

Opportunities to improve antimicrobial use in paediatric intensive care units: a nationwide survey in Spain

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Abstract

Improving antimicrobial use is a complex process that requires an accurate assessment of ongoing problems and barriers. Paediatric intensive care units (PICU) have seldom been assessed from this perspective. Two Internet-based, self-administered surveys were conducted nationwide in Spain between January and February 2014. The first survey aimed to assess those characteristics of Spanish PICUs that could influence antimicrobial prescribing or antimicrobial stewardship. The second survey targeted Spanish PICU physicians and pursued to assess their attitudes and perceptions regarding antimicrobial resistance and antimicrobial use. Information about 29/39 contacted PICUs was obtained. A total of 114/206 (55.3%) paediatric intensivists responded. PICUs were heterogeneous regarding years since foundation, number of beds, type of patients admitted and staffing. Only 11 (37.9%) PICUs had available e-prescribing systems. Procalcitonin was available in 24 (89.1%) PICUs, but there were no procalcitonin-based protocols in 14 (60.9%) of them. Half of surveyed PICUs had implemented antimicrobial stewardship activities. Ninety-eight of the 114 PICU physicians (86%) who participated considered that antimicrobial resistance was a significantly relevant problem for their daily and that improving antimicrobial use in their PICU should be a priority (103; 90.4%). The main perceived problems regarding antimicrobial use were the excessive use of antimicrobials in patients with nonconfirmed infections and excessive use of broad-spectrum antimicrobials. The most valued antimicrobial stewardship interventions were the implementation of protocols to guide antimicrobial therapy. Spanish PICU doctors are aware of the relevance of the problem of antimicrobial resistance and the need to improve antimicrobial use. Targeted interventions should take into account their difficulties and preferences when feasible.

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Introduction

Optimal antimicrobial prescribing is a complex decision-making process requiring the integration of clinical, epidemiological, microbiologic and pharmacologic variables with prescriber's knowledge and expertise on these fields [1]. Frequently this

process is interfered with by sociocultural beliefs, ethical concerns and logistic barriers [2]. Optimization of antimicrobial prescribing often requires behavioural changes at the prescriber level. A key issue in achieving prescribing changes leading to optimal antimicrobial use is to involve prescribers in the improvement process [3,4]. Deepening of prescribers' attitudes and beliefs regarding antimicrobial resistance and antimicrobial use can help to tailor interventions aiming to facilitate changes in antimicrobial prescribing [5–9]. In addition, surveying prescribers might help identify logistic barriers to optimal antimicrobial prescribing.

Intensive care units (ICU) deal with the most critically ill patients within hospitals. Severe infections are among the most frequently causes of hospitalization among patients hospitalized in the ICU. In addition, during their stay, these patients have an increased risk of acquiring nosocomial infections or conditions that mimic infections. Indeed, ICUs are among hospital wards with highest antimicrobial consumption. Interestingly, intensive care physicians are role models for other physicians for the treatment of infections in hospitalized patients. These facts make ICUs preferential substrates of antimicrobial stewardship interventions [1]. While antimicrobial stewardship in adult ICUs has been subject of multiple interventions, there are scarce data about paediatric intensive care units (PICU) that are focused on neonatal ICUs [10,11].

The aim of this survey was to evaluate the attitudes and beliefs of Spanish PICU physicians about antimicrobial resistance and antimicrobial prescribing through a nationwide online survey in order to identify and prioritize antimicrobial stewardship interventions in this setting.

Materials and Methods

We conducted two different surveys which were endorsed by the Spanish Society of Paediatric Intensive Care (SECIP) at its institutional website (<http://www.secip.com>). Both surveys consisted of self-administered, anonymous, nonincentivized questionnaires that were Internet based in the professional medical platform Navandú (<http://www.navandu.es>). Responses were single answer, multiple response and Likert scaled. Questionnaires were carefully designed with the aims of simplicity, consistency and clarity, as pointed by Sinkowitz-Cochran [12]. The usability and technical functionality of both questionnaires were tested at Hospital Universitario La Paz by PICU physicians. The questionnaires are available as Supplementary Information.

The first survey aimed to assess those characteristics of PICUs that could influence antimicrobial prescribing or antimicrobial stewardship. The questionnaire was designed based on literature review and expert advice [13,14]. It included

questions about institutional governance as well as about the number of beds and staffing issues. Questions were included regarding the available type of prescribing system, the available support from the microbiology laboratory and the hospital pharmacy service, as well as the existence of hospital- or unit-based antimicrobial therapy protocols or other ongoing antimicrobial stewardship activities. The survey was distributed by e-mail among the members of the SECIP Infectious Diseases Study Group the second week of January 2014 and remained available until the end of February 2014. One senior paediatric intensive care doctor per institution was selected to participate in this survey. Paediatric intensive care doctors selected to participate in this survey acted as local coordinators of the second survey in their respective institutions too.

The second survey, which was cross-sectioned, aimed to assess the attitudes and perceptions of Spanish senior paediatric intensive care doctors regarding antimicrobial resistance and antimicrobial use in Spanish PICUs. We developed the questionnaire after a literature review of similar studies [5–9]. Paediatric intensive care doctors at Hospital Universitario La Paz participated in pilot testing. The survey included a cover letter providing a brief description of the purpose of the survey, which also addressed the relevance of the participation of targeted physicians in order to identify areas of improvement in antimicrobial prescribing. The questionnaire initially explored demographic and professional characteristics of respondents and their institutions. The next section included the evaluation of the perception of respondents about the relevance of antimicrobial resistance in their daily practice as well as their overall perception of the quality of antimicrobial prescribing and the implementation of infection control measures in their units. Then paediatric intensive care doctors were asked to assess the difficulties found in several steps of the antimicrobial prescribing process and to prioritize areas of improvement. Finally, they were asked about their preferences among several antimicrobial stewardship interventions. SECIP officials distributed the link to the online questionnaire via e-mail among its members the second week of January 2014, and it remained available until the end of February 2014. Further e-mail reminders were sent 2 and 4 weeks after the initial message. In addition to the e-mails sent by SECIP, local coordinators fostered additional responses.

The survey results were analysed by SPSS 11.5 (IBM, Armonk, NY, USA). Percentages were calculated for the categorical data, with scaled items analysed both as quantitative variables.

Results

We obtained response from 29 of the 39 PICUs that were contacted (74.3%). All Spanish autonomous communities

(regions) were represented in the survey. The main characteristics of PICUs are summarized in Table 1. The structural environment for antimicrobial prescribing is summarized in Table 2.

Response from 114/206 (55.3%) paediatric intensive care doctors included in the initial e-mailing list was obtained. Sixty-two respondents (54.4%) were aged between 30 and 40. Only 9 (7.9%) and 1 (0.9%) were above 60 and below 30, respectively. Twenty-nine PICUs from all Spanish autonomous communities were represented among respondents. Ninety-eight (86%) respondents considered that antimicrobial resistance was a relevant problem to their daily practice. Among several multidrug-resistant microorganisms, respondents considered extended-spectrum β -lactamase-producing *Enterobacteriaceae* to be the most relevant to their daily practice (64; 56.1% said that these microorganisms were relevant/very relevant). There was also a high degree of agreement that improving antimicrobial use should be a priority in their respective units: 103 (90.4%) participants were totally (80; 70.2%) or almost totally (23; 20.2%) in agreement with the prior statement. Nevertheless, the median rate of the quality of antimicrobial prescribing in

respondents PICU was 7/10; 23/114 (20.2%) rated it below 5/10 (1 = lowest quality, 10 = highest quality). Ratings of the problems related to antimicrobial prescribing in PICU and perception of difficulties found by participants are presented in Figs. 1 and 2, respectively.

Self-assessment of the compliance with some of the principles of antimicrobial use was also explored. Where available, respondents endorsed high compliance with local protocols to guide empirical antimicrobial therapy. They reported to follow local protocols always (33/90; 35.9%) or frequently (47/90; 51.1%), respectively. All participants reported to request cultures and other microbiologic tests before starting antimicrobial therapy always (72; 63.2%) or at least almost always (42%; 36.8%), respectively. More specifically, when asked about microbiologic assessment of patients with suspected ventilator-associated pneumonia, 90 (78.9%) paediatric intensivists considered that it was performed within accepted standards. In this regard, most respondents (65; 57%) stated that bronchoalveolar lavage was seldom performed (in less than 10% of opportunities) while bronchial aspirate was performed in more than 75% of opportunities. Regarding the microbiologic assessment for suspected catheter-related infection, only 30

TABLE 1. Overall characteristics of institutions and PICUs

Characteristic	Value
Governance	
Public	27 (93.1%)
Private not-for-profit	1 (3.4%)
Private for profit	1 (3.4%)
No. of paediatric beds (hospital)	
Range	26–350
Median	80
No. of PICU beds	
Median	8
Range	3–18
P ₂₅ –P ₇₅	6–12
Institutions performing transplantations	
No transplant procedure	13 (44.8%)
Haematopoietic stem cell transplantation	13 (44.8%)
Kidney transplant	5 (17.2%)
Liver transplant	3 (10.3%)
Lung transplant	2 (6.9%)
Heart transplant	2 (6.9%)
Intestinal, multivisceral or pancreas	1 (3.4%)
PICU routinely admits transplant patients	
Yes	9 (31%)
PICU admits neonates	
No	19 (65.5%)
Years since PICU foundation	
>40 years	2 (7.4%)
30–40 years	12 (44.4%)
20–30 years	2 (7.4%)
10–20 years	5 (18.5%)
<10 years	6 (22.2%)
No. of PICU staff doctors	
Median	7
Range	3–21
P ₂₅ –P ₇₅	5–8
No. of staff members during night shifts	
1	23 (79.3%)
2	5 (17.2%)
3	1 (3.4%)
No. of residents during night shifts	
1	2 (6.9%)
2	24 (82.8%)
3	3 (10.3%)

PICU, paediatric intensive care unit; P₂₅–P₇₅, 25th to 75th percentiles.

TABLE 2. Structural environment for antimicrobial stewardship in surveyed PICUs

Feature	n (%)
Prescribing system	
Handwriting	11 (37.9)
Text processor	9 (31)
E-prescribing software	9 (31)
Does hospital pharmacy regularly provide input on antimicrobial consumption?	
Yes	18 (62.1)
No	11 (37.9)
Does your institution have an on-site microbiology laboratory?	
Yes	28 (96.6)
Is there a microbiologist available during night shifts?	
Yes (24/7)	11 (37.9)
Yes (on call)	6 (20.7)
No	12 (41.4)
Does your institution have hospital-based (paediatric) antimicrobial therapy protocols?	
Yes	23 (79.3)
No	6 (20.7)
Does your PICU have specific unit-based antimicrobial therapy protocols?	
Yes	19 (65.5)
No	10 (34.5)
Is there any restricted antimicrobial agent in your PICU?	
Yes	10 (34.5)
No	19 (65.5)
Is procalcitonin measurement available at your institution?	
Yes	24 (82.8)
No	5 (17.2)
Is there any procalcitonin-based protocol to guide antimicrobial therapy?	
Yes	9 (39.1)
No	14 (60.9)
Is there an ongoing antimicrobial stewardship program at your institution?	
Yes	14 (48.3)
No	10 (34.5)
Does not know	5 (17.2)
Has any antimicrobial stewardship activity been conducted at your institution?	
Yes	15 (51.7)
No	12 (41.4)
Does not know	2 (6.9)

PICU, paediatric intensive care unit.

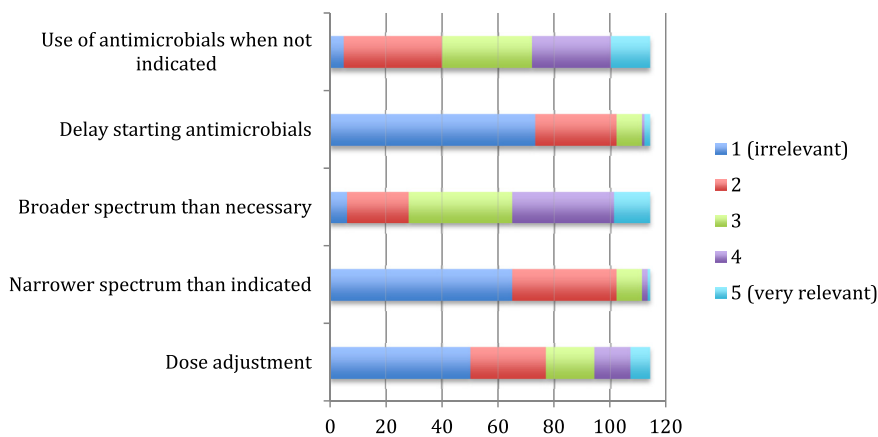


FIG. 1. Rating of the relevance of the following problems regarding antimicrobial use in respondents' PICU (1 = irrelevant, 5 = very relevant); x-axis indicates number of respondents. PICU, paediatric intensive care unit.

(26.3%) acknowledged obtaining paired blood samples from the catheter and a peripheral vein in more than 75% of opportunities. Fifty-six respondents (59.1%) were not satisfied with the microbiologic assessment for suspected catheter-related infection.

Most respondents stated that either always (39; 34.2%) or at least frequently (55; 48.2%) they reevaluated antimicrobial therapy approximately 72 hours after its start in order to adjust antimicrobial therapy to microbiologic data. In addition, 42 (36.8%) respondents endorsed that they frequently used procalcitonin to guide decisions regarding antimicrobial therapy. To explore attitudes and beliefs about duration of antimicrobial therapy, they were asked about how long they would use antibiotics in a patient with ventilator-associated pneumonia caused by nonfermenter Gram-negative microorganisms with a favourable clinical course after the first 48 hours of therapy. The most frequently self-reported length of therapy in this clinical scenario was 7 to 9 days (64; 56.1%), followed by 11 to 14 days (24; 21.1%) and 9 to 11 days (22; 19.3%), respectively.

Finally, participants were asked to rate the perceived utility of several interventions or activities aiming to improve antimicrobial use at their units (Fig. 3). For the surveyed paediatric intensive care doctors, the most valuable antimicrobial stewardship interventions were the availability of locally adapted protocols to guide both empiric antimicrobial therapy and streamlining. The least valuable interventions were those related to e-prescribing.

Discussion

This survey, which most of Spanish PICUs participated in, shows that almost universally, Spanish paediatric intensive care doctors consider antimicrobial resistance to be a clinically relevant problem in their practice and that improving antimicrobial prescribing is considered a priority. These results are concordant with those observed by Patel et al. [15] when they surveyed US neonatologists in 2010.

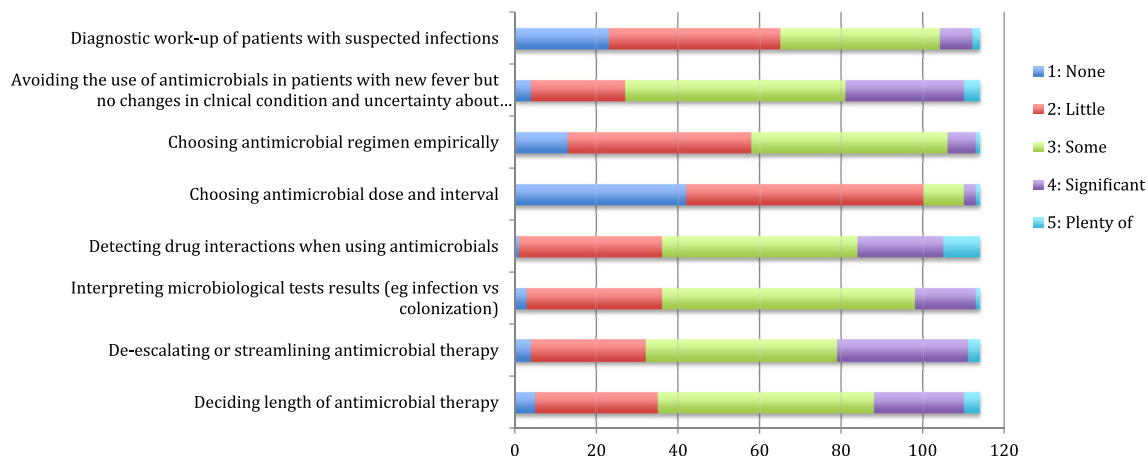


FIG. 2. Difficulty found in facets of antimicrobial use and diagnostic assessment in patients with suspected infection.

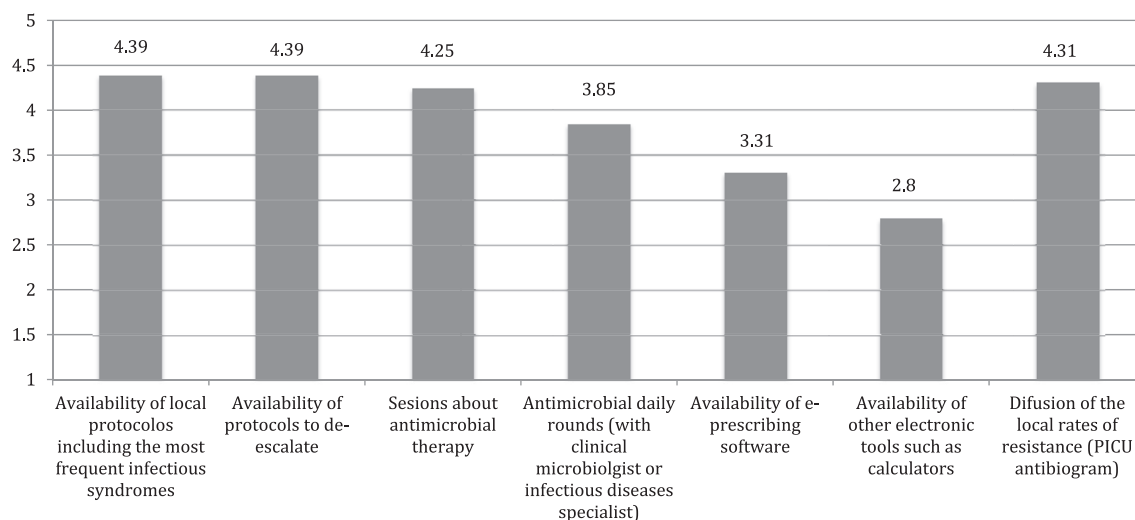


FIG. 3. Rating of usefulness of several interventions/activities to improve antimicrobial use (1 = useless, 5 = extremely useful).

The acknowledgement of antimicrobial resistance as a real problem and the need to react draws a favourable environment to design and implement participatory antimicrobial stewardship interventions. Given that experiences actively involving prescribers have been successful, it may be possible to accomplish changes aimed at quality improvement in complex scenarios such as PICUs, where the input provided might help foster this type of intervention. Interestingly, despite considering that improving antimicrobial use should be a priority in Spanish PICUs, participants had a significantly high self-perception of the quality of antimicrobial use in their units. This apparent discrepancy might have several explanations. First, surveyed paediatric intensive care doctors believe that even if they do not find much room for improvement, optimizing antimicrobial use in PICU is still relevant, given the relevance of the problem of antimicrobial resistance. On the other hand, as perceptions are subjective, the aforementioned discrepancy might hint at the need to use different approaches when exploring self-perceptions regarding antimicrobial use.

For Spanish paediatric infectious diseases doctors, the main problems found regarding antimicrobial utilization are the overuse of antimicrobials in patients with unproven infectious conditions and the abuse of broad-spectrum antimicrobials. Paradoxically, the selection of empirical therapy was considered to be one of the least difficult decisions to make in the antimicrobial prescribing process. Considering that empirical therapy is frequently guided by protocols and that the availability of local protocols is the most widely accepted antimicrobial stewardship intervention, elaborating protocols to guide decisions in patients with new fevers and adapting protocols to local microbiology would probably be priority interventions to improve antimicrobial use in the PICU.

The difficulties found by participants in streamlining antibiotic regimens might also contribute to the perception of the overuse of broad-spectrum antimicrobials as an antimicrobial prescribing problem. Respondents thought that protocols to target antimicrobial therapy would be quite useful. Another possible intervention to facilitate de-escalation would be the implementation of infectious disease and/or microbiology rounds that bring updated clinical and microbiologic without delay to the point of care. This intervention was not as well rated as the availability of protocols because it might be perceived as time-consuming or as a loss of the prescribers' autonomy. As observed in other settings, optimization of the length of antimicrobial therapy was not considered one of the main problems regarding antimicrobial use in the PICU setting [16]. Nevertheless, many participants, when asked about the length of therapy in a clinical scenario of a patient with ventilator-associated pneumonia, would provide significantly longer treatment than that recommended by (adult) guidelines [17]. Given that real practice decisions tend to be even further from recommendations than acknowledged, improving the length of antimicrobial therapy should be considered a priority too. Including specific and explicit recommendations on the duration of antimicrobial therapy in paediatric guidelines regarding the most frequent infectious syndromes could also help.

This study also provided previously unpublished input regarding the characteristics of Spanish PICUs that might be useful when tailoring interventions to improve antimicrobial use. Firstly, there is significant heterogeneity regarding years since foundation, number of beds, type of patients admitted and staffing. Remarkably, the implementation of e-prescribing tools in Spanish PICUs is low. The study shows that procalcitonin is widely available in Spanish PICUs and that it is a tool that many

consider useful, despite the scarce data available in the critically ill paediatric population. Finally, we note that nearly half of PICUs acknowledge having implemented antimicrobial stewardship activities or interventions, which suggests an improvement compared to previously reported data [18]. Spanish paediatric intensive care doctors favoured interventions consisting of local protocol adaptation as well as input on local antimicrobial resistance patterns and did not have many expectations with regard to electronic tools assisting antimicrobial prescribing. We did not expect such reluctance towards information technologies, so we cannot speculate further on the reasons behind it. These perceptions should be taken into account when designing and implementing antimicrobial stewardship interventions, such as stated by Luyt *et al.* [19] in a review about the design and implementation of antimicrobial stewardship interventions in the ICU.

The main limitation of the study, inherent to the self-administered questionnaire survey design, derives from the fact that it did not observe prescribing patterns but registered self-perceptions, which might not reflect the actual patterns of prescribing behaviour. Several efforts were made to obtain the best possible unbiased information from participants. The recruiting strategy was quite efficacious: information from most Spanish PICUs was obtained, and more than 55% of surveyed paediatric intensive care doctors responded the survey.

In conclusion, Spanish PICU doctors are aware of the relevance of the antibiotic crisis and are willing to improve antimicrobial use in their daily practice. A wide range of interventions is feasible, but they should be tailored to take into account local circumstances.

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Transparency Declaration

All authors report no conflicts of interest relevant to this article.

References

- [1] Rodríguez Baño J, Paño-Pardo JR, Alvarez-Rocha L, Asensio A, Calbo E, Cercenado E, *et al.* [Programs for optimizing the use of antibiotics (PROA) in Spanish hospitals: GEIHSEIMC, SEFH and SEMPSPH consensus document]. *Enferm Infecc Microbiol Clin* 2012;30:22.e1–22.e23.
- [2] Hulscher MEJL, Grol RPTM, van der Meer JWM. Antibiotic prescribing in hospitals: a social and behavioural scientific approach. *Lancet Infect Dis* 2010;10:167–75.
- [3] Sbarbaro JA. Can we influence prescribing patterns? *Clin Infect Dis* 2001;33(Suppl. 3):S240–4.
- [4] van Buul LW, Sikkens JJ, van Agtmael MA, Kramer MHH, van der Steen JT, Hertogh CMPM. Participatory action research in antimicrobial stewardship: a novel approach to improving antimicrobial prescribing in hospitals and long-term care facilities. *J Antimicrob Chemother* 2015. *in press.*
- [5] Wester CW, Durairaj L, Evans AT, Schwartz DN, Husain S, Martinez E. Antibiotic resistance: a survey of physician perceptions. *Arch Intern Med* 2002;162:2210–6.
- [6] Srinivasan A, Song X, Richards A, Sinkowitz-Cochran R, Cardo D, Rand C. A survey of knowledge, attitudes, and beliefs of house staff physicians from various specialties concerning antimicrobial use and resistance. *Arch Intern Med* 2004;164:1451–6.
- [7] Abbo LM, Sinkowitz-Cochran R, Smith L, Ariza-Heredia E, Gómez-Marín O, Srinivasan A, *et al.* Faculty and resident physicians' attitudes, perceptions, and knowledge about antimicrobial use and resistance. *Infect Control Hosp Epidemiol* 2011;32:714–8.
- [8] Pulcini C, Williams F, Molinari N, Davey P, Nathwani D. Junior doctors' knowledge and perceptions of antibiotic resistance and

- prescribing: a survey in France and Scotland. *Clin Microbiol Infect* 2011;17:80–7.
- [9] Dyar OJ, Pulcini C, Howard P, Nathwani D. ESGAP (ESCMID Study Group for Antibiotic Policies). European medical students: a first multicentre study of knowledge, attitudes and perceptions of antibiotic prescribing and antibiotic resistance. *J Antimicrob Chemother* 2014;69:842–6.
- [10] Cantey JB, Patel SJ. Antimicrobial stewardship in the NICU. *Infect Dis Clin North Am* 2014;28:247–61.
- [11] Patel SJ, Saiman L. Principles and strategies of antimicrobial stewardship in the neonatal intensive care unit. *Semin Perinatol* 2012;36:431–6.
- [12] Sinkowitz-Cochran RL. Survey design: to ask or not to ask? That is the question.... *Clin Infect Dis* 2013;56:1159–64.
- [13] Arnold HM, Micek ST, Skrupky LP, Kollef MH. Antibiotic stewardship in the intensive care unit. *Semin Respir Crit Care Med* 2011;32:215–27.
- [14] Njoku JC, Hermsen ED. Antimicrobial stewardship in the intensive care unit: a focus on potential pitfalls. *J Pharm Pract* 2010;23:50–60.
- [15] Patel SJ, Rosen E, Zaoutis T, Prasad P, Saiman L. Neonatologists' perceptions of antimicrobial resistance and stewardship in neonatal intensive care units. *Infect Control Hosp Epidemiol* 2010;31:1298–300.
- [16] Navarro-San Francisco C, Del Toro MD, Cobo J, De Gea-García JH, Vañó-Galván S, Moreno-Ramos F, Rodríguez-Baño J, et al. Knowledge and perceptions of junior and senior Spanish resident doctors about antibiotic use and resistance: results of a multicenter survey. *Enferm Infecc Microbiol Clin* 2013;31:199–204.
- [17] American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005;171:388–416.
- [18] Paño-Pardo JR, Padilla B, Romero-Gómez MP, Moreno-Ramos F, Rico-Nieto A, Mora-Rillo M, et al. [Monitoring activities and improvement in the use of antibiotics in Spanish hospitals: results of a national survey]. *Enferm Infecc Microbiol Clin* 2011;29:19–25.
- [19] Luyt CE, Bréchet N, Trouillet JL, Chastre J. Antibiotic stewardship in the intensive care unit. *Crit Care* 2014;18:480.