems. Fortunately, the comparison of the LTCF did not show a bias towards larger or smaller LTCF (data not shown).

The request to LTCF to collect additional data on current residents was pragmatic, taking into consideration staff workload, as a request to retrospectively review data from the HALT 2016 survey was likely to have discouraged the reporting of additional data or limited participation. Therefore, replacing residents with similar characteristics from the HALT 2016 with current residents for whom additional information was collected, thus comparing patients having AMU/HAI with patients who may or may not have AMU/HAI, could have introduced bias. Although a change in outcome is not anticipated by this action, such a bias cannot be checked for nor its direction be anticipated. However, collection of limited additional information on all residents in future HALT studies may show this association to be stronger than was found by our study.

In a PPS, participating residents' outcome and exposure are measured at the same time, which makes it difficult to derive the direction of the associations found [37]. Finally, the quality of data collected in any PPS depends on good participation and is subject to bias. It is possible that the LTCF that participated in HALT 2016 may have improved awareness of antimicrobial

Figure 3

Predicted probabilities of (A) antimicrobial use and (B) healthcare-associated infections by long-term care facility types, HALT 2016 and additional database, Ireland, 2017



HALT: healthcare-associated infections and antimicrobial use in long-term care facilities; LTCF: long-term care facilities.

stewardship and HAI prevention, and were therefore more likely to volunteer to participate in a PPS.

Comparison with existing literature

Antimicrobial stewardship provides standard, evidence-based approaches to encourage judicious AMU [38]. Some perceived barriers in antimicrobial stewardship programmes are physician practice/compliance (69%) and patient/family expectations (15%) [39]. Risk factors identified in relation to clinical practice are the 'treat first attitude' and the lack of knowledge regarding effectiveness of antimicrobials, e.g. asymptomatic bacteriuria [40]. In our study, the presence of a coordinating physician, coupled with feedback on antimicrobial consumption, and particularly having an antimicrobial stewardship committee in place, was associated with significantly reduced AMU prevalence. However, only five of 224 LTCF from HALT 2016 and three of 80 LTCF from the additional database reported having an antimicrobial stewardship committee. A nursing home study from Northern Ireland showed appropriate prescribing was associated with regular physician visits [41]. Our study showed the impact of medical care provided by a personal GP in reducing AMU, as GP were considered to be more familiar with the resident's medical history and conditions over time, which seemed to limit antimicrobial prescribing. Prescribing practices by medical staff other than the personal GP would have been by physicians who were not as familiar with the individual resident's history [41-44]. Our study supports the appointment of an internal coordinating physician and the maintenance of medical care by personal GP in resident care to support antimicrobial stewardship.

In general, nurses are primarily responsible for resident care in LTCF, supported by HCA who may have more direct resident contact, assisting with personal care, meals and mobility, as required. Some studies suggest that this may result in higher antimicrobial prescribing, specifically for asymptomatic bacteriuria, while other studies suggest that their involvement in prescribing education reduces inappropriate AMU [43,45,46]. Even though nurses and HCA do not prescribe antimicrobials in LTCF in Ireland, our study found no difference in either increased or decreased AMU with a higher or lower number of WTE nurses, but found a modest reduction in AMU with higher WTE HCA in LTCF. This modest reduction may indicate higher involvement of HCA in the direct care of the resident. The HCA role and the nurse to HCA skill mix within LTCF warrants further investigation.

Our study found the practice of taking a microbiological sample before starting antimicrobials to be a key predictor of increased AMU in LTCF, which is similar to a previous study conducted in nursing homes in 2009 [47]. It suggested that the routine of sample taking may be a reminder or justification for prescribing. However, qualitative studies are required to understand such potential association.

In our study, urinary catheterisation was an important resident risk factor associated with higher AMU

prevalence. A 2014 study also reported that UTIs were associated with catheter use in both acute care facilities (20%) and LTCF (50%) [48]. A previous study from our group reported an association between AMU and urinary catheterisation, in particular that AMU in catheterised residents was more likely to be prophylactic. According to guidelines, catheterisation is not a sufficient indication for any antimicrobial, either therapeutic or prophylactic [49]. Hence, this is an area where AMU could be improved substantially.

Conclusion

Collection of some limited additional resident risk factor data after HALT 2016 facilitated multi-level model analysis and thus identification of significant individual and institutional risk factors for AMU and HAI in Irish LTCF, with significant inter-facility variation for both conditions. Our analysis shows the benefit of collecting limited additional information on all residents, which could be considered for inclusion in future HALT PPS. Factors associated with reduced AMU were the presence of a coordinating physician and an antimicrobial stewardship committee, medical care provided by personal GP and antimicrobial consumption feedback to LTCF staff and prescribers. Feedback on IPC practices was associated with lower HAI prevalence.

Acknowledgements

Funding: MT is funded by the National University of Ireland, School of Medicine, Ph.D. grant College of Medicine, Nursing and Health Science (CMNHS) Scholarship.

Conflict of interest

None declared.

Authors' contributions

MT and AV conceived of the study. KB is the national coordinator of the HALT PPS in Ireland. KB, HM and SH coordinated the additional data collection and the HALT PPS in 2016. MT performed the final analysis and drafted the article. AV supported writing and analysis and shaped the discussion. KB, HM and MC contributed to the discussion and writing the manuscript. All authors approved the final version of the manuscript.

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Mitteilungen der Sanitätsverwaltung
Bundesministerium für Gesundheit Familie und Jugend, Vienna
Monthly, print only. In German.
http://www.bmgfj.gv.at/cms/site/thema.html?channel=CH0951

Belgium

Vlaams Infectieziektebulletin
Department of Infectious Diseases Control, Flanders
Quarterly, print and online. In Dutch, summaries in English.
http://www.infectieziektebulletin.be

Bulletin d'information de la section d'Epidémiologie
Institut Scientifique de la Santé Publique, Brussels
Monthly, online. In French.
http://www.iph.fgov.be/epidemio/epifr/episcoop/episcoop.htm

Bulgaria

Bulletin of the National Centre of Infectious and Parasitic Diseases, Sofia
Print version. In Bulgarian.
http://www.ncipd.org/

Cyprus

Newsletter of the Network for Surveillance and Control of Communicable Diseases in Cyprus
Medical and Public Health Services, Ministry of Health, Nicosia
Biannual, print and online. In Greek.
http://www.moh.gov.cy

Czech Republic

Zpravy CEM (Bulletin of the Centre of
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Centrum Epidemiologie a Mikrobiologie Státního
Zdravotního Ústavu, Prague
Monthly, print and online. In Czech, titles in English.
http://www.szu.cz/cema/adefaultt.htm

EPIDAT (Notifications of infectious diseases in the Czech Republic)
http://www.szu.cz/cema/epidat/epidat.htm

Denmark

EPI-NEWS
Department of Epidemiology, Statens Serum Institut, Copenhagen
Weekly, print and online. In Danish and English.
http://www.ssi.dk

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Department of Infectious Disease Epidemiology, National Public Health Institute, Helsinki
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http://www.ktl.fi/portal/suomi/osastot/infe/tutkimus/tartuntatautien_seuranta/tartuntatautilaakarin_kommentit/

France

Bulletin épidémiologique hebdomadaire
Institut de veille sanitaire, Saint-Maurice Cedex
Weekly, print and online. In French.
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Germany

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Robert Koch-Institut, Berlin
Weekly, print and online. In German.
http://www.rki.de/DE/Content/Infekt/EpidBull/epid__bull__node.html

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HCDCP Newsletter
Hellenic Centre for Disease Control and Prevention (HCDCP/KEELPNO), Athens
Monthly, online. In English and Greek.
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Hungary

Epinfo (az Országos Epidemiológiai Központ epidemiológiai információs hetilapja)
National Center For Epidemiology, Budapest
Weekly, online. In Hungarian.
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Landlæknisembættið
Directorate Of Health, Seltjarnarnes
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http://www.landlaeknir.is

Ireland

EPI-INSIGHT
Health Protection Surveillance Centre, Dublin
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http://www.hpsc.ie/hpsc/EPI-Insight

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Notiziario dell'Istituto Superiore di Sanità
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
http://www.iss.it/publ/noti/index.php?lang=1&tipo=4

Bolletino Epidemiologico Nazionale (BEN)
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
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Epidemiologijas Bileteni
Sabiedribas veselibas agentura
Public Health Agency, Riga
Online. In Latvian.
http://www.sva.lv/epidemiologija/bileteni

Lithuania

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Online. In Lithuanian.
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Infectieziekten Bulletin
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National Institute of Public Health and the Environment, Bilthoven
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http://www.rivm.nl/infectieziektenbulletin

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Folkehelseinstituttet, Oslo
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http://www.folkehelsa.no/nyhetsbrev/msis

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Panstwowy Zaklad Higieny,
National Institute of Hygiene, Warsaw
Fortnightly, online. In Polish and English.
http://www.pzh.gov.pl

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http://www.dgs.pt

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http://www.insp.gov.ro/cnscbt/index.php?option=com_docman&Itemid=12

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Inštitut za varovanje zdravja, Center za nalezljive bolezni, Institute of Public Health, Center for Infectious Diseases, Ljubljana
Monthly, online. In Slovene.
http://www.ivz.si

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Boletín Epidemiológico Semanal
Centro Nacional de Epidemiología, Instituto de Salud Carlos III, Madrid
Fortnightly, print and online. In Spanish.
http://revista.isciii.es

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Folkhälsomyndighetens nyhetsbrev
Folkhälsomyndigheten, Stockholm
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http://www.folkhalsomyndigheten.se/

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Weekly, online only. In English.
https://www.gov.uk/government/collections/health-protection-report-latest-infection-reports

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Communicable Diseases Monthly Report
Communicable Disease Surveillance Centre, Northern Ireland, Belfast
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http://www.cdscni.org.uk/publications

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http://europa.eu

European Commission - Public Health

The website of European Commission Directorate General for Health and Consumer Protection (DG SANCO).
http://ec.europa.eu/health/

Health-EU Portal

The Health-EU Portal (the official public health portal of the European Union) includes a wide range of information and data on health-related issues and activities at both European and international level.
http://ec.europa.eu/health-eu/

European Centre for Disease Prevention and Control

European Centre for Disease Prevention and Control (ECDC)
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http://www.ecdc.europa.eu

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TQ-AD-18-004-EN-C

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Paper TQ-AD-18-004-EN-C ISSN 1025-496X
PDF TQ-AD-18-004-EN-N ISSN 1560-7917

Publications Office