

ORIGINAL ARTICLE

Cefazolin restriction and a guideline to improve the use of antimicrobials for prevention of surgical site infection

Astridia Marilia de Souza Fontes¹, Bruno de Oliveira Burjaili², Vinício Marques Martins², Miguel Tanús Jorge^{1,3}

- 1. Hospital Infection Control Service, Clinical Hospital of the Federal University of Uberlândia, Minas Gerais, Brazil
 - 2. Medicine School of the Federal University of Uberlândia, Minas Gerais, Brazil
- Postgraduate Program in Health Sciences, Clinical Hospital of the Federal University of Uberlândia, Minas Gerais, Brazil

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Abstract

The aim of this study was to determine the effectiveness of an intervention (a guideline distribution associated with the restriction of the use of cefazolin) in order to improve the use of antimicrobials in the prevention of surgical site infection (SSI). The design of the study was a prospective one, before-after intervention. It was conducted at the Clinical Hospital of the Federal University of Uberlândia, a teaching institution with 510 beds. Two interventions were effected: a guideline for antimicrobial prevention of SSI was made available; and also the use of cefazolin was restricted. The suitability of the indication and of the prescribed antibiotic, and also the time of its use were evaluated in the prevention of SSI. This study was divided into three periods: I baseline data collection; II - data collection after creation and availability of the guideline; III - data collection during cefazolin restriction period.

The indication of prevention of SSI was considered adequate in the three collection periods. In the orthopaedic trauma ward, the choice of the antibiotics was considered adequate in the three periods. In the general surgery ward however, it was adequate in 20%, 63.9% and 61.5% of cases in periods I, II and III, respectively. The length of time for antimicrobial prevention was considered adequate in 23% in period I; 46.15% in period II and 82.46% in period III. In conclusion, educational, but especially administrative interventions can increase the adequacy of the use of an antimicrobial in surgical infection prevention.

Keywords: Antibiotic prophylaxis; Surgical wound infection and prevetion and control; cefazolin.

Corresponding Author

Astridia Marilia de Souza Fontesa

Serviço de Controle de Infecção Hospitalar do Hospital de Clínicas da UFU, Universidade Federal de Uberlândia. Av. Pará 1720 – Campus Umuarama. 38400-902 – Uberlândia, Minas Gerais, Brazil.

Fax: 055 34 3218 2199.

E-mail: alasti@uol.com.br (Astridia Fontes).

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Introduction

A nosocomial infection, also known as a hospital-acquired infection (HAI),¹ is a global public health problem.² Several strategies have been proposed to reduce the HAI incidences associated with four devices and procedures: catheter-associated bloodstream infection; ventilation-associated pneumonia; catheter-associated urinary tract infections and surgical site infection (SSI).³

SSI is the third major cause of HAI and it is also the main complication during surgeries. It can increase morbidity and mortality rates,⁴ time in the hospital and associated costs.⁵

The risk of SSI and, therefore, the indication of prophylactic antimicrobials are directly related to the degree of contamination in different surgical procedures. Surgeries are classified as clean, potentially contaminated, contaminated and dirty or infected. The prophylactic antimicrobial is indicated primarily for contaminated and potentially contaminated surgeries. In clean surgeries it is indicated where prosthetic material is used, or when the SSI is catastrophic, such as in many heart surgeries. In dirty or infected surgeries the antimicrobial is indicated as a therapeutic.

The objective of prevention with antimicrobials in surgery, is to reduce the rate of SSI and, consequently, morbidity and mortality rates and the associated financial costs.^{7,8} When the indication is correct, it is proven to be beneficial.⁹ However, there is a cost and the use of antibiotics can cause adverse effects such as toxicity, allergy, idiosyncratic reactions and, above all, infection by multidrug-resistant and opportunistic pathogens.^{10,11} Any of these adverse effects is not justified if the indication is inadequate.^{12,13}

Antimicrobial prophylaxis is in reality only one of the measures necessary for the prevention of SSI. The indiscriminate use of prophylactic antimicrobials can lead to sensations of security and to disregard for other more effective measures, such as hospitalization for a minimum period of time prior to surgery, use of trichotomy only when necessary, tonsure devices only in the smallest possible area, adequate antisepsis of the patient's skin and of the hands of the surgical team. An adequate surgical technique should be applied,

which includes surgery in the shortest possible time, a minimum amount of trauma and tissue necrosis, efficient haemostasis and the prevention of leaving empty spaces or hematomas.^{6,7}

As there are no general and absolute rules for the prevention of SSI with use of antimicrobials, it is important to know the specific norms for each surgery and for each specific situation.^{7,14} A large portion of prophylactic conduct for SSI with antimicrobials has been evaluated by careful studies and there are already governmental and specialist society directives to serve as a guide.^{6,15}

It is known that the control of the use of antimicrobials by hospitals increases the quality of the prescription of these drugs, reduces costs and contributes to the control of infections. It also reduces emergence and the dissemination of resistant microorganisms. 16,17

The use of the antibiotic for prevention of SSI remains one of the most important errors in the administration of medications in hospitals worldwide. Administration of the antibiotics for long periods of time is one of the main mistakes in the prevention of SSI. Many studies were held comparing a single dose to multiple doses of antimicrobials in the prevention of SSI, almost always showing that one dose is sufficient. Administration of SSI, almost always showing that one dose is sufficient.

Different strategies have been used in the control of antimicrobials, such as the use of software systems in hospitals; the creation of local directives based on scientific evidence and the restriction of the use of unduly prescribed antimicrobials.^{24,25}

In August 2002, the Centers for Medicare and Medicaid Services and the Centers for Disease Control and Prevention (CDC) implemented a national Surgical Infection Prevention Project,⁸ with the goal of reducing the rate of mortality and morbidity associated with SSI. For this reason, the proposal to intensify the observance of the following three basic guidelines was created:

- Administration of the antimicrobial up to one hour before surgery (two hours for vancomycin or fluoroquinolones);¹⁵
- Use of antimicrobials consistent with "current recommendations";
- Discontinued use within 24 hours after surgery.

Though the prescriptions and forms of prevention for SSI with antimicrobials are already relatively established, it is difficult to find effective ways to make these standards accepted in practice by medical surgeons. In this context, the aim of this study was to determine the effectiveness of an intervention (a guideline distribution associated with the restriction of the use of cefazolin) in order to improve the use of antimicrobials in the prevention of SSI.

Methods

This study was conducted in the Clinical Hospital (HC) of the Federal University of Uberlândia, a 510 bed teaching hospital. HC is a public institution that offers tertiary care to an area with a population of over 3 million inhabitants. The surgeries evaluated are those that are submitted to the hospital infection surveillance team who use the methodology of the National Healthcare Safety Network. 1 This surveillance is routinely performed by a hospital infection control nurse. The surgeries evaluated were those in which the patient was already in the orthopaedic trauma ward or general surgery ward. The use of antibiotic prophylaxis was analyzed regarding the proper use, the kind of antimicrobial prescribed and the time of use. The data were obtained from surgery reports at the surgical centre and also from the records of the hospitalised patients. Cefazolin consumption data were obtained at the Clinical Pharmacy of the HC.

Data were taken for all patients who underwent one of the selected surgical procedures. The collection time was set at eight weeks. Patients that lacked the required information were excluded from the study. The data were collected in three periods: period I (baseline); period II (after the guidelines were created and made available); and period III (during restriction of cefazolin). Period I, consisting of collection of baseline data, took place in the months of February and March 2007. Period II, the intervention period, took place from March to September 2007. During this period the "Guide for Prevention with Antimicrobials in Surgery" was composed. It contained basic rules for the antimicrobial prophylaxis for SSI, the antimicrobials suggested, the form of administration, the length of the time and dosage for adult and paediatric patients (Intervention I) and instructions for most surgeries.

It was based on existing literature, above all on the guidelines of specialist associations and on original scientific articles. Discussions were held with all the surgical teams of the HC whose specialty was considered in the Guide, which was to be accepted by the surgeons. The Guide was made available in September 2007 and placed permanently on the HC Intranet for consultation or printing. In November and December 2007, data were collected, for eight weeks, after the Guide was made available. The goal was to evaluate the change in conduct of the surgeons regarding the use of prophylactic antibiotics.

Period III began in April 2008 when the Guide was permanently available (Intervention I). Meetings were held with the surgery departments of the HC, and the Guide for the use of cefazolin was fixed on the notice board of these surgical clinics. Whenever cefazolin was prescribed within the surgical centre, it was released as a kit containing only three 1g doses of the antimicrobial. Prescriptions outside the surgical centre were only released after filling out a form for the release of restricted antimicrobials and an evaluation by the doctor in charge of infection control (Intervention II). In the months of July and August 2008 (eight weeks), data were collected in the same manner as in previous periods.

The successes and errors related to the indication of prophylaxis, the chosen antimicrobial and the time of use was based on the guideline.

The chi-squared test (X²) and, when necessary, the Yates correction or the Fisher exact test were used to analyze the secondary variables. Regarding the permanence time of the prophylactic antimicrobial in orthopaedic trauma surgery, period I was compared to period II (Yates), II with III (Yates), and I with III (Fisher). The calculations were performed with Epi Info, CDC software, version 3.51. The value of p<0.05 was used as an indication of statistical significance.

The proposal for this study was approved by the Research Ethics Committee of the Federal University of Uberlândia (registered number 002/05).

Results

Two hundred and fourteen patients were evaluated and, 5 were excluded during Period I, 1 during Period II and 7 during Period III, because they used the antimicrobial with a therapeutic purpose. Thus, remained 57 in Period I, 78 in Period II and 66 in Period III.

The number of male patients was 24 (42.11%), 37 (47.44%) and 26 (39.39%) for Periods I, II and III, respectively (p=0.6105) and the number of patients between the ages of 30 and 60 was 43 (75.44%), 49 (62.82%) and 44 (66.67%), respectively (p=0.2951). The percentage of participation in the specialty surgeries in the different periods can be observed in Table I.

The prescribed antimicrobial for the prevention of SSI was considered adequate in most cases and there was no difference in the evaluated periods (Table II). The use of the correct antimicrobial occurred in 37 (74.00%), 46 (77.97%) and 38 (79.17%) of cases in Periods I, II and III, respectively (p=0.8135). These percentages are different in general surgery and orthopaedic trauma (Table III). The prolonged use of the antimicrobial for the prevention was the main inadequacy found. The time of use was separately evaluated in periods I, II and III for the two surgical specialties (Table IV). After it was restricted, the consumption of cefazolin was reduced by 35.7%, from 5,424 phials in 2007, to 4,016 in 2008. In 2009 the number of bottles consumed was 3,488 (p<0.0001).

	1	II	II
Clinical Specialty Wards	n (%)	n (%)	n (%)
General Surgery	22 (38.60)	55 (70.51)	36 (54.55
Orthopaedic Trauma Surgery	35 (61.40)	23 (29.49)	30 (45.45
Total	57 (100)	78 (100)	66 (100

	1	II	III
Use of the antimicrobial	n (%)	n (%)	n (%)
CORRECT	51 (89.47)	63 (80.77)	55 (83.33)
It was indicated and prescribed ^a	50 (87.72)	59 (75.64)	48 (72.73)
It was not indicated and not prescribed ^a	1 (1.75)	4 (5.13)	7 (10.60)
INAPPROPRIATE	6 (10.53)	15 (19.23)	11 (16.67)
It was indicated but not prescribed	4 (7.02)	9 (11.54)	2 (3.03)
It was not indicated but was prescribed	2 (3.51)	6 (7.69)	9 (13.64)
Total	57 (100)	78 (100)	66 (100)

Note. a Correct in 89.47%, 80.77% and 83.33% of the cases in Periods I, II and III, respectively (p =0.3858).

Table III. Adequate choice of the prophylactic antimicrobial prescribed in General Surgery and Orthopaedic Trauma in periods I, II and III

		II	III	p value
Adequate antimicrobial	n (%)	n (%)	n (%)	n (%)
General Surgery ^a	03 (20.0)	23 (63.9)	16 (61.5)	0.011
Orthopaedic Trauma	34 (97.1)	23 (100)	22 (100)	0.5215

Note. ^aPeriods I and II, p=0.0108; I and III, p=0.0248; II and III, p=0.9384.

Table IV. Time of permanence of the prophylactic antimicrobial in General Surgery and Orthopaedic Trauma in periods I, II and III.

	I	II	III	p value
Adequate permanence time	n (%)	n (%)	n (%)	n (%)
General Surgery ^a	2(11.76)	28(66.67)	20(68.97)	0.0002
Orthopaedic Trauma ^b	10(28.57)	2(8.70)	27(96.43)	0.0001
Total	12(23)	30(46.15)	47(82.46)	0.0000

Note. ^aPeriods I and II, p=0.0004; I and III, p=0.0006; II and III, p=0.9565. ^bPeriods I and II, p=0.1345; I and III, p<0.001; II and III, p<0.0001.

Discussion

The adequate use of antimicrobials for the prevention of SSI remains a global challenge. The most common recommendations from guides and professional consensus on this subject refer to the right choice of the antimicrobial, administration within one hour before surgical incision and early suspension, generally within twenty-four hours.^{25,26}

There is an association between the moment the first dose of the prophylactic antibiotic and the rates of SSI.²⁷ The moment of the first dose was not an evaluation target for this study. However in HC, the administration of the first dose of the antibiotic was already routinely applied at the same time as the anaesthetic in the surgical centre.

There was a difference in the percentage of the right antibiotic, and this was probably due to the Guide. One of the traditional routine prophylaxis at the HC included ceftriaxone. This antibiotic is not recommended by the vast majority of guidelines nor by many authors such as Weed,²⁸ neither is it part of

the routine suggested by the Guide. Other authors also demonstrate a reduction in the inadequate prescriptions of prophylactic antibiotics when the standardization of the local protocol was established.^{12,25,29,30}

According to the Surgical Care Improvement Project and to the American Academy of Orthopedic Surgeons, the preferred antimicrobial for patients submitted to a total arthroplasty of the hip or knee is cefazolin or cefuroxime.^{31,32} Because cefazolin was already used in almost 100% of the cases of orthopaedic trauma in period I, there was no possibility of its greater use with the introduction of the Guide.

As in this study, one of the main errors found in the prophylactic use of antimicrobials in the prevention of SSI was its use for a greater period of time than recommended.^{20,21} It has also been shown that overuse should be avoided, since it doesn't reduce the SSI, and it can lead to increased bacterial resistance.^{33,34,35}

Just as in this study, a multi-centric study involving 13 hospitals in The Netherlands showed good adherence to local guidelines.³⁶ A French study of local directives for the use of an antimicrobial in the prevention of SSI showed an increase in correct use from 31% to 82%.31 However, Brusaferro and colleagues,³⁷ showed a modest increase in the correct use of the prophylactic antimicrobial and suggested the monitoring and the identification of critical points that can increase adherence to protocol. In this present study, the presence of the Guide did not guarantee the correct use of the prophylactic antimicrobial regarding the timeframe in orthopaedic trauma. Therefore, it is correct to conclude that the same intervention may have different effects on different professional team or situations. So, scientific information about this subject is not easily applied in practice.

The greater impact of the second intervention in the timeframe of use of the antimicrobial in orthopaedic trauma could have occurred due to its greater previous incorrect use and due to the fact that, in most surgeries, cefazolin was the antimicrobial used in prevention.^{7,24} The substantial reduction in the consumption of cefazolin, from 2007 to 2009, reinforces this point.

The success of the use of kits like those of this study was also found in other studies such as that of Carlès *et al.*³⁸ which compared the unrestricted use of the antimicrobial in the prevention of SSI (41% correct use) to that of the antibiotic in the kits (82% correct use). The kits used in this way are, therefore, an effective tool in the implementation of directives for the use of antibiotics in the prevention of SSI. On the other hand, educational programs, such as continued medical education or continuous professional development, do not always show effective change in medical behaviour. A study conducted in Spain, with the creation of local protocol, along with an integrated dispensation system, also showed a significant increase in the correct use of prevention.³⁹

We conclude that one of the most common nonconformities in the use of antimicrobials in the prevention of SSI is there excessively long timeframe. A guide made with the participation of the surgeons along with control of the use of the antimicrobial can improve its use. The same strategy can have very

different results depending on the situation in which it is used.

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References

- Edwards JR, Peterson KD, Andrus ML, Dudeck MA, Pollock DA, Horan TC. National Healthcare Safety Network (NHSN) report, data summary for 2006 through 2007, issued November 2008. Am J Infect 2008; 36: 609-626. http://dx.doi. org/10.1016/j.ajic.2008.08.001
- 2. Casey AL, Elliott TS. Progress in the prevention of surgical site infection. *Curr Opin Infect Dis* 2009; **22:** 370–375. http://dx.doi.org/10.1097/QCO.0b013e32832c4048
- Yokoe DS, Mermel LA, Anderson DJ, et al. A compendium of strategies to prevent healthcare-associated infections in acute care hospitals. *Infect Control Hosp Epidemiol* 2008; 29: S12-21. http://dx.doi.org/10.1086/591060
- Astagneau P, Rioux C, Golliot F, Brücker G, INCISO Network Study Group. Morbidity and mortality associated with surgical site infections: results from the 1997–1999 INCISO Surveillance. J Hosp Infect 2001; 48: 267–274. http://dx.doi. org/10.1053/jhin.2001.1003
- Quinn A, Hill AD, Humphreys H. Evolving issues in the prevention of surgical site infections. *Surgeon* 2009; 7: 170-172. http://dx.doi.org/10.1016/S1479-666X(09)80041-3
- Mangram AJ, Horan TC, Pearson, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. *Infect Control Hosp Epidemiol* 1999; 20: 247-278. http://dx.doi.org/10.1086/501620
- 7. ASHP Therapeutic Guidelines on Antimicrobial Prevention in Surgery. American Society of Health-System Pharmacists. *Am J Health Syst Pharm* 1999; **56:** 1839-1888.
- 8. Bratzler DW, Hunt DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clinic Infect Dis* 2006; **43:** 322-330. http://dx.doi.org/10.1086/505220
- Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery* 1961; 50: 161-168.
- Wong ES. Surgical site infections. In: Mayhall CG, editors. Hospital Epidemiology and Infection Control. 3rd ed. (PH): Lippincott Williams & Wilkins; 2004; 287-310.
- 11. Harbarth S, Samore MH, Lichtenberg D, Carmeli Y. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. *Circulation* 2000; **101:** 2916-2921. http://dx.doi.org/10.1161/01.CIR.101.25.2916
- Gómez MI, Acosta-Gnass SI, Mosqueda-Barboza L, Basualdo JA. Reduction in surgical antibiotic prophylaxis expenditure and the rate of surgical site infection by means of a protocol that controls the use of prevention. *Infect Control Hosp Epidemiol* 2006; 27: 1358-1365. http://dx.doi.org/10.1086/509845
- 13. Shapiro M. Perioperative prophylactic use of antibiotics in surgery: principles and practice. *Infect Control* 1982; **3:** 38-40.
- Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the national surgical infection prevention project. *Clin Infect Dis* 2004; 38: 1706-1715. http://dx.doi.org/10.1086/421095

- Anderson DJ, Kaye KS, Classen D, et al. Strategies to prevent surgical site infections in acute care hospitals. *Infect* Control Hosp Epidemiol 2008; 29: S51-61. http://dx.doi. org/10.1086/591064
- Hecker MT, Aron DC, Patel NP, Lehmann MK, Donskey CJ. Unnecessary use of antimicrobials in hospitalized patients: current patterns of misuse with an emphasis on the antianaerobic spectrum of activity. *Arch Intern Med* 2003; 163: 972-978. http://dx.doi.org/10.1001/archinte.163.8.972
- 17. Saizy-Callaert S, Causse R, Furhman C, Le Paih MF, Thébault A, Chouaïd C. Impact of a multidisciplinary approach to the control of antibiotic prescription in a general hospital. *J Hosp Infect* 2003; **53:** 177-182. http://dx.doi.org/10.1053/jhin.2002.1307
- Burke JP. Maximizing appropriate antibiotic prophylaxis for surgical patients: an update from LDS Hospital, Salt Lake City. Clin Infect Dis 2001; 33: S78-83. http://dx.doi. org/10.1086/321861
- 19. Gorecki P, Schein M, Rucinski JC, Wise L. Antibiotic administration in patients undergoing common surgical procedures in a community teaching hospital: the chaos continues. *World J Surg* 1999; **23:** 429-432; discussion 433. http://dx.doi.org/10.1007/PL00012319
- Young B, Ng TM, Teng C, Ang B, Tai HY, Lye DC. Nonconcordance with surgical site infection prevention guidelines and rates of surgical site infections for general surgical, neurological, and orthopedic procedures. *Antimicrob Agents Chemother* 2011; 55: 4659-4663. http://dx.doi.org/10.1128/AAC.00562-11
- 21. Ehrenkranz NJ, Meakins JL. Surgical infections. In: Bennett JV, Brachman PS, editors. *Hospital infections*. 3th ed. (PH): Lippincott-Raven 1992; 685-710.
- 22. Auerbach AD. Chapter 20. Prevention of Surgical Site Infections. In: Shojania KG, Duncan BW, McDonald KM, Wachter RM, Making Healthcare Safer: A Critical Analysis of Patient Safety Practices. San Francisco: AHRQ 2001.
- 23. Bratzler DW, Dellinger EP, Olsen KM, *et al.* Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health-Syst Pharm* 2013; **70:** 195–283. http://dx.doi.org/10.2146/ajhp120568
- 24. Gagliardi AR, Fenech D, Eskicioglu C, Nathens AB, Mcleod R. Factors influencing antibiotic prophylaxis for surgical site infection prevention in general surgery: a review of the literature. *Can J Surg* 2009; **52:** 481-489.
- 25. Khan SA, Rodrigues G, Kumar P, Rao PG. Current challenges in adherence to clinical guidelines for antibiotic prophylaxis in surgery. *J Coll Physicians Surg Pak* 2006; **16:** 435-437.
- Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med* 1992; 326: 281-286. http://dx.doi.org/10.1056/ NEJM199201303260501

- 27. Steinberg JP, Braun BI, Hellinger WC, et al. Timing of antimicrobial prevention and the risk of surgical site infections: results from the trial to reduce antimicrobial prevention errors. *Ann Surg* 2009; **250:** 10-16. http://dx.doi.org/10.1097/SLA.0b013e3181ad5fca
- 28. Weed HG. Antimicrobial prophylaxis in the surgical patient. *Med Clin North Am* 2003; **87:** 59-75. http://dx.doi.org/10.1016/S0025-7125(02)00145-1
- 29. Ribeiro Filho N, Lopes HV, Grinbaum RS. Uso profilático de antibióticos em clínica e em cirurgia. In: Fernandes AT, editor. *Infecção hospitalar e suas interfaces na área da saúde. São Paulo: Atheneu* 2000; **2:** 1535-1549. [Portuguese]
- Talon D, Mourey F, Touratier S, et al. Evaluation of current practices in surgical antimicrobial prophylaxis before and after implementation of local guidelines. J Hosp Infect 2001; 49: 193–198. http://dx.doi.org/10.1053/jhin.2001.1033
- 31. Meehan J, Jamali AA, Nguyen H. Prophylactic antibiotics in hip and knee arthroplasty. *J Bone Joint Surg Am* 2009; **91:** 2480-2490. http://dx.doi.org/10.2106/JBJS.H.01219
- 32. Prokuski L. Prophylactic antibiotics in orthopaedic surgery. *J Am Acad Orthop Surg* 2008; **16:** 283-293.
- De Chiara S, Chiumello D, Nicolini R, et al. Prolongation of antibiotic prophylaxis after clean and clean-contaminated surgery and surgical site infection. *Minerva Anestesiol* 2010; 76: 413-419.
- Manniën J, van Kasteren ME, Nagelkerke NJ, et al. Effect of optimized antibiotic prophylaxis on the incidence of surgical site infection. *Infect Control Hosp Epidemiol* 2006; 27: 1340-1346. http://dx.doi.org/10.1086/509842
- Terpstra S, Noordhoek GT, Voesten HG, Hendriks B, Degener JE. Rapid emergence of resistant coagulase-negative staphylococci on the skin after antibiotic prophylaxis. *J Hosp Infect* 1999; 43: 195-202. http://dx.doi.org/10.1053/jhin.1999.0636
- van Kasteren ME, Kullberg BJ, de Boer AS, Mintjes-de Groot J, Gyssens IC. Adherence to local hospital guidelines for surgical antimicrobial prophylaxis: a multicentre audit in Dutch hospitals. *J Antimicrob Chemother* 2003; 51: 1389-1396. http://dx.doi.org/10.1093/jac/dkg264
- Brusaferro S, Rinaldi O, Pea F, Faruzzo A, Barbone F. Protocol implementation in hospital infection control practice: an Italian experience of preoperative antibiotic prophylaxis. *J Hosp Infect* 2001; 47: 288-293. http://dx.doi.org/10.1053/ jhin.2001.0946
- 38. Carlès M, Gindre S, Aknouch B, Mousnier A, Raucoules-Aimé M. Improvement of surgical antibiotic prophylaxis: a prospective evaluation of personalized antibiotic kits. *J Hosp Infect* 2006; **62**: 372-375. http://dx.doi.org/10.1016/j.jhin.2005.09.004
- 39. Alerany C, Campany D, Monterde J, Semeraro C. Impact of local guidelines and an integrated dispensing system on antibiotic prophylaxis quality in a surgical centre. *J Hosp Infect* 2005; **60:** 111-117. http://dx.doi.org/10.1016/j. jhin.2004.07.022