Original Research

Effects of a computerized provider order entry and a clinical decision support system to improve cefazolin use in surgical prophylaxis: a cost saving analysis

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ABSTRACT*

Background: Computerized Provider Order Entry (CPOE) and Clinical Decision Support System (CDSS) help practitioners to choose evidence-based decisions, regarding patients' needs. Despite its use in developed countries, in Brazil, the impact of a CPOE/CDSS to improve cefazolin use in surgical prophylaxis was not assessed yet.

Objective: We aimed to evaluate the impact of a CDSS to improve the use of prophylactic cefazolin and to assess the cost savings associated to inappropriate prescribing.

Methods: This is a cross-sectional study that compared two different scenarios: one prior CPOE/CDSS versus after software implementation. We conducted twelve years of data analysis (3 years prior and 9 years after CDSS implementation), where main outcomes from this study included: cefazolin Defined Daily Doses/100 bed-days (DDD), crude costs and product of costs-DDD (cost-DDD/100 bed-days). We applied a Spearman rho non-parametric test to assess the reduction of cefazolin consumption through the years.

Results: In twelve years, 84,383 vials of cefazolin were dispensed and represented 38.89 DDD/100 bed-days or USD 44,722.99. Surgical wards were the largest drug prescribers and comprised >95% of our studied sample. While in 2002, there were 6.31 DDD/100 bed-days, 9 years later there was a reduction to 2.15 (p<0.05). In a scenario without CDSS, the hospital would have consumed 75.72 DDD/100 bed-days, which is equivalent to USD 116 998.07. It is estimated that CDSS provided USD 50,433.39 of cost savings.

Conclusion: The implementation of a CPOE/CDSS helped to improve prophylactic cefazolin use by reducing its consumption and estimated direct costs.

Keywords: Cost Savings; Clinical Pharmacy Information Systems; Decision Support Systems, Clinical; Medical Order Entry Systems; Anti-Bacterial Agents; Hospitals; Pharmacists; Brazil

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INTRODUCTION

A publication has once stated the four habits that comprise high value healthcare organizations, and one that deserves special attention includes the use of Computerized Provider Order Entry (CPOE), Clinical Decision Support Systems (CDSS) and treatment algorithms.[1]

CPOE/CDSS is a technology designed to help health practitioners to choose the best evidence-based decision regarding patients' needs.[2] Such technologies are associated with significant improvements in health care assistance. One systematic review published in 2014 included seven randomized trials, which assessed CDSS to improve antibiotics use. The authors concluded that it improved antimicrobial agents prescribing behavior.[3,4]

Cefazolin is a 1st generation cephalosporin that covers gram positive skin bacteria but also has a marginal effect and little clinical use to treat gram negative microorganisms. Clinicians mainly use cefazolin 2g for prophylactic purposes and its indications include skin and soft tissue-related procedures (3g apply for patients weighing >120 kg and 50 mg/kg for children or adolescents with less than 40 kg).[5]

Nonetheless, cefazolin inappropriate use in clinical settings has been extensively described since 1980,[6,7] but still is a concern in many institutions.[8] As fact, inadequate use of antimicrobial agents is associated to higher healthcare expenditures, microbial selection, resistant species prospection and other negative clinical outcomes.[8-10]

Despite many initiatives, middle and low income countries, likewise Brazil, has poorly assessed and published the impact of implementing CPOE/CDSS. Herein, in a quality improvement perspective, we aimed to assess the impact of this technology in twelve years: three years pre-CDSS and nine years post-CDSS implementation. Our objective was to evaluate the impact of a CDSS to improve the prophylactic use of cefazolin and to assess the cost savings associated with inappropriate prescribing in a large university hospital in Southern Brazil.

METHODS

Study Design

This is a cross-sectional study that included twelve years (2002 to 2013, 144 months) of historical registries of prophylactic cefazolin use, from a Southern Brazilian University Hospital.

Inclusion Criteria and Data Collection

Intravenous cefazolin (Anatomical Therapeutic Code number J01DB04) from pharmacy dispensing registries were included in this study considering the aforementioned period: pre-CDSS (January 2002 to December 2004) and post-CDSS implementation (January 2005 to December 2013). Ophthalmic cefazolin preparations were excluded as they did not comprise our study's objectives. Furthermore, different concentrations of such drug were also standardized[11], whereby 1 vial with 500 mg of cefazolin was equivalent to half vial of cefazolin 1g.

Data were collected by two independent post-graduated level researchers. Main findings were discussed with experienced Infectious Diseases (ID) physicians and the Infection Control Service.

CPOE/CDSS: Historical Implementation, Aims and Process

Prior to 2002, the aforementioned hospital did not have a clinical pharmacist to assess whether cefazolin was prescribed according to international guidelines on surgical prophylaxis.[5] In January 2003, a full time dedication clinical pharmacist started an Antimicrobial Stewardship Program and assessed the possibility to implementing a CPOE/CDSS directed to improve prophylactic cefazolin use among surgical wards.

Herein, in the same year, an official document was sent to all surgical specialty wards to collect data regarding current prophylactic practices, which included: (a) name of surgical procedure; (b) prophylactic antimicrobial agent; (c) dosing regimen; and (d) duration of prophylaxis.

Next, hospital's Infection Control Service analyzed each response according to international guidelines on prophylactic use of antimicrobials.[5]

In 2004, all discrepancies identified in the survey were discussed with each surgery specialists and resulted in one clinical algorithm for prophylactic cefazolin use in surgeries (Figure 1). The algorithm was sent to our technology and informatics team and, in January 2005, the final CDSS version was incorporated into hospital's computerized system. In summary, three different scenarios were highlighted and are depicted in this research report:

- In 2002 there were was no cefazolin use assessment;

- In 2003 and 2004 there was a clinical pharmacist who assessed cefazolin and made interventions to improve the use of this antibiotics;

- In 2005, the CPOE/CDSS was implemented and served as an electronic algorithm to guide physicians' surgical prophylaxis prescriptions.
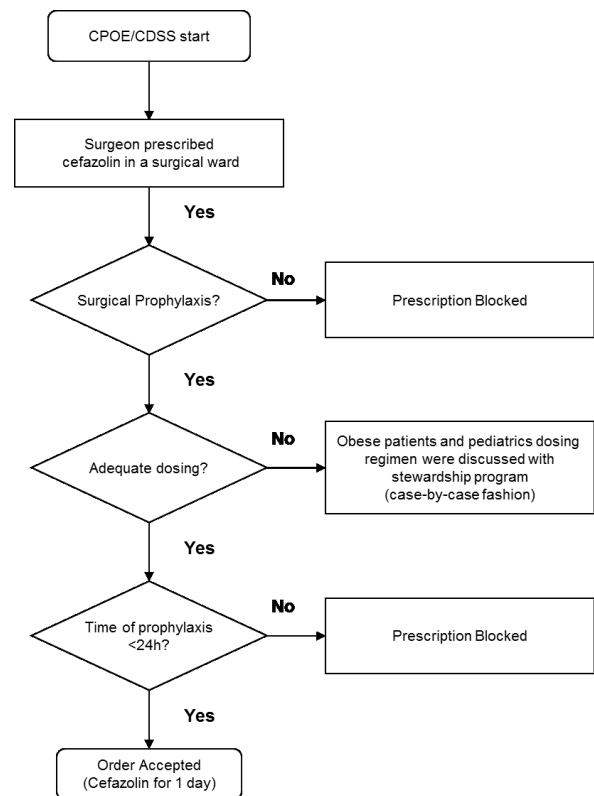

Figure 1 – Clinical decision support rationale.

Figure 1 shows the final algorithm that CDSS performs every time cefazolin is prescribed in one surgical prophylaxis scenarios. In summary, doses and intervals are manually prescribed by clicking on pre-set options: prophylaxis use, therapeutic use, dosing strategy, procedure type and duration. Different doses prescribed to pediatrics, obese and renal injury situations were assessed daily by our hospital's Antimicrobial Stewardship Team, composed by a clinical pharmacist and ID physicians.[12]

Main Outcomes and Definitions

Main outcome was expressed as Defined Daily Doses per 100 bed-days (DDD/100 bed-days). Developed by the World Health Organization, this tool was standardized and validated to compare drug consumption between health institutions.[11] Moreover, as cefazolin use may vary according to the number of inpatients, DDD has as denominators: number of beds and occupation rate, whereby each unit of DDD can be compared to any institution size or occupation rate.

We also assessed the potential cost savings and and cost-DDD per hundred bed-days, by comparing the real DDD consumption versus one hypothetical scenario with no CDSS implementation (no changes on cefazolin consumption through the years).

For this purpose, the average cost of cefazolin was defined as BRL 1.25 ±0.22, where 1 BRL was equivalent to 0.42 USD (dollar). In other words, each cefazolin 1g vial cost 0.53 USD. Exchange values were calculated based on 2014 data, which can be found elsewhere [reuters.com/finance] and

each unit of cefazolin cost was consulted within hospital's Financial and Acquisition Department.

Cost Savings Assessment and Data Analysis

We performed a partial economic analysis by comparing the real cefazolin consumption with one hypothetical scenario without CDSS (extrapolated from 2002), where we assumed that antibiotics consumption would permanently stay the same along the years. DDD and cost-DDD difference between the aforementioned hypothetic scenario was compared with the real cefazolin consumption.

DDD, cost-DDD and crude costs were compared through twelve years horizon, whereby 2002 did not have any cefazolin control; 2003 to 2004 had a dedicated pharmacist to antimicrobial stewardship; and 2005 accounted for the 1st year of CDSS implementation.

Because both data are continuous variables, we performed a Spearman non-parametric correlation to establish whether such effect sustained along years by interpreting its linear function. Regarding "Spearman rho", we considered the r-squared value as "highly correlated association" when $-0.6 > r^2 > +0.6$. For hypothesis testing, we considered a two-tailed analysis and p-values under 0.05 were statistically significant.

Ethics

This quality improvement project complies with Helsinki's Declaration. It is part of an approved project to assess the impact of rationalizing antimicrobial agents in the aforementioned hospital, which was submitted and approved by Local Ethics Committee.

RESULTS

Overview of Cefazolin Use

Through twelve years, there were 84,383 vials of cefazolin dispensed that represented 38.89 DDD per hundred bed-days. The amount of 1st generation cephalosporin consumed was equivalent to USD 44,722.99.

Our sample consisted mainly in surgical wards, as they accounted for 95% of all prescribed drugs (95% = 80,125 vials or USD 42,466.70). Figure 2 illustrates the absolute number of cefazolin consumption in the analyzed period.

As shown in Figure 3, there was a significant decrease in DDD value from 2002 to 2013 (6.31 vs 2.15), representing almost three times reduction if both periods were directly compared. Yearly, there was an average 0.53 (±0.73) DDD reduction. We also observed a decrease in cefazolin consumption through the years (R^2=0.8, p<0.001).

Still in this graph, it is possible to observe three patterns of cefazolin consumption:

- In 2002, the highest consumption of cefazolin was observed, as the hospital neither had cefazolin restriction policies, nor it was assessed by a Stewardship Team;

- A clinical pharmacist started to assess cefazolin use in 2003 and 2004 and also helped to develop and implement a CPOE/CDSS. This professional contributed with the first reduction of cefazolin consumption;

- In 2005, CDSS was finally implemented and it ensured a sustained reduction on DDD consumption in the next years (2005 to 2013).
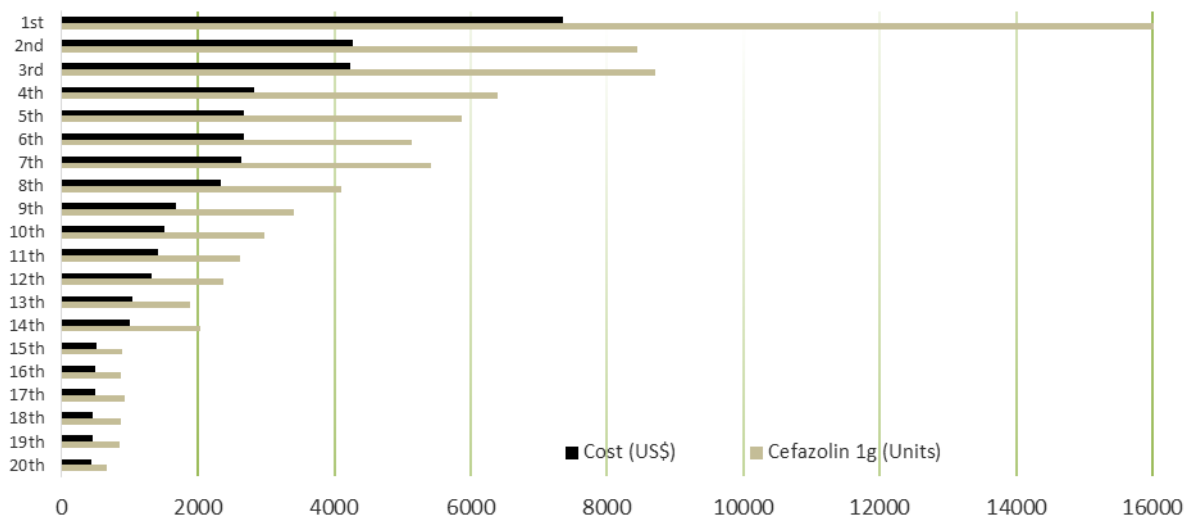

Figure 3. DDD per hundred bed-days and correlation analysis.
Legend: From 1st to 20th (wards that were classified as "top twenty" cefazolin prescribers): Orthopedics, Urology surgery, Gynecologic surgery, Plastic surgery, General surgery, Pediatric surgery, Adult intensive care, Obstetrics, Neurology surgery, Cardiology intensive care, Otolaryngology surgery, Digestive surgery, Vascular surgery, Pediatric intensive care, Thoracic and cardiovascular surgery, Internal medicine (male), Internal medicine (female), Adult emergency room, Infectology and Pediatric emergency room.
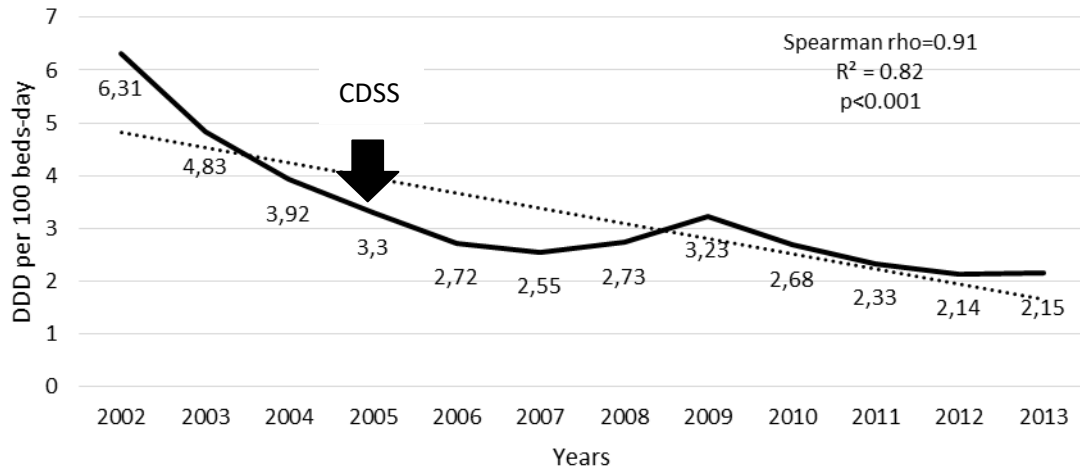
Figure 3. DDD per hundred bed-days and correlation analysis.

Cost Savings

If DDD was hypothetically sustained through the twelve years (considering 2002 DDD value), there would be 75.72 DDD/100 bed-days, which is equivalent to 40.13 USD DDD/100 bed-days. Therefore, we estimated that the difference between non-CDSS and CDSS scenarios (after 2005) generated 32.64 DDD/100 bed-days of cefazolin savings, or 17.3 USD DDD/100 bed-days avoided.

Another estimation regarding Figures 3 and 4 would include an analysis of the crude monetary values: in a scenario without CDSS there would be USD 116,998.07 of cefazolin-related expenditures; however, with CDSS implementation (after 2005), we consumed only USD 66,564.67. We estimated that USD 50,433.39 was avoided due to CPOE/CDSS implementation.

One should note that 2003 and 2004 was not included in cost-savings analysis because it reflected clinical pharmacist's efforts to ensure that cefazolin was properly used in our institution. Nonetheless, clinical pharmacist's interventions in that time accounted for a 2.39 DDD/100 bed-days reduction in 2 years of dedication. If cefazolin was constantly consumed at 6.31 DDD/100 bed-days per year, it would represent USD 19,499.67 of cefazolin cost savings. After 2005, we observed that CDSS/CPOE sustained a cefazolin consumption average of 2.65 ± 0.4 DDD/100 bed-days.

DISCUSSION

This quality improvement project suggested that the CPOE/CDSS had positive impact on rationalizing the prophylaxis use of cefazolin among the years.
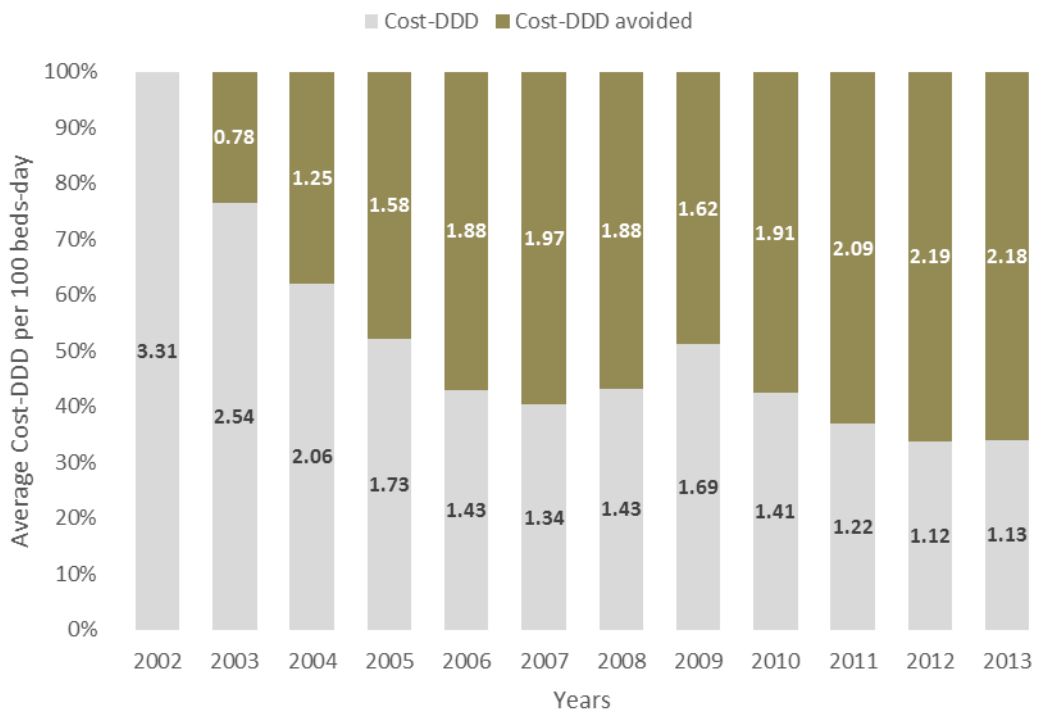

Figure 4. Cost-DDD per 100 bed-days and avoided cost-DDD.

Notably, this is the first report to assess the feasibility of such technology in Brazil.

By analyzing our experience, two issues determined the successful implementation of the clinical decision support system in the hospital's computerized order entry: the necessity to improve human and financial resources allocation in a large public health hospital in Brazil; and the collaboration of many health care professionals through CPOE/CDSS process of development and implementation.

CPOE/CDSS helped to improve cefazolin use

One could discuss that in 12 years, there could be many significant changes, but regarding cefazolin use in surgical prophylaxis scenario, few issues has changed.[5] Moreover, long-term assessment of efficient technologies is of special interest in health systems with scarce resources.

Our main findings corroborate with other CDSS researches. However, none of them reported the results of CDSS implementation results of nine years period.

Recently, one study[13] showed that CDSS-based algorithm improved the rate of adequate surgical prophylaxis, whereby excessive treatment duration reduced from 77% to 44.7% (p<0.001), and improved the number of surgery-related infections (18.5% to 12%). Nonetheless, in 1 year of data analysis, the DDD/procedure also reduced the costs from 36,420 to 21,465 Euros. Our cost savings were smaller if we consider 9 years of CDSS/CPOE implementation. However, we focused only on cefazolin, while the previous considered clindamycin, metronidazole and cefuroxime, which are considerably more expensive. The drawback from this interesting study[13] is the prophylaxis optimization process, which included inspections and feedback to prescribers. Such interventions are time-consuming and may lose effectiveness, as it is dependent on persons' behavior. Our CDSS blocked inappropriate prescribing and explained why it still is effective after years of implementation.

The largest research about CDSS and surgical prophylaxis was an observational study conducted in the United States of America with almost 163 thousand patients.[14] Their study differed from ours because they did additional analysis on preoperative and postoperative consumption of antibiotics, clinical outcomes (rates of adverse drug events, antimicrobial resistance, length of stay and mortality) and cost savings. The seven years-based study suggested a 22.8% decrease on antibiotics consumption, and a cost reduction of antibiotics per patient from USD 122 to USD 52.[14]

Finally, a recent before-and-after study conducted in Korea, compared the effects of implementing a CDSS on length of stay, antimicrobial consumption and resistance rates.[15] Their interrupted series analysis suggested an 8.71 DDD/1000 patient-days reduction and decreased length of stay after CDSS implementation. They also found a reduction on beta-lactamase producing E. coli, carbapenemase-producing P. aeruginosa and methicillin-resistant S.

aureus. In our study, we did not attempt to study the number of cefazolin resistant bacteria, because first generation cephalosporin resistant species has little clinical value on gram positive infections.[16] Skin and soft tissue-related infections can be further treated with many therapeutic options, such as broader spectrum cephalosporins, oxacillin, clindamycin and vancomycin.[17] On the other hand, length of stay might be an interesting outcome for future studies to assess the impact of CDSS/CPOE implementation in our hospital.

CDSS Implementation Process Determined the Results

A previous systematic review reported that future studies should investigate what CDDS characteristics are crucial for high acceptance and institutional improvements on cefazolin prescribing.[4] In our study, CDSS succeeded due to a stepwise strategy to implement such initiative, which included all surgery wards (main assistant physicians and chair professors). All medical staff suggestions were considered and discussed to elaborate our institutional prophylaxis guidelines and forthcoming updates were continuously incorporated to CDSS. Other determinant situations included the active participation from our infectious disease professionals and institution's involvement. Comparatively, other studies had reported promising results after recruiting and involving hospital's surgeons to improve prescribing behavior.[8,13]

Our CDSS/CPOE was substantially cheap, as we were supported by hospital's informatics staff who developed the software in a few months. The most expensive part of developing software, likewise we did, is the dedication of long periods to continuously develop the most adequate protocol with all interested parties.

Limitations

Our study is not free of limitations. Firstly, cost saving studies lack sensitivity analysis and clinical outcomes, thus, it is unknown whether uncertainty of the included variables (e.g.: currency variation, DDD range and discounts through 12 years of assessment) could influence final result. In addition, we used an unusual way to analyze cost savings by hypothetically assuming that cefazolin consumption would not change along the years in a scenario without CDSS. However, we believe that our findings are robust by considering figure 3, where we demonstrated a sustained reduction in cefazolin use after CDSS implementation, after 2005.

Secondly, it is necessary to say that clinical pharmacist's efforts to ensure adequate use of cefazolin in 2003 and 2004 could have promoted a residual effect in the following years, especially on 2005, the first year of CDSS/CPOE implementation. On the other hand, there was little involvement of clinical pharmacist's activity after 2005, as the software accounted for most of necessary interventions, and he could dedicate to more complex infectious diseases cases in the hospital.

Thirdly, prophylaxis guidelines have been suffering consistent changes through the years. However, surgery prophylaxis with cefazolin still is the main antimicrobial choice due to its narrow spectrum and lack of cross-resistance among other anti-infectious antibiotics. Since 2002, cefazolin remains as valid option to prevent skin incisions-related bacteremia.[5]

Our research was conducted in a single-center in Southern Brazil, so our results might not be replicated in other hospitals and countries. Criticism on the acceptance of the software and amount of cost savings are relevant issues to consider when interpreting our data.

Finally, retrospective studies have intrinsic bias associated to quality of clinical documentation and data collection. We believe that these problems were attenuated by involving ID experienced professionals during data analysis and article processing.

CONCLUSIONS

In a context of resource scarceness in many health systems, better human and financial resources are imperative to guarantee more efficiency. In our casuistic, the CDSS improved cefazolin use and reduced costs, by reducing the number of inappropriate prescriptions. We also considered that CDSS/CPOE rationalized pharmacist's daily activities, and directed him to other cognitive activities, rather than screening for prophylactic surgery inadequate prescriptions.

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CONFLICT OF INTEREST

References

1. Bohmer RM. The four habits of high-value health care organizations. N Engl J Med. 2011 Dec 1;365(22):2045-7. doi: 10.1056/NEJMp1111087

2. Sim I, Gorman P, Greenes RA, Haynes RB, Kaplan B, Lehmann H, Tang PC. Clinical decision support systems for the practice of evidence-based medicine. J Am Med Inform Assoc. 2001;8(6):527-534.

3. O'Sullivan D, Fraccaro P, Carson E, Weller P. Decision time for clinical decision support systems. Clin Med (Lond). 2014;14(4):338-341. doi: 10.7861/clinmedicine.14-4-338

4. Holstiege J, Mathes T, Pieper D. Effects of computer-aided clinical decision support systems in improving antibiotic prescribing by primary care providers: a systematic review. J Am Med Inform Assoc. J Am Med Inform Assoc. 2015;22(1):236-242. doi: 10.1136/amiajnl-2014-002886

5. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70(3):195-283. doi: 10.2146/ajhp120568

6. Appleby DH, John JF Jr. Use, misuse, and cost of parenteral cephalosporines at a county hospital. South Med J. 1980;73(11):1473-1475.

7. Katz E, Schlamowitz S. Savings achieved through cephalosporin surveillance. Am J Hosp Pharm. 1978;35(12):1521-1523.

8. Rana DA, Malhotra SD, Patel VJ. Inappropriate surgical chemoprophylaxis and surgical site infection rate at a tertiary care teaching hospital. Braz J Infect Dis. 2013;17(1):48-53. doi: 10.1016/j.bjid.2012.09.003

9. Harbarth S, Samore MH. Antimicrobial resistance determinants and future control. Emerg Infect Dis. 2005;11(6):794-801.

10. Howard DH, Scott RD 2nd. The economic burden of drug resistance. Clin Infect Dis. 2005 Aug 15;41(Suppl 4):S283-S286.

11. World Health Organization Collaborating Center for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment 2013. WHO: Oslo; 2012. Available at: http://www.whocc.no/atcddd/ (accessed September 24, 2014).

12. Okumura LM, Silva MM, Veroneze I. Effects of a bundled antimicrobial stewardship program on mortality: a cohort study. Braz J Infect Dis. 2015;19(3):246-252. doi: 10.1016/j.bjid.2015.02.005

14. Bozkurt F, Kaya S, Gulsun S, Tekin R, Deveci Ö, Dayan S, Hoşoglu S. Assessment of perioperative antimicrobial prophylaxis using ATC/DDD methodology. Int J Infect Dis. 2013 Dec;17(12):e1212-e1217. doi: 10.1016/j.ijid.2013.08.003

14. Pestotnik SL, Classen DC, Evans RS, Burke JP. Implementing antibiotic practice guidelines through computer-assisted decision support: clinical and financial outcomes.. Ann Intern Med. 1996;124(10):884-890.

15. Huh K, Chung DR, Park HJ, Kim MJ, Lee NY, Ha YE, Kang CI, Peck KR, Song JH. Impact of monitoring surgical prophylactic antibiotics and a computerized decision support system on antimicrobial use and antimicrobial resistance. Am J Infect Control. 2016. [Epub ahead of print] doi: 10.1016/j.ajic.2016.01.025

16. Jonkers D, Swennen J, London N, Driessen C, Stobberingh E. Influence of cefazolin prophylaxis and hospitalization on the prevalence of antibiotic-resistant bacteria in the faecal flora. J Antimicrob Chemother. 2002;49(3):567-571.

Okumura LM, Veroneze I, Burgardt CI, Fragoso MF. Effects of a computerized provider order entry and a clinical decision support system to improve cefazolin use in surgical prophylaxis: a cost saving analysis. Pharmacy Practice 2016 Jul-Sep;14(3):717. doi: 10.18549/PharmPract.2016.03.717

17. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59(2):e10-e52. doi: 10.1093/cid/ciu444