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Comparison of antimicrobial stewardship programmes in acute-care hospitals in four European countries: A cross-sectional survey

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ABSTRACT

Antimicrobial stewardship programmes (ASPs) are designed to improve antibiotic use. A survey was systematically developed to assess ASP prerequisites, objectives and improvement strategies in hospitals. This study assessed the current state of ASPs in acute-care hospitals throughout Europe. A survey containing 46 questions was disseminated to acute-care hospitals: all Dutch ($n = 80$) and Slovenian ($n = 29$), 215 French (25%, random stratified sampling) and 62 Italian (49% of hospitals with an infectious diseases department, convenience sampling) acute-care hospitals, for a Europe-wide assessment. Response rates for the Netherlands (Nl), Slovenia (Slo), France (Fr) and Italy (It) were 80%, 86%, 45% and 66%. There was variation between countries in the prerequisites met and the objectives and improvement strategies chosen. A formal ASP was present mainly in the Netherlands (90%) and France (84%) compared with Slovenia (60%) and Italy (60%). Presence of an antimicrobial stewardship (AMS) team ranged from 42% (Fr) to 94% (Nl). Salary support for AMS teams was provided in 68% (Fr), 51% (Nl), 33% (Slo) and 12% (It) of surveyed hospitals. Quantity of antibiotic use was monitored in the majority of hospitals, ranging from 72% (Nl) to 100% (Slo and Fr) of acute-care hospitals. Participating countries varied substantially in the use of 'prospective monitoring and advice' as a strategy to improve AMS objectives. ASP prerequisites, objectives and improvement activities vary considerably across Europe, with room for improvement. Stimulating appropriate system prerequisites throughout Europe, e.g. by introducing staffing standards and financial support for ASPs, seems a first priority.

1. Introduction

Antimicrobial resistance is a major threat to global public health [1,2]. New resistance mechanisms have emerged and spread globally, whilst there is a steady decline in the discovery of new antibiotics [1]. A global action plan to reduce antimicrobial resistance has been adopted by the World Health Assembly, with all member states committing themselves to prepare national action plans [3]. As part of this initiative, antimicrobial stewardship

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programmes (ASPs), 'a coherent set of actions which promote using antimicrobials responsibly', have been introduced to improve the quality of antibiotic use and patient outcomes and to reduce antimicrobial resistance rates [4–6].

Antimicrobial stewardship (AMS) guidelines provide three sets of recommendations, or 'building blocks', for successful development and implementation of ASPs (Supplementary Fig. S1) [4,7,8]. The first building block includes recommendations on appropriate structural or system prerequisites that should be met when establishing an ASP, e.g. the availability of a financially compensated multidisciplinary AMS team [9]. The second block includes recommendations on appropriate use at the patient level, which constitute the objectives (the 'WHAT') of the AMS teams, e.g. timely intravenous (IV) to oral switch [10]. The third building block encompasses recommendations on improvement strategies that AMS teams have to perform at the professional or institutional level (the 'HOW') in order to guarantee that these objectives are met, e.g. monitoring and advice or education [11].

Recently, we systematically developed a survey based on these building blocks for successful AMS (Supplementary Fig. S2) [12]. In the present study, the AMS survey was used to assess the current state of ASPs in acute-care hospitals in four European countries.

2. Materials and methods

We developed an AMS survey in 2015 [12]. In short, a literature review on surveys for AMS was performed. In addition, potentially relevant survey questions were selected from two published checklists: (i) a checklist including core elements of hospital ASPs by the US Centers for Disease Control and Prevention (CDC); and (ii) a checklist on structure and process indicators for hospital ASPs by the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR). Potential survey questions were extracted and categorised. During a face-to-face consensus meeting, the list with categorised questions was presented to five of the authors. These stewardship experts discussed, combined and rephrased the questions. The final survey was piloted in 42 Dutch hospitals in order to test clinimetric properties of the questions and to reach consensus on the content of the survey.

In June 2017, four European countries were invited through ESGAP (ESCMID Study Group for Antimicrobial Stewardship) to participate in a stewardship survey: the Netherlands (Nl), Slovenia (Slo), France (Fr) and Italy (It) (Supplementary Fig. S2). The survey was disseminated to 80 hospitals in the Netherlands [12] and to 29 hospitals in Slovenia, which comprised all acute-care hospitals for these countries. France invited 215 hospitals (private and public) based on a randomisation procedure in which 25% of the total number of hospitals with more than 50 acute-care beds was selected to participate in the survey [13]. Stratification was based on the type of hospital (e.g. teaching hospitals, non-teaching public hospitals, cancer institutes, non-profit and for-profit private clinics) and on the number of acute-care beds. Italy participated with 62 hospitals, which was 6% of the total number of acute-care hospitals and 49% of the hospitals with an infectious diseases (ID) department in Italy. These hospitals were invited based on the fact that an ID physician was present in these hospitals (convenience sample) (Fig. 1). The survey, originally designed in English (Supplementary Fig. S2), was translated into French and Slovenian for these countries by CP, AS and BB. Italian subtitles were provided for Italian participants by RM. Dutch participants used the original English translation of the survey. For France, some survey answers were slightly adapted to fit the French context and organisation of care. All survey questions were mandatory, indicating that the participant was not able to proceed if the question was not filled out.

An online survey tool (LimeSurvey v.2.6.4) was used to send the survey to a national co-ordinator for each country. The national co-ordinators disseminated personalised survey links to one contact person per hospital, preferably a member of the AMS team. Reminders were sent to the non-responding hospitals every 4 weeks. In the Netherlands and Italy, non-responders were contacted after 12 weeks by telephone for a last reminder. The survey deadline was 1 November 2017 for Dutch participants, 1 March 2018 for French and Slovenian participants, and 1 April 2018 for Italian participants.

Descriptive statistics were used to assess frequencies, percentages and averages using IBM SPSS Statistics v.23.0 (IBM Corp., Armonk, NY). Differences between hospitals were studied using the χ^2 test. All filled out questions were included in the analyses.

3. Results

3.1. Survey response and hospital characteristics

Response rates for the Netherlands, Slovenia, France and Italy were, respectively, 80% ($n = 64$), 86% ($n = 25$), 45% ($n = 97$) and 66% ($n = 41$). Dutch participants completed all questions in 56 (88%) of 64 surveys. In the remaining 12%, participants stopped the survey prematurely. Slovenia completed 23 (92%) of 25 surveys, France completed 86 (89%) of 97 surveys, and Italy completed 39 (95%) of 41 surveys. The majority of participating hospitals were non-university teaching hospitals, except for Italy where mainly academic hospitals participated (59%). In France, both public and private hospitals were invited but the response rate of public hospitals was significantly higher than the response rate of private hospitals [59% (60/102) vs. 33% (37/113); $P < 0.001$]. There was no significant difference in response rates between different types of hospitals (i.e. academic, non-academic teaching, non-teaching) for the Netherlands, Slovenia and Italy.

An ID specialist was present in all participating Italian hospitals as this was the selection criterion for participation in the survey. A clinical microbiologist was mostly located in the hospital, except for Slovenia where a clinical microbiologist was consulted from an external location in the majority of hospitals (56%). A clinical pharmacist with a specific interest in the field of antibiotics was present in nearly all Dutch and French hospitals (92% and 97%, respectively); in Italy a clinical pharmacist was present in 46% of hospitals (19/41). Further hospital characteristics are provided in Table 1.

3.2. Stewardship prerequisites

3.2.1. Antimicrobial stewardship team and antimicrobial stewardship programme organisation

Presence of an AMS team (i.e. a multidisciplinary team, larger than one staff member, that monitors antibiotic use and supports clinical decisions to ensure appropriate antibiotic use) ranged from 42% for France to 94% for the Netherlands. Remarkably, Dutch AMS teams were established recently, between 2010 and 2017 (Table 2). Nearly all French hospitals without an AMS team had at least one person officially in charge of the ASP, an 'ASP lead' (i.e. a person who co-ordinates a local ASP).

Key members of the AMS team were a clinical microbiologist (range 67–100% between countries), a clinical pharmacist (range 80–100%) and an ID specialist (range 67–100%). A clinical pharmacist and a clinical microbiologist were present in particular in all Dutch AMS teams. Remarkably, participating Italian AMS teams included an infection prevention specialist in 76% and a nurse in 68%. In France, 80% of the ASP leads had received specialised stewardship training (i.e. training in AMS-related topics in addition to the standard specialty training for an ID specialist, clinical microbiologist or clinical pharmacist, such as the annual ESCMID Study Group

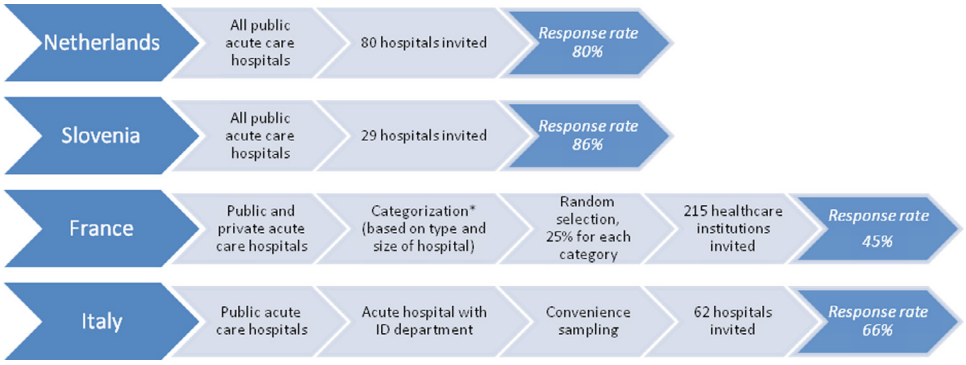

Fig. 1. Selection criteria of invited hospitals and response rate in each country. ID, infectious diseases.
*Categories identified: 1. Teaching hospitals, 2. Public hospitals <200 acute care beds; 3. Public hospitals >200 acute care beds; 4. Cancer institutes; 5. Nonprofit private hospitals <130 acute beds; 6. Nonprofit private hospitals >130 acute beds; 7. For profit private hospitals <110 acute beds; 8. For profit private hospitals >110 acute beds. Hospitals with <50 acute care beds were excluded. The different cut-off concerning acute care bed number was established in function of the median number of beds for that category of health care facility.

Table 1
Hospital characteristics in the four countries[a].

	Nl	Slo	Fr	It
No. of hospital beds [median (range)]	483 (50–1048)	211 (23–2200)	250 (36–3000)	790 (200–2500)
Hospital type				
University	5 (8)	5 (20)	10 (10)	24 (59)
Non-university teaching	37 (58)	16 (64)	NA	6 (15)
General non-teaching	22 (34)	4 (16)	50 (52)	11 (27)
Private not-for-profit	NA	NA	14 (14)	NA
Private for-profit	NA	NA	23 (24)	NA
Part of a collaborative hospital group	18 (28)	13 (52)	25 (26)	17 (41)
Residency programmes				
Internal medicine	40 (63)	14 (56)	32 (33)	27 (66)
Infectious diseases (ID)	7 (11)	5 (20)	20 (21)	27 (66)
Clinical microbiology	23 (36)	2 (8)	30 (31)	22 (54)
Clinical pharmacy	34 (53)	9 (36)	43 (44)	17 (41)
None of these	0	6 (24)	43 (44)	1 (2)
Presence of a specialist				
Clinical microbiologist[b]				
Available with clinical tasks	57 (89)	4 (16)	63 (65)	25 (61)
Available without clinical tasks	1 (2)	3 (12)	NA	14 (34)
Can be consulted from external location (samples are sent outside)	6 (9)	14 (56)	34 (35)	1 (2)
Clinical pharmacist with specific field of interest in antibiotics[c]	59 (92)	15 (60)	94 (97)	19 (46)
ID specialist[d]	42 (66)	9 (36)	48 (49)	41 (100)
None of the above	0	3 (12)	0	0
Total no. of respondents	64	25	97	41

Nl, the Netherlands; Slo, Slovenia; Fr, France; It, Italy; NA, not applicable (this item was not available in the survey).
[a] Numbers are *n* (%) unless otherwise indicated.
[b] Clinical microbiologists supervise microbiology laboratory testing, report results of microbiological tests, and provide advice on diagnostics, prophylaxis and treatment of infections to physicians, and are involved in infection prevention and control.
[c] Clinical pharmacists are trained pharmacists working in a hospital. They work directly with physicians to optimise the use and dosing of antibiotics.
[d] ID specialists treat patients with (presumed) infectious diseases in the hospital as well as in outpatient clinics.

for Antibiotic Policies (ESGAP) course or a university degree on antimicrobial prescribing and stewardship). AMS team meetings were held most frequently in the Netherlands and Italy (71% and 75% of teams, respectively, met once a month or more often), whilst the majority of teams met once every 2 months or less in France and Slovenia (75% and 73%, respectively). A formal ASP was present in 60% of the Italian and Slovenian participating hospitals, up to 84% of the French hospitals and 90% of the Dutch hospitals. Antibiotic champions (e.g. professionals who publicise appropriate use of antibiotics and help AMS teams to implement AMS activities on their ward) were present only in the minority of hospitals, ranging from 23% in France up to 69% in Italy.

Details on AMS team composition and ASP organisation are listed in Table 2 and Supplementary Table S1.

Slovenian AMS teams reported the highest time investment per week in AMS activities (median 39 h/week/500 beds; range 0–373 h/week/500 beds), whilst the Netherlands reported the lowest time investment per week (median 17 h/week/500 beds; range 2–96 h/week/500 beds). Furthermore, 17% of participating hospitals with an AMS team available were not able to quantify the salary support for their members. Salary support was provided to 68% of AMS teams in France, 51% in the Netherlands, 33% in Slovenia and 12% in Italy. Moreover, 28% of the AMS teams with salary support received >1 full-time equivalent (FTE)/500 beds (33% in Italy, 17% in Netherlands, 40% in Slovenia and 37% in France). AMS team salary support provided ranged from a median of 0.3 FTE/500 beds (Italy) to a median of 0.9 FTE/500 beds in France (Supplementary Table S2).

3.2.2. Hospital resources for antimicrobial stewardship programmes

Presence of an electronic medical record (EMR) ranged from 54% in Italy to 100% in the Netherlands. In Slovenia an EMR was present in 79% of participating hospitals but data on medication, microbiology and radiology were available in only one-half of these EMRs.

Table 2
Antimicrobial stewardship (AMS) prerequisites for the four countries: AMS team composition and resources for an antimicrobial stewardship programme (ASP) (for other prerequisites, see Supplementary Table S2)[a].

ASP organisation	Nl	Slo	Fr	It
Formal ASP[b]	57/63 (90)	15/25 (60)	80/95 (84)	24/40 (60)
Annual report[c]	35/63 (56)	18/25 (72)	65/95 (68)	19/40 (48)
Presence of AMS team[d]	59/63 (94)	15/25 (60)	40/96 (42)	25/40 (63)
AMS team in preparation	4/63 (6)	4/25 (16)	1/96 (1)	11/40 (28)
No AMS team but there is one single person officially in charge of the AMS programme ('ASP lead')	NA	NA	55/96 (57)	NA
No AMS team and no ASP lead	0	6/25 (24)	0	4/40 (10)
Year of establishment (range)	2010–2017	1996–2017	2000–2017	1999–2018
AMS team composition (at least one member of the profession present)				
Clinical microbiologist	59/59 (100)	10/15 (67)	32/40 (80)	21/25 (84)
Clinical pharmacist	59/59 (100)	13/15 (87)	38/40 (95)	20/25 (80)
ID specialist	40/59 (68)	10/15 (67)	27/40 (68)	25/25 (100)
Internist	24/59 (41)	9/15 (60)	6/40 (15)	10/25 (40)
Paediatrician	9/59 (15)	4/15 (27)	NA	1/25 (4)
Quality-of-care officer	4/59 (7)	5/15 (33)	NA	10/25 (40)
Infection prevention specialist	6/59 (10)	4/15 (27)	10/40 (25)	19/25 (76)
Nurse	8/59 (14)	4/15 (27)	NA	17/25 (68)
Epidemiologist	5/59 (8)	2/15 (13)	NA	11/25 (44)
Other	14/59 (24)	8/15 (53)	12/40 (30)	8/25 (32)
Frequency of AMS team meetings[e]				
Daily	4/55 (7)	1/15 (7)	0	1/24 (4)
Twice a week	2/55 (4)	0	0	5/24 (21)
Once a week	11/55 (20)	2/15 (13)	5/40 (13)	2/24 (8)
Once every 2 weeks	10/55 (18)	0	0	6/24 (25)
Once a month	12/55 (22)	1/15 (7)	5/40 (13)	4/24 (17)
Once every 2 months	8/55 (15)	4/15 (27)	1/40 (3)	4/24 (17)
Four times a year or less	8/55 (15)	7/15 (47)	29/40 (73)	2/24 (8)
AMS team (or ASP) leader appointed				
No AMS team leader	19/59 (32)	5/19 (26)	1/94 (1)	5/35 (14)
Clinical microbiologist	25/59 (42)	2/19 (11)	4/94 (4)	0
Clinical pharmacist	0	4/19 (21)	15/94 (16)	0
ID specialist	11/59 (19)	5/19 (26)	39/94 (41)	28/35 (80)
Internist	2/59 (3)	3/19 (16)	13/94 (14)	0
Other	2/59 (3)	0	22/94 (23)	2/35 (6)
Specialised ASP training for AMS team (or ASP) leader	27/40 (45)	10/14 (71)	74/93 (80)	17/30 (57)
Stewardship included in leader's job description or annual review	19/40 (48)	7/14 (50)	47/93 (51)	18/30 (60)
Presence of a named senior executive officer with accountability for ASP leadership	16/59 (27)	3/25 (12)	11/94 (12)	18/39 (46)
Guidelines and antibiotic formulary				
Local antibiotic formulary[f]	55/59 (93)	19/24 (79)	92/94 (98)	27/39 (69)
Containing a list of restricted antibiotics[g]	35/55 (64)	13/19 (68)	70/92 (76)	21/27 (78)
Local guidelines for common infectious diseases[h]	55/59 (93)	15/24 (63)	88/94 (94)	28/39 (72)
Based on local antimicrobial susceptibility	53/55 (96)	14/15 (93)	47/88 (53)	24/28 (86)
Defined standard criteria for:				
IV-to-oral switch	45/59 (76)	14/24 (58)	27/94 (29)	10/39 (26)
Streamlining/de-escalation of empirical therapy	27/59 (46)	11/24 (46)	68/94 (72)	12/39 (31)
Dose optimisation (TDM)*	46/59 (78)	13/24 (54)	24/94 (26)	5/39 (13)
Discontinuation of therapy	19/59 (32)	9/24 (38)	26/94 (28)	11/39 (28)
Surgical prophylaxis	53/59 (90)	11/24 (46)	80/94 (85)	37/39 (95)
None of these	3/59 (5)	5/24 (21)	4/94 (4)	2/39 (5)
Available IT support of AMS team (or ASP lead)				
Official IT support (in FTEs)	5/59 (8)	0	1/94 (1)	5/39 (13)
IT support can be applied for if needed	32/59 (54)	10/24 (42)	50/94 (53)	11/39 (28)
Limited IT support available	3/59 (5)	1/24 (4)	NA	NA
No IT support available	19/59 (32)	13/24 (54)	43/94 (46)	22/39 (56)
IT support for specific ASP-related activities				
Selection of specified patient categories	26/40 (65)	6/11 (55)	22/51 (43)	5/17 (29)
Data reporting	28/40 (70)	5/11 (45)	43/51 (84)	8/17 (47)
Point prevalence survey	20/40 (50)	2/11 (18)	38/51 (75)	8/17 (47)
Decision support (i.e. clinical rules)	17/40 (43)	1/11 (9)	9/51 (18)	8/17 (47)
Other	3/40 (8)	0	7/51 (14)	2/17 (12)

Nl, the Netherlands; Slo, Slovenia; Fr, France; It, Italy; NA, not applicable (this item was not available in the survey); ID. infectious diseases; IV, intravenous; TDM, therapeutic drug monitoring; IT, information technology; FTE, full-time equivalent.

[a] Numbers are *n*/*N* (%) unless otherwise indicated (where *N* is the number of respondents).

[b] Co-ordinated hospital programme that promotes the appropriate use of antibiotics by professionals to reduce the development of antimicrobial resistance.

[c] Summary of antibiotic use and/or practice initiatives to improve the appropriateness of antibiotic use.

[d] Multidisciplinary team, larger than one staff member, that monitors antibiotic use and supports clinical decisions to ensure appropriate antibiotic use.

[e] Meetings in which co-ordinating issues referring to local AMS activities are discussed. Only the hospitals with an established AMS team were selected.

[f] List of antibiotics that the hospital pharmacy stocks, along with information about each specific drug (this may be part of a general drug formulary in the hospital).

[g] Antibiotics needing prior or post-authorisation by an AMS team member.

[h] Facility-specific evidence-based treatment recommendations that assist professionals in their decision-making on diagnostics and treatment.

* There is possible confounding in these results as we could not deduce from the survey whether TDM was available but simply not performed (i.e. not considered relevant) or that TDM was not available because the drug was not prescribed in that hospital.

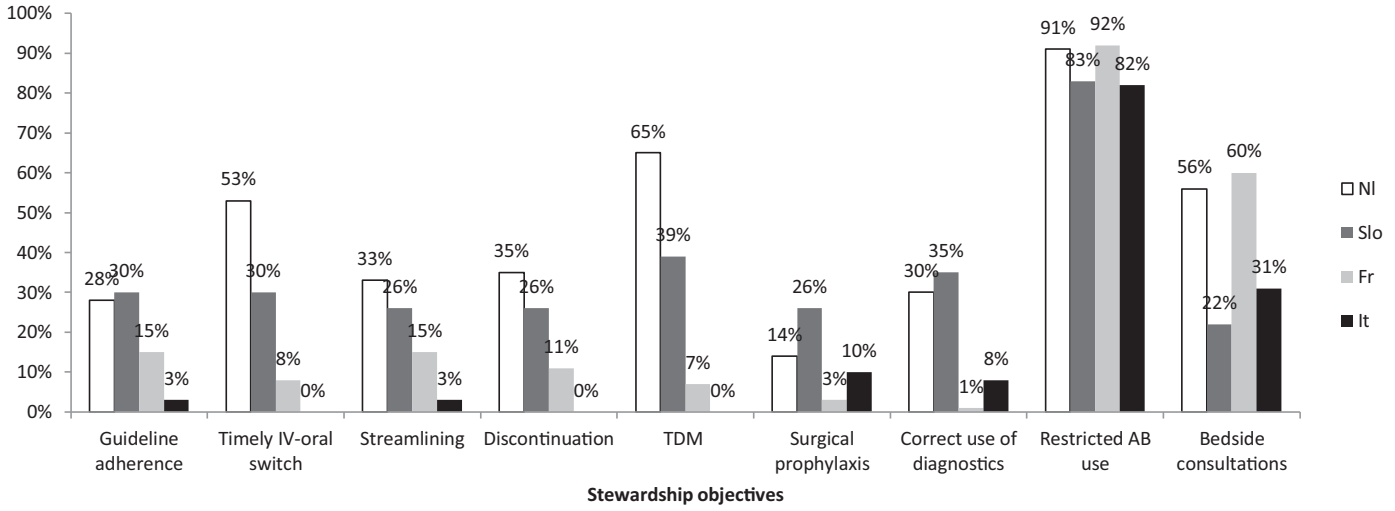

Fig. 2. Frequency of monitoring and advice for antimicrobial stewardship objectives in the four countries studied. Nl, the Netherlands; Slo, Slovenia; Fr, France; It, Italy; IV, intravenous; TDM, therapeutic drug monitoring; AB, antibiotic.

Presence of a local antibiotic formulary ranged from 69% (It) to 98% (Fr). A list with restricted antibiotics was available in 64% of the Dutch antibiotic formularies up to 78% in Italian antibiotic formularies. The formularies could predominantly be consulted via intranet (range 43–76%). Remarkably, 23% of Dutch hospitals used mobile applications to consult the local antibiotic formulary. Presence of local guidelines for common infectious diseases ranged from 63% (Slo) to 94% (Fr). Nearly all participating hospitals based these guidelines on local antimicrobial susceptibility, except for France (53%). Local guidelines could also be consulted mainly via intranet (range 40–85%), whilst many Slovenian and Italian hospitals also used a printed version in the physician's room (47% and 32%, respectively). Moreover, 53% of the Slovenian hospitals used a daily care bundle.

Available information technology (IT) support for the AMS team ranged from 41% (It) to 68% (Nl). Dedicated IT support was available only in the Netherlands (8%) and Italy (13%), whilst in other countries it could only be applied for if needed.

3.3. Stewardship objectives and their related improvement strategies

3.3.1. Quantity of antibiotic use and susceptibility reports

The quantity of antibiotic use (either all antibiotics or specific agents) was monitored by the majority of participating hospitals, ranging from 72% (Nl) to 100% (Slo and Fr); defined daily doses (DDD) was the most frequently applied metric (range 64–91%). Cumulative susceptibility reports were available to the AMS team in most of the participating hospitals (Nl 83%, Fr 84% and It 82%), except for Slovenia (39%).

3.3.2. Appropriateness of antibiotic use

There was large variation between the participating countries in the use of monitoring and advice as a strategy to improve AMS objectives (Fig. 2). Hospital AMS teams primarily monitored the following objectives: restricted antibiotics (range 82–92%); therapeutic drug monitoring (TDM) (range 0–65%); timely IV-to-oral switch (range 0–53%); streamlining (range 3–33%); and discontinuation (range 0–35%). Monitoring of TDM (65%) and IV-to-oral switch (53%) was most frequently performed in Dutch hospitals. Monitoring of guideline-adherent empirical therapy (30%), surgical prophylaxis (26%) and correct use of diagnostics (35%) was most frequently performed in Slovenian hospitals. Monitoring the use of restricted agents (92%) and bedside consultation (60%) was performed most frequently in French hospitals.

Overall, restricted use of antibiotics was monitored most frequently in all countries. Strategies to improve restricted use are listed in Table 3. Patient categories involved as well as the frequency and timing of monitoring are listed in Supplementary Table S3.

3.3.3. Point prevalence survey (PPS) or audit

The performance of a PPS (i.e. 'a cross-sectional assessment of the quality of antibiotic use at patient level in the hospital' [14]) ranged from 22% (Nl) to 67% (Fr) of hospitals. Use of surgical prophylaxis was most frequently measured by means of a PPS or audit (i.e. 'a systematic collection of data from patient records to assess the appropriateness of professionals' performance or patient outcomes and to provide feedback') compared with other stewardship objectives. Remarkably, TDM was not measured by means of a PPS or audit in the Netherlands and Slovenia.

Patients categories involved as well as the frequency and timing of PPSs and audits are listed in Supplementary Table S3.

3.3.4. Type of advice

Dutch hospitals mainly advised on AMS objectives by telephone. Italian and French hospitals, on the other hand, mainly gave face-to face advice. Advice through computerised alerts was mainly used in France, ranging from 27% of hospitals who advised on the use of surgical prophylaxis and correct use of diagnostics to 68% of hospitals who advised on streamlining of antibiotic therapy. Further details are shown in Supplementary Table S4.

3.3.5. Education on antimicrobial stewardship

Education for residents was provided in 39% (Slo) to 66% (Fr) of hospitals. Overall, such education was provided approximately two times per year. Many Dutch hospitals provided education more frequently than twice a year. Slovenian hospitals provided education to residents mostly once a year (44%) or on demand (33%). Education for specialists was provided in all four countries, ranging from 28% (Nl) to 54% (It) of hospitals. Overall, the average frequency of stewardship education for specialists was approximately one to two times per year; Italian and Dutch hospitals provided education more frequently. Details on education are provided in Table 4.

4. Discussion

Here we present data regarding the characteristics of ASPs in acute-care hospitals from four different European countries (the

Table 3
Improvement strategies for restricted agents[a,b].

	Nl	Slo	Fr	It
Pre-authorisation[c]	9/52 (17)	12/19 (63)	23/82 (28)	22/32 (69)
Post-authorisation[d]	22/52 (42)	6/19 (32)	18/82 (22)	4/32 (13)
Formulary restriction[e]	15/52 (29)	10/19 (53)	0	9/32 (28)
Antibiotic order forms[f]	3/52 (6)	12/19 (63)	62/82 (76)	18/32 (56)
Computerised alert	14/52 (27)	0	25/82 (30)	4/32 (13)
Check for diagnostic tests	10/52 (19)	2/19 (11)	17/82 (21)	5/32 (16)
Mandatory bedside consultation	1/52 (2)	3/19 (16)	3/82 (4)	9/32 (28)
Stop orders	1/52 (2)	5/19 (26)	11/82 (13)	8/32 (25)
Post-prescription review	25/52 (48)	8/19 (42)	32/82 (39)	2/32 (6)

Nl, the Netherlands; Slo, Slovenia; Fr, France; It, Italy.
[a] Numbers are *n*/*n* (%).
[b] Antimicrobials requiring prior authorisation by an infectious diseases specialist, clinical microbiologist or clinical pharmacist.
[c] Prescribing restricted agents only after authorisation.
[d] Continuation of a specific agent requires authorisation after the first administration.
[e] Restricted agents are not available.
[f] Documenting clinical indication when prescribing restricted agent.

Table 4
Education as an antimicrobial stewardship intervention[a].

Education	Nl	Slo	Fr	It
Education provided for residents	33/57 (58)	9/23 (39)	58/88 (66)	24/39 (62)
Voluntary	19/33 (58)	6/9 (67)	27/58 (47)	17/24 (71)
Mandatory	14/33 (42)	3/9 (33)	31/58 (53)	7/24 (29)
Frequency of education for residents				
Daily	0	0	0	0
Once a week	1/33 (3)	0	1/58 (2)	1/24 (4)
Once a month	5/33 (15)	0	1/58 (2)	1/24 (4)
Once every 2 months	2/33 (6)	0	1/58 (2)	1/24 (4)
4 times per year	7/33 (21)	1/9 (11)	5/58 (9)	3/24 (13)
2 times per year	6/33 (18)	1/9 (11)	46/58 (79)	7/24 (29)
Once every year	7/33 (21)	4/9 (44)	2/58 (3)	4/24 (17)
On demand	3/33 (9)	3/9 (33)	2/58 (3)	6/24 (25)
Other	2/33 (6)	0	0	1/24 (4)
Education subjects for residents				
Antimicrobial resistance	31/33 (94)	8/9 (89)	49/58 (84)	24/24 (100)
Specific syndromes (e.g. pneumonia)	31/33 (94)	7/9 (78)	42/58 (72)	19/24 (79)
Restricted medication	17/33 (52)	5/9 (56)	32/58 (55)	12/25 (50)
IV-to-oral switch	20/33 (61)	7/9 (78)	33/58 (57)	20/24 (83)
Streamlining or de-escalation	20/33 (61)	7/9 (78)	52/58 (90)	20/24 (83)
Dose optimisation (TDM)	13/33 (39)	5/9 (56)	18/58 (31)	12/24 (50)
PPS or audit	5/33 (15)	1/9 (11)	2/58 (3)	8/24 (33)
Other subjects	5/33 (15)	2/9 (22)	2/58 (3)	0
Education provided for specialists	16/57 (28)	10/23 (43)	35/88 (40)	21/39 (54)
Voluntary	14/16 (88)	8/10 (80)	34/35 (97)	16/21 (76)
Mandatory	2/16 (13)	2/10 (20)	1/35 (3)	5/21 (24)
Frequency of education for specialists				
Daily	1/16 (6)	0	0	2/21 (10)
Once a week	0	0	0	2/21 (10)
Once a month	2/16 (13)	0	1/35 (3)	2/21 (10)
Once every two months	1/16 (6)	0	0	2/21 (10)
4 times per year	4/16 (25)	0	3/35 (9)	3/21 (14)
2 times per year	2/16 (13)	2/10 (20)	10/35 (29)	4/21 (19)
Once every year	5/16 (31)	5/10 (50)	10/35 (29)	2/21 (10)
On demand	1/16 (6)	3/10 (30)	7/35 (20)	4/21 (19)
Other	0	0	4/35 (11)	0
Education subjects for specialists				
Antimicrobial resistance	15/16 (94)	7/10 (70)	31/35 (89)	19/21 (90)
Specific syndromes (e.g. pneumonia)	15/16 (94)	8/10 (80)	28/35 (80)	19/21 (90)
Restricted medication	10/16 (63)	8/10 (80)	22/35 (63)	11/21 (52)
IV-to-oral switch	9/16 (56)	10/10 (100)	15/35 (43)	16/21 (76)
Streamlining or de-escalation	12/16 (75)	9/10 (90)	25/35 (71)	18/21 (86)
Dose optimization (TDM)	10/16 (63)	8/10 (80)	10/35 (29)	12/21 (57)
PPS or audit	6/16 (38)	2/10 (20)	10/35 (29)	6/21 (29)
Other subjects	0	1/10 (10)	2/35 (6)	0

Nl, the Netherlands; Slo, Slovenia; Fr, France; It, Italy; IV, intravenous; TDM, therapeutic drug monitoring; PPS, point prevalence survey.
[a] Numbers are *n*/*N* (%) (where *N* is the number of respondents).

Netherlands, Slovenia, France and Italy). The findings show that the ASP prerequisites met as well as the objectives and improvement strategies chosen vary considerably among the four European countries.

In 2002–2005, Bruce et al. used a survey to investigate a selection of ASP indicators on resources and activities in 170 hospitals from 32 European countries [15]. The results showed that ASPs were more developed in Northern and Western European countries compared with Southern and South-Eastern European countries. However, the survey was distributed directly through the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the hospitals participating were all self-selected, leading to an important response bias [15]. In 2012, a global survey showed high variability in ASPs between continents; data from European hospitals showed a relatively good level of ASP implementation, however different countries were pooled together, whereas European countries are known to differ in terms of antibiotic use policies [16,17].

Efforts have been taken to implement and standardise policies by distributing European guidelines on the prudent use of antimicrobials as well as the TATFAR indicators for hospital ASPs [18,19]. In a recent consensus paper, ASP core elements, and related checklist items, that should be present in all hospitals worldwide have been identified [20]. Comparing the current results with these core elements, European Centre for Disease Prevention and Control (ECDC) recommendations and TATFAR indicators, several elements of ASPs could be identified as highly variable among the hospitals participating in the survey, providing room for improvement. For example, the presence of an AMS team ranged from 42–94% even though nearly all French hospitals without an AMS team did have an 'ASP lead' in place. Also, there was considerable variation between the participating countries related to the presence of a local antibiotic formulary or local guidelines for infectious diseases, the availability of IT support and provision of salary support for an AMS team.

A formal ASP was present in the Netherlands and France more often than in Slovenia and Italy. ASPs are mandatory in the Netherlands and France [21]. The Dutch healthcare inspectorate monitors the presence of AMS teams, and the Dutch Working Party on Antibiotic Policy (SWAB) had facilitated AMS teams in their functioning since 2012 [22–24]. In France, ASPs are mandatory as signed by their Ministry of Health in 2007 [25]. ASPs are also mandatory in Slovenia, as signed by their Ministry of Health in 2011, yet only 60% of the hospitals have an official ASP and AMS team present. A recent paper by Beović et al. showed large heterogeneity and insufficiency in legal ASP frameworks in European hospitals and concluded that if ASPs are mandatory, this does not always imply ASPs are implemented accordingly [21]. Thus, special attention should be paid to the implementation of regulations and the sustainability of AMS activities [21]. In Italy, ASPs are not yet mandatory [21,26]. Also, the percentage of ASPs present in Italy (60%) would probably be lower when investigated nationwide as hospitals were selected based on the presence of an ID specialist.

Despite the prevailing evidence that a multidisciplinary team should lead an ASP, AMS teams were only widely implemented in the Netherlands, whereas in France, Italy and Slovenia their presence was substantially lower. In France, for example, an AMS team was present in only 42% of participating hospitals. The mandatory composite indicator for hospital ASPs in France (ICATB2) [27], required for national hospital accreditation standards, advocates the need for one ASP lead and not for a multidisciplinary team, which does not live up to the 2015 recommendation by the French Task Force on Antimicrobial Resistance to have a multidisciplinary team in each hospital [28].

Lack of support from the hospital management was an issue in all four countries investigated; salary support and time investment by the AMS teams was likely not sufficient to optimally develop and maintain ASPs. In 2016, the ECDC recommended that salary support and time investment should be established for the AMS team [18]. Based on existing national standards, salary support for the AMS teams should range between 1–3 FTE/500 beds [23,29] depending on the country's organisation of care, which is considerably higher than the current median (Supplementary Table S2) in all four countries. For many AMS teams it was difficult to define the time spent on AMS activities as the activities and salary support provided for ASPs is rarely well defined in job contracts/descriptions. These results must therefore be interpreted with caution. For example, the Netherlands reported the lowest time investment per week (median 17 h/week/500 beds; range 2–96 h/week/500 beds), whilst according to Fig. 2 the Netherlands is engaged in the most stewardship activities. Also, Slovenian hospitals were found to spend substantially more time on AMS activities compared with the other participating countries. However, the difficulty in defining time investment, the relatively small number of Slovenian hospitals and hospital size could have influenced the results.

The 2002–2005 survey conducted by Bruce et al. concluded that accessibility for AMS resources was suboptimal [15]. The current results highlighted substantial improvements on prerequisites for ASPs, such as the presence of antibiotic formularies and local guidelines for the main infectious syndromes. Moreover, use of an intranet is now preponderant in most countries. Also, the medical record has turned electronic in nearly all hospitals, which should facilitate ASPs.

Recently, a similar survey by Nhan et al. described the implementation of ASPs in the USA [30]. In that study, 82% of participating US hospitals had an active ASP in place and 48% had a dedicated budget for their ASP, which is comparable with France, higher than Slovenia and Italy, but lower compared with the Netherlands. Similar results were found for the implementation of local guidelines for common infectious diseases. The most frequently applied optimisation strategy in the USA was IV-to-oral switch (93%), whilst ASPs in European hospitals focused more often on restricted antibiotic use. Remarkably, nearly all US hospitals (92%) used days of antibiotic therapy (DOT), whilst Europe used DDD more often (range 64–91%). Moreover, education was provided considerably more often in the USA. However, we need to take into account that results from the US survey were based only on the top-ranked US hospitals and the response rate was 50%, which is prone to response bias and might overestimate US results.

The main strength of the current study is that, to our knowledge, this is the first survey that simultaneously evaluated ASP prerequisites but also stewardship objectives and their improvement strategies (the three building blocks of an ASP) in a considerable number of hospitals in four different European countries, with systematic sampling performed in three of the four countries.

The main limitation of this study is that in Italy convenience sampling was performed based on the presence of an ID department. Therefore, Italian respondents were probably those most concerned with and interested in AMS, which might have given an optimistic view of the Italian results (response bias). For the other countries, sampling was performed systematically. The Netherlands and Slovenia invited all acute-care hospitals to respond and the response rates were 80% and 86%, respectively, therefore the representability of these results should be considered as high. In addition, Dutch non-responders were contacted and 81% were confirmed to have an AMS team present or in preparation. The main reason for non-response was lack of time. In France, as the national health system includes a very high number of hospitals and acute care is provided from public as well as private hospitals, randomised sampling after stratification based on the type of hospital was performed in order to include all the categories

of acute-care hospitals. The absolute number of respondents in France was high ($n = 97$), however the response rate was lower than in other countries (45%), in particular for private clinics: if respondents are those most interested in ASPs, we can presume that ASPs in the private French sector are not as well implemented as in public hospitals.

In conclusion, this survey demonstrated large variation in the presence of AMS prerequisites, AMS objectives and related improvement strategies chosen by AMS teams of hospitals in four different European countries. Despite the many efforts made in the last years to fight antimicrobial resistance and to implement AMS at the national and international level, there is room for improvement. As this study demonstrates variation between hospitals and countries in meeting the prerequisites of AMS, stimulating appropriate system prerequisites throughout Europe, e.g. by introducing staffing standards and financial support for ASPs, seems a first priority.

Declaration of Competing Interest

None declared.

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Ethical approval

Not required.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2019.06.005.

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