

# Use of ECDC PPS HAI&AU data to evaluate adherence to national guidelines for antimicrobial treatment of community-acquired pneumonia

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## KEY WORDS

antimicrobial policy,  
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## ABSTRACT

**INTRODUCTION** Point prevalence surveys are widely described as a useful tool for evaluating antimicrobial policy and adherence to guidelines.

**OBJECTIVES** We aimed to investigate if data from the European Centre for Disease Prevention and Control (ECDC) point prevalence survey of healthcare-associated infections and antimicrobial use (PPS HAI&AU) can be used to evaluate adherence to national guidelines for the treatment of community-acquired pneumonia (CAP) and to analyze the quality of treatment regimens.

**PATIENTS AND METHODS** Data for 72 698 patients were collected in Poland between the years 2012 and 2015 according to the ECDC Protocol v.4.2. CAP was an indication for antimicrobial treatment in 3608 patients. Patients hospitalized longer than 48 hours were excluded. A total of 667 patients met the inclusion criteria, and 79 regimens were recorded and evaluated as concordant or discordant with the guidelines. Afterwards, 7 experts scored the regimens from 1 to 5. The averages were calculated, and the results below 3.0 were considered as not optimal and those of 3.0 or higher—as optimal. Coherence of the experts' scores was evaluated.

**RESULTS** Of all patients, 153 (22.8%) were treated exactly according to the guidelines. Nineteen regimens (24.0%) were optimal but discordant with the guidelines; they were administered to 346 patients (51.9%). The remaining 50 regimens (63.3%) were evaluated as discordant and not optimal and were used in 169 patients (25.3%). The correlation results of the experts' scores were significant.

**CONCLUSIONS** ECDC PPS HAI&AU data can be efficiently used to assess adherence to guidelines. Despite low adherence (22.8%), almost 75% of patients received optimal antimicrobial treatments. Actions promoting the guidelines and time-series studies analyzing improvement of adherence should be considered.

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**INTRODUCTION** Point prevalence surveys (PPSs) are widely described as a useful tool for evaluation of antimicrobial policy and adherence to guidelines.<sup>1-3</sup> International guidelines are developed by scientific societies to improve the quality of care as well as patient safety. They are based on the results of clinical studies, epidemiological data, as well as on drug pharmacokinetics, pharmacodynamics, and pharmacoecconomy. National guidelines are based on local epidemiology, which may differ between countries, especially in the aspect of increasing antimicrobial resistance.

The guidelines for antimicrobial use in Poland are elaborated by the National Antimicrobial Protection Programme ([www.antybiotyki.edu.pl](http://www.antybiotyki.edu.pl)). The first edition of the guidelines for the management of community-acquired respiratory tract infections was published in 2010,<sup>4</sup> and then revised in 2016.<sup>5</sup> The guidelines were approved by the Polish Ministry of Health.

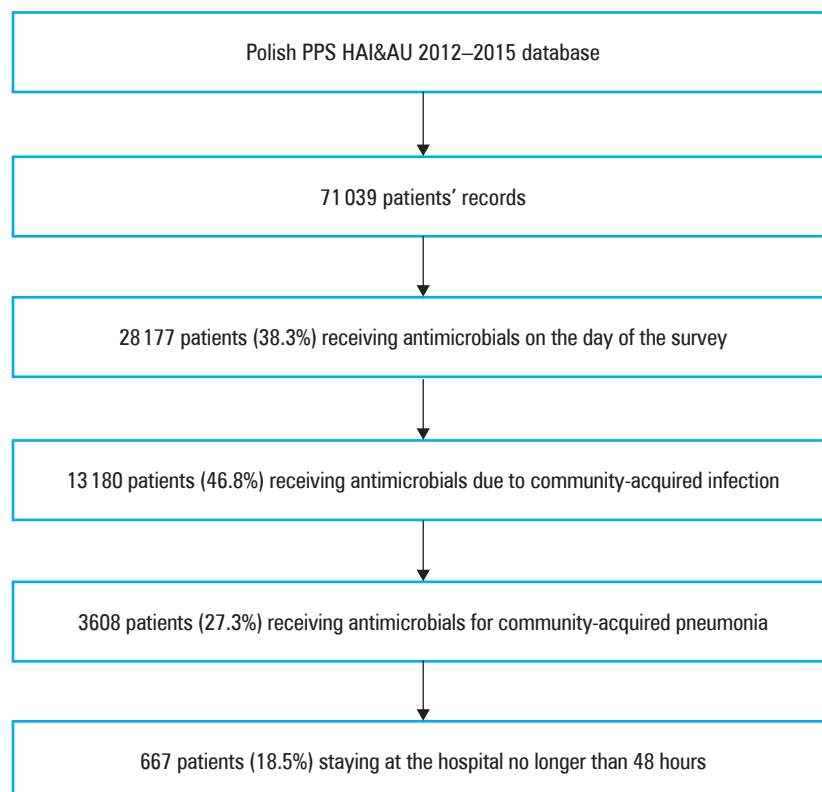
The European Centre for Disease Prevention and Control (ECDC) point prevalence survey of healthcare-associated infections and antimicrobial use (PPS HAI&AU) has been organized in Poland yearly since 2012. We decided to use aggregated data collected between 2012 and 2015 on antimicrobial use to evaluate adherence to the national guidelines for the treatment of community-acquired pneumonia (CAP), as one of the most frequent infections that result in admission to acute care hospitals. The analysis was possible because all the required data are being collected during PPS HAI&AU (diagnosis, site of infection, and prescribed antimicrobial).

**PATIENTS AND METHODS** During 4 years, data for 72 698 patients were collected according to the ECDC Protocol of PPS HAI &AU v.4.2.<sup>6</sup> The data selection process is shown in **FIGURE 1**. Briefly, of the 72 698 patients, 28 177 received antimicrobials on the day of the survey. Community-acquired infection was an indication for treatment in 13 180 patients. Out of this group, CAP was an indication in 3608 patients. To eliminate the effect of microbiology results and to capture the initial empirical treatment, we decided to exclude patients staying at acute care hospitals more than 2 days. Finally, 667 patients met the inclusion criteria and 79 treatment regimens were recorded.

Initially, the first author (AD) evaluated the regimens as concordant or discordant with the national guidelines. According to the available guidelines, amoxicillin, ampicillin, cefotaxime, ceftriaxone, clarithromycin, and azithromycin were recommended to treat CAP.  $\beta$ -lactam drug or macrolide could be used alone or in combination. In the second step, 7 experts (WH, AM-K, GD, MZ, TO, AŻ, and AD) scored the 79 regimens from 1 to 5 to evaluate how optimal they could be in the treatment of CAP. From the expert scores, the averages were calculated for each regimen, and the results below 3.0 were considered as nonoptimal and those equal 3.0 or higher—as optimal.

**Statistical analysis** To evaluate the coherence between the 7 experts, the Spearman correlation rank coefficient was used. Based on the Shapiro–Wilk test results, the nonparametric test was used. The differences at a *P* level of less than

**FIGURE 1** Flowchart of the study  
Abbreviations: PPS HAI&AU, point prevalence survey of healthcare-associated infections and antimicrobial use



**TABLE 1** Regimens evaluated as concordant with the national guidelines

No.	Basic drug/monotherapy	Combination treatment (2nd compound)	Expert evaluation (average)	No. of patients	% of patients
1	Amoxicillin (orally)		5	17	2.5
2	Ampicillin (IV)		5	28	4.2
3	Cefotaxime		5	22	3.3
4	Cefotaxime	Clarithromycin	5	2	0.3
5	Ceftriaxone		5	60	9.0
6	Ceftriaxone	Azithromycin	5	1	0.1
7	Ceftriaxone	Clarithromycin	5	4	0.6
8	Clarithromycin		5	18	2.7
<b>TOTAL</b>				<b>152</b>	<b>22.8</b>

**TABLE 2** Regimens discordant with the national guidelines, but evaluated as optimal by the experts

No.	Basic drug/monotherapy	Combination treatment (2nd compound)	Combination treatment (3rd compound)	Expert evaluation (average)	No. of patients	% of patients
1	Amoxicillin (orally)	Ciprofloxacin		3.57	1	0.1
2	Amoxicillin/clavulanate			3.14	164	24.6
3	Amoxicillin/clavulanate	Clarithromycin		3.43	10	1.5
4	Ampicillin/sulbactam			3	7	1.0
5	Cefepime			3	1	0.1
6	Cefotaxime	Ciprofloxacin		3.14	1	0.1
7	Ceftriaxone	Ampicillin (IV)		3.14	1	0.1
8	Ceftriaxone	Ciprofloxacin		3.57	10	1.5
9	Ceftriaxone	Doxycycline		4.32	1	0.1
10	Ceftriaxone	Levofloxacin		4.57	6	0.9
11	Ceftriaxone	Metronidazole		3.43	5	0.7
12	Ceftriaxone	Vancomycin	Clarithromycin	3.14	1	0.1
13	Cefuroxime			3.43	123	18.4
14	Cefuroxime	Clarithromycin		3.43	4	0.6
15	Cefuroxime	Clindamycin		3.14	3	0.4
16	Cefuroxime	Levofloxacin		3.14	2	0.3
17	Cefuroxime	Metronidazole		3.57	2	0.3
18	Clarithromycin	Metronidazole		3.71	1	0.1
19	Levofloxacin			3.57	3	0.4
<b>TOTAL</b>					<b>346</b>	<b>51.9</b>

0.05 were considered significant. Correlation results  $r_{xy} = 0$  were considered as lack of correlation;  $0 < r_{xy} < 1$ , little correlation,  $0.1 \leq r_{xy} < 0.3$ , weak correlation;  $0.3 \leq r_{xy} < 0.5$ , average correlation;  $0.5 \leq r_{xy} < 0.7$ , high correlation;  $0.7 \leq r_{xy} < 0.9$ , almost full correlation; and  $0.9 \leq r_{xy} < 1$ , full correlation.<sup>7</sup>

**RESULTS** CAP was a predominant indication for the treatment of community-acquired infections, recorded in 3608 of the 13 180 patients (27.4%).

The regimens fully concordant with the national guidelines, together with expert scores and the number of patients receiving those regimens, are listed in **TABLE 1**. The most common drug was ceftriaxone used as monotherapy as well as in combination with macrolides (clarithromycin or azithromycin), and 153 patients (22.8%)

included in the study were treated exactly according to the guidelines.

**TABLE 2** shows regimens that were not concordant with the guidelines, but the experts evaluated them as optimal in accordance with their knowledge and clinical experience. This category included 19 regimens (24%). The most common antimicrobials were amoxicillin/clavulanate and cefuroxime (both used mostly as an intravenous formulation; data not shown) and combinations of these 2 antimicrobials with other antimicrobials. Interestingly, the remaining regimens were not so common. Despite the lack of concordance with the national guidelines, 346 patients (51.9%) received antimicrobial treatment that in the experts' opinion could be potentially effective for CAP.

**TABLE 3** Regimens discordant with the national guidelines and evaluated as not optimal by the experts

No.	Basic drug/monotherapy	Combination treatment (2nd compound)	Combination treatment (3rd compound)	Expert scores average	No. of patients	% of patients
1	Amikacin			1	4	0.6
2	Amoxicillin (orally)	Clindamycin		2.71	2	0.3
3	Amoxicillin/clavulanate	Amikacin		1.86	4	0.6
4	Amoxicillin/clavulanate	Amikacin	Fluconazole	1.14	1	0.1
5	Amoxicillin/clavulanate	Cefotaxime		1.37	2	0.3
6	Amoxicillin/clavulanate	Ceftazidime		1.27	1	0.1
7	Amoxicillin/clavulanate	Ceftriaxone	Metronidazole	1	1	0.1
8	Amoxicillin/clavulanate	Cefuroxime		1	1	0.1
9	Amoxicillin/clavulanate	Cefuroxime	Clarithromycin	1.37	5	0.7
10	Amoxicillin/clavulanate	Ciprofloxacin		2.71	21	3.1
11	Amoxicillin/clavulanate	Ciprofloxacin	Amikacin	2.71	1	0.1
12	Amoxicillin/clavulanate	Ciprofloxacin	Metronidazole	1.43	2	0.3
13	Amoxicillin/clavulanate	Fluconazole		1.71	2	0.3
14	Amoxicillin/clavulanate	Doxycycline	Fluconazole	1.43	2	0.3
15	Amoxicillin/clavulanate	Ketoconazole		1	1	0.1
16	Amoxicillin/clavulanate	Levofloxacin		2.29	1	0.1
17	Amoxicillin/clavulanate	Meropenem		1	1	0.1
18	Amoxicillin/clavulanate	Metronidazole		1.29	5	0.7
19	Amoxicillin/clavulanate	Metronidazole	Gentamicin	1.14	2	0.3
20	Amoxicillin/clavulanate	Piperacillin/tazobactam		1	1	0.1
21	Amoxicillin/clavulanate	Piperacillin/tazobactam	Amikacin	1	1	0.1
22	Cefazolin			1	1	0.1
23	Cefotaxime	Amikacin		2	2	0.3
24	Cefotaxime	Clindamycin		1.43	1	0.1
25	Ceftazidime			2.57	4	0.6
26	Ceftazidime	Ciprofloxacin		1.71	1	0.1
27	Ceftazidime	Metronidazole		1.14	1	0.1
28	Cefuroxime	Amikacin		1.43	1	0.1
29	Cefuroxime	Amikacin	Fluconazole	1.27	2	0.3
30	Cefuroxime	Ciprofloxacin		1.86	13	1.9
31	Cefuroxime	Co-trimoxazole		2.71	1	0.1
32	Cefuroxime	Vancomycin		1.57	1	0.1
33	Ciprofloxacin			1	45	6.7
34	Ciprofloxacin	Fluconazole		1	1	0.1
35	Ciprofloxacin	Fluconazole	Clindamycin	1	1	0.1
36	Doxycycline			1.71	4	0.6
37	Doxycycline	Amikacin		1.29	2	0.3
38	Erythromycin			1.14	1	0.1
39	Fluconazole			1	1	0.1
40	Gentamicin			1	1	0.1
41	Clarithromycin	Amikacin		2.71	1	0.1
42	Clindamycin			1.14	7	1.0
43	Co-trimoxazole			1.71	3	0.4
44	Levofloxacin	Clindamycin		1.71	1	0.1
45	Meropenem	Ciprofloxacin		1	1	0.1
46	Metronidazole			1	1	0.1
47	Norfloxacin			1	2	0.3
48	Piperacillin/tazobactam			2.29	5	0.7
49	Piperacillin/tazobactam	Colistin		1	1	0.1
50	Spiramycin			1.14	2	0.3
				<b>TOTAL</b>	<b>169</b>	<b>25.3</b>

**TABLE 4** Correlations of the experts' scores

Experts	AZ	WH	TO	AD	GD	MZ	AM-K
AZ	1.000000	0.680351	0.702053	0.806115	0.566019	0.692763	0.526562
WH	0.680351	1.000000	0.658435	0.752799	0.679259	0.749716	0.545818
TO	0.702053	0.658435	1.000000	0.824872	0.545573	0.742288	0.627694
AD	0.806115	0.752799	0.824872	1.000000	0.617008	0.829425	0.621707
GD	0.566019	0.679259	0.545573	0.617008	1.000000	0.761620	0.551889
MZ	0.692763	0.749716	0.742288	0.829425	0.761620	1.000000	0.593956
AM-K	0.526562	0.545818	0.627694	0.621707	0.551889	0.593956	1.000000

The 50 regimens (63.3%) that were not concordant with the guidelines and were evaluated as not optimal by the experts are listed in [TABLE 3](#). These regimens were used to treat 169 patients (25.3%) with CAP. Most of these regimens were used in the case of single patients; the most frequently used antimicrobials were amoxicillin/clavulanate in combinations, and ciprofloxacin as monotherapy or in combination. Some of the regimens would be accepted or recommended for the treatment of hospital-acquired or healthcare-associated pneumonia (piperacillin/tazobactam or ceftriaxone/ceftazidime combined with quinolone), but not for CAP.

The correlations of the expert scores are presented in [TABLE 4](#). All correlation results in the case of all experts were significant. Of the 21 correlation scores, 8 (38.1%) were between  $0.7 \leq r_{xy} < 0.9$  (almost full correlation), which means consistency of all scores of the regimens at the level of 49.0% to 68.9% (the highest Spearman  $r$  result was 0.83). The last 13 results were between  $0.5 \leq r_{xy} < 0.7$  (high correlation). The lowest Spearman  $r$  result was 0.55 (consistency at the level of 30.3%).

**DISCUSSION** There is good evidence that following the management or treatment guidelines for both community-acquired and healthcare-associated infections improves patient safety, as well as reduces treatment costs and the rates of serious health complications. Many different guidelines are developed by international or national societies and organizations; all published guidelines are evidence-based and adjusted to local (national) epidemiology and antimicrobial resistance patterns. But the availability of well-written contemporary guidelines is just the first step to establish a good antimicrobial policy; another essential step is the education of prescribers. After more than 2 years since the publication of the Polish national guidelines for the management of community-acquired respiratory tract infection,<sup>4</sup> Poland has joined the ECDC PPS HAI&AU, so the data are being collected each year and can be used for evaluation of prescription practices in participating hospitals.

Different approaches are used for evaluation of adherence to guidelines. For hospital prescription, it can be PPS<sup>1-3</sup>; for outpatient care, it is usually the prescription rate.

To our knowledge, ECDC PPS HAI&AU data have not been used so far for the evaluation of adherence to national guidelines on antimicrobial policy. Since data for over 72 000 patients were collected during 4 years of repeated studies in Poland, we considered the group as representative and performed the analyses.

A high number of regimens were recorded ( $n = 79$ ), while the national guidelines allow for 14 monotherapy or combination regimens. However, 35 regimens were recorded for single patients, and another 30 regimens—for fewer than 10 patients. Twelve monotherapy or combination regimens were used to treat the vast majority of patients—531 (79.6%). Adherence to the national guidelines was evaluated as quite low; only 22.8% of patients had been treated exactly according to the guidelines. Our results are similar to those revealed by repeated PPS in Swedish hospitals,<sup>3</sup> where 17.1% of patients with CAP were treated according to the guidelines at baseline, but after 6 years compliance increased to 24.2%. We were not able to perform a time-series analysis because within the first 2 years only slightly over 16 000 patients were included in the Polish PPS HAI&AU study, of whom 731 had CAP and only 162 met the inclusion criteria.

Since most of the recorded regimens were not concordant with the national guidelines,<sup>4</sup> we implemented expert evaluation, because it was quite obvious that some of the regimens might have been “optimal” or “sufficient” or “harmless” apart from being discordant with the guidelines. Experts acted as independent judges, so that in order to examine the experts' scores for consistency, we decided to perform a statistical analysis of coherence. Although 2 of the experts (AM-K and GD) had different clinical backgrounds than the remaining experts (intensive care and anesthesiology subspecialties together with clinical microbiology) and their scores slightly differed from the rest of the panel, the experts judged all the recorded regimens quite similarly, usually reaching an almost full or high correlation coefficient.

After expert evaluation, 19 regimens used for the treatment of 346 patients (51.9%) were judged as not concordant with the guidelines, but optimal, which means that they would do no harm to the patient, and they could be potentially effective in the treatment of CAP, although not included in the guidelines. Two most frequently prescribed

drugs in that group were amoxicillin/clavulanate and cefuroxime (174 patients [26.1%] and 134 patients [20.1%], respectively), both were administered mostly as an intravenous formulation. Neither intravenous nor oral form of amoxicillin/clavulanate was included in the Polish national guidelines for the management of community-acquired respiratory tract infections<sup>4</sup> as a therapeutic option for CAP, even after revision in 2016.<sup>5</sup> The reason for that was mainly the lack of clinical trials on the efficacy of intravenous amoxicillin/clavulanate and low activity of cefuroxime against *Streptococcus pneumoniae*.<sup>4,9,13</sup> Another reason is that  $\beta$  lactamase-producing strains are not so frequent among the etiologic agents of CAP, so clavulanate is not needed. The side effects of amoxicillin/clavulanate include liver injury<sup>10</sup> and a huge potential to promote *Clostridium difficile*-associated diarrhea<sup>11</sup> due to high activity against anaerobic gut flora, as well as to promote proliferation and toxin production by *C. difficile* 027 ribotype,<sup>12</sup> which is very frequent in Poland. Importantly, amoxicillin/clavulanate is one of the most frequently overused antimicrobial in Poland, even at intensive care units,<sup>9</sup> where there are almost no indications for its use.

Among regimens evaluated by the experts as discordant with the guidelines and not optimal, the most frequently used was ciprofloxacin (86 patients, 12.9%) given alone (46 patients, 6.9%) or in different combinations (40 patients, 6.0%). This drug has almost no activity against potential etiologic agents of CAP, so it is difficult to justify its use and this is probably why it resulted in poor experts' scores. Some of the regimens included in that category would be acceptable for the treatment of healthcare-associated pneumonia (piperacillin/tazobactam, ceftazidime), and they might be active against etiologic factors of CAP, but such broad-spectrum activity is definitely not needed for the treatment of CAP.

In some cases, penicillin allergy, even self-reported, might be a reason for choosing an agent other than  $\beta$ -lactam antibiotic,<sup>14</sup> which could partially explain using quinolones in the treatment regimens. Levofloxacin monotherapy was evaluated by the experts as not concordant with the guidelines but optimal, while ciprofloxacin was evaluated as not optimal because it does not display sufficient activity against most etiologic factors of CAP.

Our study has a potential limitation: during PPS HAI&AU only data on hospital prescriptions are collected, and some of the patients included in the study might have been treated for CAP in outpatient care. Previous antimicrobial treatment could potentially affect hospital prescriptions, but on the other hand, according to both versions of the national guidelines, outpatients should receive amoxicillin, macrolide, or a combination of the 2 antimicrobials. If they are not effective and the patient is admitted to the hospital, the guidelines recommend ceftriaxone or

cefotaxime. Therefore, it is hard to explain choices of regimens evaluated as not optimal.

Achieving higher compliance with guidelines on prescribing antimicrobials is a considerable challenge worldwide. Numerous studies have been performed on adherence and its impact on the outcome.<sup>15</sup> Also, the causes of nonadherence were analyzed,<sup>16</sup> together with social and behavioral factors influencing those practices.<sup>17</sup> Hulscher et al<sup>17</sup> published an interesting review, in which they reported that also organizational, cultural, social, socioeconomic, and religious aspects may influence adherence to antimicrobial prescription guidelines.

Clearly, further studies are needed to analyze the concordance of prescription practices with the guidelines, including time-series analysis together with assessing the causes of nonadherence, so that guideline implementation strategy considers all the aspects identified as reasons for poor adherence.

We conclude that ECDC PPS HAI&AU data can be efficiently used to evaluate adherence to guidelines on antimicrobial treatment of CAP, but some conditions must be considered. Adherence to the guidelines in Polish acute care hospitals was low and only 22.8% of patients received adequate treatment. However, almost 75% of patients received antimicrobial regimens judged by the experts as at least optimal. More educational actions should be undertaken to promote responsible antimicrobial use and adherence to the guidelines. Time-series studies should be conducted to assess improvement in adherence.

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