Repeated nationwide point-prevalence surveys of antimicrobial use in Swedish hospitals: data for actions 2003–2010

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This study sought to analyse antimicrobial pressure, indications for treatment, and compliance with treatment recommendations and to identify possible problem areas where inappropriate use could be improved through interventions by the network of the local Swedish Strategic Programme Against Antibiotic Resistance (Strama) groups. Five point-prevalence surveys were performed in between 49 and 72 participating hospitals from 2003 to 2010. Treatments were recorded for 19 predefined diagnosis groups and whether they were for community-acquired infection, hospital-acquired infection, or prophylaxis. Approximately one-third of inpatients were treated with antimicrobials. Compliance with guidelines for treatment of community-acquired pneumonia with narrow-spectrum penicillin was 17.0% during baseline 2003–2004, and significantly improved to 24.2% in 2010. Corresponding figures for quinolone use in uncomplicated cystitis in women were 28.5% in 2003–2004, and significantly improved, decreasing to 15.3% in 2010. The length of surgical prophylaxis improved significantly when data for a single dose and 1 day were combined, from 56.3% in 2003–2004 to 66.6% in 2010. Improved compliance was possibly the effect of active local feedback, repeated surveys, and increasing awareness of antimicrobial resistance. Strama groups are important for successful local implementation of antimicrobial stewardship programs in Sweden.

Introduction

The Swedish Strategic Programme Against Antibiotic Resistance (Strama) was established during the 1990s to promote rational use of antibiotics [1]. At that time in Sweden, data on antimicrobial use in hospitals was

limited to statistics on the total amount of deliveries from hospital pharmacies [2]. While such data allow analysis over time and comparison of patterns of antimicrobial use among hospitals and regions, they do not include the indication for therapy and thus do not permit assessment of compliance with recommendations. Knowledge of antimicrobial use in Swedish hospitals was largely restricted to local projects [3] when the national Strama board [1] initiated the nationwide point-prevalence survey (PPS) in 2003. In a PPS, data is registered during one day and gives a cross-sectional figure over, in this case, antibiotic use for different diagnosis groups. Numbers are small when looking only at one hospital but if data are collected for several hospitals, and surveys are repeated, data becomes more reliable.

This paper presents an analysis of antimicrobial use related to diagnosis in Swedish hospitals and experiences from interventions based on findings in five PPS from 2003 to 2010.

Methods

Sweden has 21 county councils and ca 80 public acute-care hospitals, all of which were invited to participate in the studies. Participation was optional and between 19 and 21 county councils and 49 and 72 acute-care hospitals (somatic care only, that is, excluding psychiatric care) over the study years. The mean length of stay (LOS) was 5.4 days in 2003, 5.3 days in 2004, 5.1 days in 2006, 5.0 days in 2008, and 4.8 days in 2010 [4].

FIGURE 1

Distribution of antibiotics given to patients in the nationwide hospital point-prevalence surveys, Sweden, 2003–2010

Excludes antibiotics given as prophylaxis.

The studies were performed as PPS during one day within a two-week period in November 2003, 2004, 2006, 2008, and 2010. Data were collected by infectious-disease specialists at 08:00 from the medical records of all patients receiving systemic antibacterials. The total number of admitted patients was used as the denominator. The survey protocol is available online [5]

Therapy was defined as the conjunction of the drug(s) dispensed, diagnosis and whether the prescription was for community-acquired infection (CAI), hospital-acquired infection (HAI), or prophylaxis [5]. More than one therapy could be registered for one patient, and one therapy could consist of more than one antibiotic.

The following patient data were collected: age, sex, prescribed drug(s), dose per administration, number of doses, route of administration, focus of the infection (or for prophylaxis) and significant risk factors for infection such as immunosuppression, presence of foreign material and invasive medical devices.

The assessment also included whether the indication for treatment was documented in the records and whether a relevant culture was done before initiation of treatment. A final assessment of the therapy was made by the surveyors as directed therapy, empirical therapy, or deviating from recommendations.

Duration of surgical prophylaxis was classified as single dose, 1 day, or more than 1 day.

FIGURE 2

Distribution of indications for antimicrobial treatment according to predefined diagnosis groups, nationwide hospital point-prevalence surveys, Sweden, 2003–2010

Excludes antibiotics given as prophylaxis, includes antimycotics and tuberculostatic treatments.

Antimicrobials were classified according to the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) Classification System [6]. The defined daily dose (DDD) was used as indicator for antimicrobial pressure and calculated from the amounts of antibiotics given per day according to the WHO definitions, with the exception of oral vancomycin, for which the prescribed daily dose of 500 mg was chosen. DDDs were not registered for children under 16 years. Drugs recorded in this study were: antibiotics (oral vancomycin (A07AA09), terbinafine (D01BA02), oral imidazoles (P01AB) and antibacterials for systemic use (J01), excluding methenamine), antimycotics (J02A) and tuberculostatics (J04A).

Coded patient identity and study data were entered into a web-based interface (Neotide Ltd, Vaasa, Finland) by each local Strama group. A standardised validation

was performed, and incongruences were addressed for reassessment by each Strama group.

A systematic approach in feeding back the results to hospitals was achieved by including the local Strama groups in the process. Together with the research team, Strama representatives were involved in formulating three main messages for interventions, based on data from the 2003 and 2004 surveys. These representatives could then present and discuss the study results in their own counties while including relevant local aspects. Interventions also took the form of information leaflets addressing main messages that were sent to all hospital prescribers and displayed in participating hospitals in visible areas such as in lifts and on bulletin boards.

TABLE 1

Demographics in five nationwide hospital point-prevalence surveys of antimicrobial use, Sweden, 2003–2010

	2003	2004	2006	2008	2010
Number of available beds in Sweden	22,471	22,454	21,628	21,302	21,019
Number of admitted patients in survey					
Tertiary care hospitals	4,808	3,191	6,675	5,269	6,849
Secondary care hospitals	5,977	5,536	7,049	7,189	6,804
Primary care hospitals	2,751	2,621	3,412	3,529	3,429
Specialised geriatric hospitals	NA	NA	NA	331	621
Total (% of available beds)	13,536 (60.2%)	11,348 (50.5%)	17,136 (79.2%)	16,318 (76.6%)	17,703 (84.2%)
Number of patients in survey with antimicrobial treatment (% of admitted patients in survey)	4,178 (30.9%)	3,622 (31.9%)	5,588 (32.6%)	5,339 (32.7%)	5,928 (33.5%)
Age of treated patients in survey (% of treated patients in survey)					
0–16 years	266 (6.4%)	183 (5.1%)	280 (5.0%)	268 (5.0%)	336 (5.7%)
17–60 years	1,102 (26.4%)	913 (25.2%)	1,439 (25.8%)	1,266 (23.7%)	1,453 (24.5%)
61–79 years	1,624 (38.9%)	1,465 (40.4%)	2,187 (39.1%)	2,168 (40.6%)	2,326 (39.2%)
≥80 years	1,186 (28.4%)	1,061 (29.3%)	1,682 (30.0%)	1,637 (30.7%)	1,813 (30.6%)
Number of patients in ICUs					
Number of adults in ICUs with antimicrobial treatment (% of all treated adults)	176 (4.5%)	154 (4.5%)	266 (5.0%)	227 (4.5%)	240 (4.3%)
Number of children in ICUs with antimicrobial treatment (% of all treated children)	25 (9.4%)	27 (14.8%)	41 (14.6%)	26 (9.7%)	49 (14.6%)

ICU: intensive care unit; NA: not available.

Statistical calculations of changes over time were performed only for the three intervention areas. The average percentage from the first two surveys were used as baseline measurements and counted as one time period (2003–2004). Changes over time were examined using chi-squared tests. First, a comprehensive test including all study years was performed. If the result of this test showed statistical significance ($p < 0.001$), additional chi-squared tests in pairs were performed. Further statistical calculations were not considered appropriate in this descriptive survey because of the high coverage of admitted patients within somatic hospital care.

The survey was assessed by the Regional Ethical Review Board in Lund on 24 September 2003, registration number LU 596-03.

Results

Study demographics are presented in Table 1. The number of admitted patients included varied between 11,348 and 17,703 and the number of patients with antimicrobial treatment varied between 3,622 and 5,928. The proportion of women varied between 48.7% and 49.9%. The median age was 73 years old for women (range: 0–108 years, interquartile range (IQR): 27 years) and 70 years old for men (range: 0–108 years, IQR: 23 years).

The observed prevalence of CAI, HAI, and prophylaxis in different hospital categories is shown in Table 2. Tertiary hospitals and specialised geriatric hospitals had a higher prevalence of treatment for HAI, and tertiary hospitals also had a higher proportion of patients on medical prophylaxis compared with the other hospital categories.

The mean antimicrobial pressure within adult specialties was 40.3 DDD per 100 admitted patients in 2003, 43.1 in 2004, 43.5 in 2006, 45.9 in 2008, and 45.6 in 2010. Antibiotics represented an average of 92.1%, antimycotics, 2.4%, and tuberculostatics, 5.5% of the total DDD per 100 admitted patients, respectively.

The documented indication for antibiotic treatment in medical records varied over the study years between 82.3–85.2%. After oral completion of information from the staff, an indication for treatment could be obtained in 94.9% of patients. The distribution of all given antibiotics used for treatment of infections in adults (prophylaxis excluded) is shown in Figure 1. Cephalosporins and fluoroquinolones were the most frequently used antibiotics, although use decreased over the years of the study. The use of penicillins increased during the study period, especially penicillins in combination with piperacillin.

As shown in Figure 2, pulmonary infections were the most common of the 19 predefined diagnosis groups.

TABLE 2

Prevalence of community-acquired infection, hospital-acquired infection, and surgical and medical prophylaxis in five nationwide hospital point-prevalence surveys of antimicrobial use, Sweden, 2003–2010

	Number of therapies (% of admitted patients)				
	2003	2004	2006	2008	2010
Community-acquired infection					
Tertiary care hospitals	836 (17.4%)	535 (16.8%)	1,096 (16.4%)	850 (16.1%)	1,112 (16.2%)
Secondary care hospitals	1,022 (17.1%)	1,048 (18.9%)	1,334 (18.9%)	1,294 (18.0%)	1,404 (20.6%)
Primary care hospitals	446 (16.2%)	464 (17.7%)	629 (18.4%)	721 (20.4%)	724 (21.1%)
Specialised geriatric hospitals	NA	NA	NA	52 (15.7%)	65 (10.5%)
Total	2,304 (17.0%)	2,047 (18.0%)	3,059 (17.9%)	2,917 (17.9%)	3,305 (18.7%)
Hospital-acquired infection					
Tertiary care hospitals	510 (10.6%)	365 (11.4%)	841 (12.6%)	690 (13.1%)	901 (13.2%)
Secondary care hospitals	494 (8.3%)	517 (9.3%)	657 (9.3%)	653 (9.1%)	600 (8.8%)
Primary care hospitals	235 (8.5%)	190 (7.2%)	284 (8.3%)	285 (8.1%)	281 (8.2%)
Specialised geriatric hospitals	NA	NA	NA	73 (22.1%)	85 (13.7%)
Total	1,239 (9.2%)	1,072 (9.4%)	1,782 (10.4%)	1,701 (10.4%)	1,867 (10.5%)
Surgical prophylaxis					
Tertiary care hospitals	251 (5.2%)	189 (5.9%)	332 (5.0%)	302 (5.7%)	379 (5.5%)
Secondary care hospitals	263 (4.4%)	195 (3.5%)	306 (4.3%)	294 (4.1%)	261 (3.8%)
Primary care hospitals	111 (4.0%)	125 (4.8%)	158 (4.6%)	171 (4.8%)	120 (3.5%)
Specialised geriatric hospitals	NA	NA	NA	1 (0.3%)	3 (0.5%)
Total	625 (4.6%)	509 (4.5%)	796 (4.6%)	768 (4.7%)	763 (4.3%)
Medical prophylaxis					
Tertiary care hospitals	120 (2.5%)	110 (3.4%)	202 (3.0%)	178 (3.4%)	301 (4.4%)
Secondary care hospitals	95 (1.6%)	84 (1.5%)	72 (1.0%)	97 (1.3%)	90 (1.3%)
Primary care hospitals	13 (0.5%)	19 (0.7%)	22 (0.6%)	22 (0.6%)	28 (0.8%)
Specialised geriatric hospitals	NA	NA	NA	3 (0.9%)	6 (1.0%)
Total	228 (1.7%)	213 (1.9%)	296 (1.7%)	300 (1.8%)	425 (2.4%)

NA: not available.

All age groups are included.

Table 3 shows the three most common diagnosis groups of CAI and the antibiotic classes used for therapy. Compliance with treatment recommendations for uncomplicated community-acquired pneumonia (CAP) improved because treatment with beta-lactamase-sensitive penicillins increased significantly from 17.0% in 2003–2004 to 24.2% ($p < 0.001$) in 2010. Likewise, compliance with treatment recommendations for women with lower urinary tract infections (UTI) improved significantly. In 2003–2004, fluoroquinolones were used in 28.5% for treatment vs 15.3% ($p < 0.001$) in 2010. Beta-lactamase-resistant penicillins (isoxazoly penicillins) were the most commonly used drugs for skin and soft-tissue infections.

Antimicrobials were administered parenterally in 43.0%, 44.4%, 47.3%, 48.2%, and 51.0% of all cases in each study year, respectively. The proportion of treatments with a relevant culture taken before therapy ranged between the study years from 67.7–75.4% for HAI and 62.1–72.6% for CAI. Before parenteral treatment, culture was recorded in a range of 69.4–78.3% of

the patients and before oral treatment in 60.3–69.6% of the patients.

The most frequently used antibiotics for surgical prophylaxis over the years were beta-lactamase-resistant penicillins (average 38.4%) and cephalosporins (average 19.4%). Surgical prophylaxis was given as a single dose in 23.7%, 25.5%, 32.4%, 26.4%, and 32.4% of all cases; during one day in 29.3%, 35.0%, 36.8%, 36.3%, and 34.2% of all cases; and for more than one day in 47.0%, 39.5%, 30.8%, 37.2%, and 33.4% of the cases in each study year, respectively. For a single dose, no clear pattern was shown but significant improvement was seen when data for a single dose and one day were combined, from 56.3% in 2003–2004 to 66.6% ($p < 0.001$) in 2010. Medical prophylaxis constituted on average 29.7% of all prophylaxis.

Discussion

A major finding in the PPS presented here was that approximately one-third of inpatients in acute-care hospitals in Sweden were treated with antimicrobials. We found that an increasing proportion, from

TABLE 3

The top six antibiotic classes used to treat the three most common community-acquired infections, nationwide hospital point-prevalence surveys, Sweden, 2003–2010

	Number of antibiotics given (%) per diagnosis				
	2003	2004	2006	2008	2010
Pulmonary infections (n=3,738)					
Beta-lactamase-sensitive penicillins (J01CE)	98 (17.0)	90 (16.9)	121 (14.3)	208 (25.5)	248 (24.2)
Cephalosporins (J01DB-J01DD)	190 (33.0)	197 (36.9)	287 (33.8)	219 (26.8)	237 (23.1)
Penicillins with extended spectrum (J01CA)	51 (8.9)	50 (9.4)	84 (9.9)	92 (11.3)	92 (9.0)
Tetracyclines (J01AA)	63 (11.0)	67 (12.5)	76 (9.0)	66 (8.1)	86 (8.4)
Fluoroquinolones (J01MA)	28 (4.9)	28 (5.2)	56 (6.6)	54 (6.6)	63 (6.2)
Combinations of penicillins (J01CR)	1 (0.2)	3 (0.6)	22 (2.6)	36 (4.4)	54 (5.3)
Skin and soft-tissue infections (n=2,064)					
Beta-lactamase-resistant penicillins (J01CF)	109 (29.1)	90 (29.1)	144 (31.8)	140 (31.0)	157 (32.9)
Lincosamides (J01FF)	78 (20.9)	64 (20.7)	90 (19.9)	95 (21.1)	77 (16.1)
Cephalosporins (J01DB-J01DD)	72 (19.3)	45 (14.6)	64 (14.1)	47 (10.4)	60 (12.6)
Beta-lactamase-sensitive penicillins (J01CE)	34 (9.1)	33 (10.7)	41 (9.1)	54 (12.0)	54 (11.3)
Combinations of penicillins (J01CR)	8 (2.1)	5 (1.6)	7 (1.5)	22 (4.9)	33 (6.9)
Fluoroquinolones (J01MA)	27 (7.2)	36 (11.7)	29 (6.4)	31 (6.9)	20 (4.2)
Female lower urinary tract infection (n=894)					
Penicillins with extended spectrum (J01CA)	54 (35.3)	58 (35.6)	94 (43.3)	101 (56.7)	97 (53.0)
Fluoroquinolones (J01MA)	37 (24.2)	53 (32.5)	41 (18.9)	21 (11.8)	28 (15.3)
Nitrofurantoin (J01XE)	6 (3.9)	8 (4.9)	5 (2.3)	21 (11.8)	19 (10.4)
Trimethoprim (J01EA)	34 (22.2)	31 (19.0)	56 (25.8)	21 (11.8)	17 (9.3)
Cephalosporins (J01DB-DD)	15 (9.8)	12 (7.4)	12 (5.5)	7 (3.9)	14 (7.7)
Trimethoprim with sulphonamides (J01EE)	3 (2.0)	1 (0.6)	7 (3.2)	5 (2.8)	4 (2.2)

Codes in parentheses are classifications from the World Health Organization Anatomical Therapeutic Chemical Classification System [6].

30.9% to 33.5%, of patients received antibiotics on the day of the survey over the study years. For comparison, the European Surveillance of Antimicrobial Consumption (ESAC) surveys, which were based on a protocol similar to ours, showed that an average of 30.1% (range 19–59%) [7] and 29.0% [8] of the patients received antimicrobials in 2006 and 2009, respectively. Standardised PPS methods for reviewing medical information is a reliable tool to describe patterns of antimicrobial use in hospitals [7,9–13]. When data are aggregated, variation is small between the separate studies, despite the expected variation in PPS methodology [14] that was previously noted in smaller studies [10,12].

We found that the prevalence of HAI treated with antimicrobials was of the same order of magnitude as reported for other European countries [15] and comparable to the 8.9–11.3% obtained in the national PPS performed twice a year since 2008 by the Swedish Association of Local Authorities and Regions (data not shown).

In our surveys, the indication for antimicrobial treatment was documented in the medical records in 82.3–85.2% of the cases, which is high compared with other studies [7,8,12]. A documented indication for treatment

is important to evaluate compliance with treatment guidelines and rational use of antibiotics [7–9,12].

When we started our surveys, recommendations for antibiotic treatment in hospitalised patients were not as standardised as for some common diagnoses treated in general practice. However, the following had been published: national recommendations for indications and duration of surgical prophylaxis since 1998 [16,17], treatment of mild to moderately severe CAP in 2004 [18], treatment of community-acquired uncomplicated lower UTI in women in 2007 [19], and recommendations for the prevention of extended-spectrum beta-lactamase-producing *Enterobacteriaceae* in 2007 [20]. Analyses after the surveys in 2003 and 2004 showed that the proportion of women with community-acquired lower UTI treated with fluoroquinolones (24.2–32.5%), and the overall use of cephalosporins (23.6–24.2% of all antibiotics), particularly in adults with CAP (33.0–36.9%), seemed too high and that the duration of surgical prophylaxis often exceeded one day. Thus, the interventions before the surveys in 2006 and onward were focused on improvement in these areas.

The surveys in 2008 and 2010 suggest that the desired improvements were achieved for UTI and CAP. Also, the proportion of lower UTIs among all treated infections decreased from a maximum of 12.7% in 2004 to 9.0% in

2010, possibly as a result of increased awareness during the feedback process not to treat asymptomatic bacteriuria. Increased use of the combination of penicillins and beta-lactamase inhibitors was probably an effect of the desire to decrease cephalosporin and quinolone use, as recommended in the ESBL-control programme [20]. Increasing awareness of antimicrobial resistance among prescribers in Sweden might also have contributed to the decreased use of cephalosporins and fluoroquinolones. These positive changes are supported by data on hospital consumption based on pharmacy sales [2]. We used an audit and feedback approach as the main intervention. Previously it has been shown that persuasive as well as restrictive approaches may affect antibiotic use [21]. However, the context in which the evidence is to be implemented plays a crucial role in the choice of methodology [22], which we addressed since feedback was given with local data. In modern interventions the role of evidence, context and facilitation is emphasised within the framework Promoting Action on Research Implementation in Health Services (PARIHS), and should be considered for future interventions [23].

It can be argued that the analysis should be restricted only to the subset of hospitals participating in all surveys, but because the coverage was so high, this should only play a minor role.

We found that compliance with evidence-based recommendations for surgical prophylaxis was poor, since the recommendation for most surgeries is only a single dose. This needs further attention, monitoring and intervention. Even if some of the prolonged prophylaxes were misclassified and were actually early treatments, they were not documented as such and were still not in accordance with existing recommendations [16,17]. Interestingly, around one-third of patients receiving prophylaxis in our surveys did so for medical, not surgical, conditions, an observation that has not previously been given much attention. These findings were unexpected and need to be investigated further. Medical prophylaxis might be of particular importance for the development and selection of antibiotic resistance in immunocompromised individuals who often receive long-term prophylaxis in low doses.

Earlier studies in different settings have also pointed to the high antimicrobial pressure in hospitals and frequent inappropriate use and/or poor compliance with guidelines [9,12,24,25]. Several specific areas for improvement suitable for quality assessment and benchmarking have been suggested, such as the high rate of intravenous administration [9,12,25], poor compliance with guidelines [9], lack of culture before treatment [9,10], and prolonged surgical prophylaxis [9,12]. The usefulness of these indicators was further discussed in the ESAC studies [7,8,26].

In our study, parenteral treatments were given in 43.0–51.0% of the cases when excluding prophylaxis.

This can be compared with more than 60% parenteral treatment in non-Swedish hospitals in other surveys [8,9,12]. One problem when comparing these figures is that it was not possible to assess the time that elapsed between admission and PPS. Duration of antibiotic treatment at time of PPS is not stated in several studies, including ours. In view of the comparatively short average LOS in Sweden, less than 50% on intravenous treatment is fairly low but can probably be decreased further, as previously shown in targeted interventions [27–29]. Our finding of a slowly increasing proportion of patients receiving intravenous antibiotics was paralleled by a slow increase of the mean antimicrobial pressure of 40.3–45.6 DDD per 100 admitted adult patients and a decrease in the average LOS in Swedish hospitals. The antibiotic pressure in acute care hospitals has continued to increase as measured by sales data [2]. These findings suggest that hospitalised patients in Sweden are more ill and require more intensive treatment than in previous years. When hospitals in the Baltic region were compared with one Swedish hospital, it was suggested that patients in Sweden were more severely ill compared with the other countries [12]. This should be kept in mind when analysing the proportion of intravenous antibiotic treatments as a quality indicator for rational antibiotic use. To improve comparative data analysis in the future, it would be advantageous to document the illness score, for instance with the McCabe score.

Relevant cultures are a prerequisite for rational antibiotic use. In Swedish hospitals, cultures were drawn before treatments in 62.1–75.4% of cases depending on the type of infection. This is more than the 19.7–64.5% reported from university hospitals in five European countries [9] but fewer than the 85% reported from Norway [10]. Cultures before treatment are becoming increasingly important for patient safety, particularly in HAI, because resistance rates are increasing and the time to adequate antibiotic treatment is the most important factor for clinical outcome in severe infections [30]. This suggests that there is room for improvement.

The strength of our PPS method was the nationwide coverage and the fact that local Strama groups were given immediate access to their own data for systematic feedback to prescribers.

Weaknesses in the PPS methodology itself [14] and differences in case mix within clinical specialties and among hospitals mean that benchmarking should be performed with caution and comparisons should be focused on the performance of the same unit over time [8,9,12,24,25,31]. Another disadvantage with the present PPS method is the laborious way that data are collected. Even though data from our surveys are somewhat ‘old’ they are still relevant for benchmarking and monitoring of compliance and treatment patterns for different diagnoses in Swedish hospitals. In contrast to other publications of PPS surveys we describe

how data have been used for widespread coordinated national feedback and interventions which were later followed up. Furthermore, our surveys informed the ESAC surveys, particularly regarding the survey protocol, and are therefore important for comparing antibiotic stewardship over time in the European Union.

We found that the repeated nationwide PPS were successfully implemented and have contributed knowledge on indications for use of antimicrobials in Swedish hospitals. The compliance with treatment recommendations for treatment of CAP and lower UTI in women has improved after interventions, while the duration of surgical prophylaxis still seems to be too long.

National and local recommendations are a cornerstone of antimicrobial stewardship. Structures like the multidisciplinary local Strama groups are of vital importance for local feedback and implementation of treatment recommendations and for the success and sustainability of antimicrobial stewardship programs. However, the laborious PPS should be replaced by IT-based systems for automatic retrieval of intention-to-treat data from digital records.

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Authors' contributions

Otto Cars: initiated study, designed and planned the study, analysed data and planned interventions. Mats Erntell designed and planned the study, collected data, validated data, analysed data and planned interventions. Johan Struwe, Peter Ulleryd, Inga Odenholt, Mårten Prag and Håkan Hanberger designed and planned the study, collected data, analysed data and planned interventions. Katarina Skärlund and Gunilla Skoog designed and planned the study, validated data, analysed data and planned interventions. Gunilla Skoog, Johan Struwe, Håkan Hanberger and Mats Erntell wrote the manuscript.

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