A Clinical Decision Support System for an Antimicrobial Stewardship Program

F. Palacios[1], M. Campos[2], J. M. Juarez[2], S. E. Cosgrove[3], E. Avdic[3], B. Canovas-Segura[2], A. Morales[2], M. E. Martínez-Nuñez[1], T. Molina-García[4], P. García-Hierro[4] and J. Cacho-Calvo[5]

[1]*Intensive Care Unit, University Hospital of Getafe, Getafe, Spain*
[2]*Computer Science Faculty, University of Murcia, Murcia, Spain*
[3]*Antimicrobial Stewardship Program, The Johns Hopkins Hospital, Baltimore, MD, U.S.A*
[4]*Pharmacy, University Hospital of Getafe, Getafe, Spain*
[5]*Microbiology, University Hospital of Getafe, Getafe, Spain*

Keywords: Decision Support System, Antimicrobial Stewardship Program.

Abstract: The World Health Organization has declared that antimicrobial resistance is a major public health issue and one of the three greatest threats to human health. Antimicrobial Stewardship Programs, ASP, are institutional approaches to curb the threat of antimicrobial resistance, improve the safety of patients receiving antibiotics, and decrease antibiotic costs. Medical informatics in all areas, particularly the Electronic Health Record (EHR), has become a paradigm of modern medicine. An intelligent system integrated in EHR can play an important role in facilitating ASP activities. In this article we describe the experience of integration of a newly developed clinical decision support system, WASPSS, into an antimicrobial stewardship program in a mid-size hospital.

1 INTRODUCTION

According to the Center of Disease Control and Prevention (CDC), each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die each year as a direct result of these infections (CDC, 2013). The European Union estimates that 25,000 people die due to the same problem, at a cost of 1.5 billion Euros per year (ECDC, 2009). Many more people die from other conditions that are complicated by an antibiotic-resistant infection.

Antibiotics are unique drugs due to their high efficacy in terms of the reduction of morbidity and mortality. At the same time, they are the only drugs in which the use of the agent in one patient can affect use in another patient via development of resistance. Almost all medical specialties use antibiotics, although it had been demonstrated that education in appropriate antibiotic use is lacking in medical school and training programs. Choosing the correct agent can also be impacted by this lack of knowledge particularly given the complexities of modern hospital patients. It is also important to bear in mind the ethical considerations of dealing with the global problem of antibiotic resistance while offering the care to the individual patient.

Antimicrobial Stewardship Programs, ASPs, have been proposed as a solution to the global threat of antibiotic resistance (Doron and Davidson, 2011; Nathan and Cars, 2014). ASPs have proven to be effective at improving patient outcomes, reducing the use of antibiotics, and controlling costs (Carling et al., 2003). A key issue in ASP is the use of Clinical Decision Support Systems (CDSSs), along with the meaningful use of Electronic Health Records (EHRs) (Blumenthal and Tavenner, 2010) that promote and incentivize the use of health information technologies, and, more specifically, the use of CDSSs in the United States.

A review of recent articles on CDSSs for infectious disease management shows that the trend in CDSSs is to focus on infection control, surveillance, alerts and reporting. In general, they are directed at a limited number of users, mainly infection preventionists and pharmacists who use this technology to identify patients that may need

Palacios, F., Campos, M., Juarez, J., Cosgrove, S., Avdic, E., Canovas-Segura, B., Morales, A., Martínez-Nuñez, M., Molina-García, T., García-Hierro, P. and Cacho-Calvo, J.
A Clinical Decision Support System for an Antimicrobial Stewardship Program.
DOI: 10.5220/0005824904960501
In *Proceedings of the 9th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2016) - Volume 5: HEALTHINF*, pages 496-501
ISBN: 978-989-758-170-0

therapy modification. Nevertheless, ASP influence goes further than those points and the CDSS should consider other functionalities to support ASP activities and ways of breaking the barriers of CDSS adoption that are not yet identified.

The University Hospital of Getafe in Spain, UHG, has recently implemented an ASP program named PAMACTA (Program for Multidisciplinary Assistance and Control of Antimicrobial Therapy). The UHG, is a mid-size hospital (approx. 600 beds), covering most medical specialties. In this paper, we describe the practical reasons that have inspired the development of a CDSS called WASPSS (Wise Antimicrobial Stewardship Program Support System). We show how the recommendations for the ASP can be translated into an intelligent system beyond the functionalities of the CDSS already described in the literature.

The PAMACTA team is composed of 9 members. In the current context of economic crisis, resources are limited, and all specialists have a modest dedication of time to the project. To begin with, the team considered the recommendations of the Infectious Diseases Society of America and Society for Hospital Epidemiology of America (IDSA/SHEA) (Dellit et al., 2007), and the objectives described by CDC (CDC, 2012). One of the most important recommendations is to define a multidisciplinary group, thus facilitating communication and collaboration in order to improve antibiotic use.

A well-known disadvantage when teams follow this methodology is the amount of time required by the ASP to review alerts: 2-3 hours/day, with an additional 1-2 hours for interventions on actionable alerts and documentation. In addition, the number of alerts increases with the number of rules, which are increasingly specific for the different protocols and clinical conditions of the patients. The team needs the support of specific software that will allow them to focus on key aspects of ASP. The birth of the WASPSS system at the same time that the team was created provides the opportunity to focus on current needs of an ASP team starting from scratch.

The rest of the paper is structured as follows. We describe the functionalities and analytic capabilities not yet identified in the CDSS literature for infection control. In the following two sections we describe the functionality of the WASPSS system for supporting the physician and the ASP team in their respective activities. The intelligent technologies included in the WASPSS system are described, and, finally, we provide the conclusions and contributions of this paper.

2 CDDS FUNCTIONALITIES NOT YET IDENTIFIED

Since the MYCIN (Buchanan and Shortliffe, 1984) project, there has been a long history of intelligent systems working on infection diagnosis and treatment, dating back to the 1980s (Evans et al., 1998; Nachtigall et al., 2014). In a previous work, some authors identified the functional requirements of a CDSS for infection control (Pestotnik, 2005). A recent review (Forrest et al., 2014) compared the functionalities of some commercial CDSSs and EHRs for infection control. Most of them only focus on surveillance, alerting, and reporting.

The general difficulties involved in creating successful CDSSs have been identified (Forrest et al., 2014), but there are no proposals from the technical point of view to overcome the economical and ethical barriers, alert fatigue, and the lack of any measure of clinical impact. More specific gaps in functionality are the limited interaction with clinical guidelines, the difficulty of following up the patient after the alert, and the difficulty involved in integrating and sharing knowledge. Regarding the last point, the number of hand-coded alerts may be very high (e.g. 1285 best practice alerts (Schulz et al., 2013)), and their management is very complex since there is no easy way of updating them or detecting conflicts.

As regards the users, most of the CDSSs are focused on prescription support for physicians, and on helping the treatment reviews carried out by pharmacists (Calloway et al., 2013). Very few works highlight the role of microbiologists in ASP (Avdic and Carroll, 2014).

We realized that the above studies did not focus on helping the ASP team, and that, some essential ideas on ASP functions have been overlooked; for example: a) CDSSs must be multidisciplinary, and must consider a view adapted for each role; b) CDSSs must promote and ease communication between all the participants; c) CDSSs must provide the most suitable information at the most appropriate moment to each specific user; d) CDSS must help in the education of clinical staff members in the management of antibiotics.

3 SUPPORTING ATTENDING PHYSICIAN IN THE TREATMENT OF INFECTIONS

We now describe a process for management of patients with infections, where we identify the knowledge needed by the ASP members and the support that can be offered by WASPSS in each phase. In general, we can define three phases respect to the treatment: a) “pre-prescription” phase where the clinician needs clinical information to diagnose, b) a “prescription” phase where the clinician selects the antibiotic according to several criteria and not only to clinical information, and c) the “post-prescription” phase with an assessment-review loop of clinical response.

In the first phase, “pre-prescription”, the actions are essentially related to the clinical assessment of the patient, and the use of protocols. The system in this case should be responsible for proposing protocols and, according to those protocols, propose short-term plans and to provide reminders about information gathering. Table 1 depicts the phases and the possible actions considered in the CDSS.

In the second phase, a key aspect where the WASPSS system intervenes is to integrate the clinical guidelines with the experts’ knowledge. The system is responsible for including information on microbiology, pharmacodynamics, pharmacokinetics as well as local policies of antibiotic use (e.g. formulary restriction) is needed in the proposal for empiric treatment. In our case, we think that visual explanation is a simple way of showing the rationale; for example, cost and coverage of most frequent pathogens in the type of culture.

An important factor would be to take advantage of microbiologists’ expertise in the interpretation of the susceptibility tests and antibiogram. The introduction of EUCAST expert rules (Leclercq et al., 2013) for intrinsic resistance and exceptional resistance phenotypes with local adaptations could help a better and wider interpretation of the test.

In the third phase, post-prescription, the role of an infectious diseases specialist, microbiologist and pharmacist in the ASP team is even more relevant. Once the culture results with susceptibilities and minimum inhibitory concentrations are available, it is possible to detect any inappropriate selection of antibiotics, and to avoid the failure of treatment due to factors such us under-dosing (not ensuring the elimination of the pathogen), adverse effects, or reinfection. At this moment, recommendations such as the early isolation of the patient according to local policies are important. For example, a local policy in the UHG is not to use ciprofloxacine against *E.coli* in urinary tract infections due to a resistance of 43%.

By including pharmacokinetics and pharmacodynamics as criteria, we facilitate the selection of both drug and dosing regimen, with the aim of inhibiting the microbe and improving the clinical response of the patient. The dosage selected should result in adequate therapeutic concentrations at the site of infection for a sufficient time without causing side effects or toxicity.

In this step, the system should enter in a loop that should include the evolution and previous assessment rather than simply evaluating each action individually to avoid false positive alerts that would eventually be overridden by the ASP team and the physician. When the clinician actually feels a patient-centered care culture involving close supervision of the patient’s evolution, it is possible to improve the treatment of the patient.

4 SUPPORTING ASP ACTIONS

Apart from patient care, the ASP team is responsible for defining actions in a wide number of contexts that are not directly related to antibiotic supervision. Some of these functions are the actions related with infection prevention, educational actions, information diffusion, and the definition of policies. In this section we describe four aspects where the WASPSS system is supporting these ASP functions.

First, the CDSS must adapt to the methodology of work proposed by the ASP team. In the case of the UHG, the use of department representatives with different roles and views in the CDSS is essential for creating a general culture of rational antibiotic use, and enable as many alerts as possible to be monitored.

At the same time, WASPSS strengthens the communication links between the attending physicians and the respective experts in pharmacy, microbiology and infectious diseases. Previous study evaluated the effect of different methods of communication of ASP recommendations using variety of technologies (phone, pager, email) (Cosgrove et al., 2007). Nevertheless, they did not focus on the content of the messages and the positive reinforcement, since the communication mode was only used to send alerts or warnings. From an educational point of view, the objective is twofold: on the one hand to report possible errors, and, on the other hand to provide feedback and positive reinforcement when the patient care is going well.

Table 1: CDSS actions in the patient management phases.

Pre-prescription	Prescription	Post-prescription
- Proposal of protocols - Calculation of severity indexes - Therapeutic threshold for antibiotic administration - Planning of tests and information gathering reminders	- Interpretation of antibiogram with expert rules - Stratified, combined and dual cross cumulative antibiogram - Visualization of therapeutic options - Sorted visualization of criteria	- Pharmacy alerts - Alert of alteration of biochemical control of organs - De-escalation proposal - Isolation proposal - Proposal of new test - Evaluation and prediction of systemic inflammatory response

We have included a bidirectional communication channel that also involves the physician in the ASP team, and that facilitates access to clinical information about the patient.

Another role of ASP team is to review the current knowledge and to evaluate the quality of care. The ASP team can leverage the analytic capabilities of the CDSS to include local habits of use of antibiotics and the local microbiology in the process of reviewing the clinical guidelines and protocols.

A third role of the ASP is the global surveillance and monitoring of antibiotic use and resistance. The monitoring of both clinical and process outcomes is important for proposing new actions, and also for removing measures or policies that are not having any real impact on patient safety, economy or antibiotic resistance. In this case, the use of business intelligence technologies allows the creation of meaningful and actionable reports that facilitate the decision-making process.

The last activity we highlight is education. Education on the best use of antibiotics may be one of the highest impact activities in patient safety through the protection of antibiotics and the reduction of resistances. The ASP team can analyze the use of the CDSS, the type of alerts fired, the type of recommendations accepted and rejected, the deviations from protocols and the local habits of use of antibiotics in a number of dimensions, such as the experience of the physicians, in order to assess the competence of the different disciplines, services and roles.

In this way, it is possible to design the content of training activities that could reduce the distance between junior and senior physicians, to unify criteria and policies in the use of antibiotics, to raise awareness on the problem of antibiotic resistance.

5 INTELLIGENT TECHNOLOGIES IN WASP

In order to cover all the above aspects, we propose the inclusion of three specific technologies in WASPSS: a) knowledge management, b) intelligent data analysis and mining, and c) visualization.

One of the main barriers in CDSSs is the integration of data. This is partially solved by means of interoperability, communication and vocabulary standards. However, we think that knowledge is far more important than data, and a knowledge management methodology is a key element in integrating experts' knowledge, clinical guidelines, local habits of use and knowledge discovered in the database. We use the same representation framework for clinical guidelines and protocols, rules for adverse effect or interactions, phenotypes to create more specific rules, and even patient clinical data.

Intelligent data analysis and data mining are used to increase the amount of knowledge available in the CDSS. There are a number of techniques that can be used for a number of tasks. In this sense, we are not only looking for classification models, but actionable knowledge that allows the ASP to act in any of their functions. For example, we use data mining techniques to discover subgroups of patients whom the antibiotic therapy is failing. Other applications include the use the data analysis to help the epidemiologist in the analysis of patterns of appearance of resistances, or analysis of the use of the CDSS to detect, for example, what antibiotics are the causes of more alerts.

We put particular emphasis on new visualization techniques of patient status, protocols, and, in general, all the criteria to assist the physician in choosing the most appropriate antibiotics. Improved CDSSs must include innovative visualization techniques to provide a simple and intuitive way of summarizing as much information as possible, both for helping in the prescription and for overall monitoring.

The use of visual analytics techniques to display patterns and models enables an agile review of discovered knowledge and its incorporation into the knowledge base. In this way, it is possible to analyze and to contrast the current local use and effect of antibiotics with respect to clinical guidelines and protocols.

6 CONCLUSIONS

In this article we have presented the first experiences of an ASP team in a mid-size hospital in Madrid, Spain, and the opportunities identified in the development of an intelligent system to help them called WASPSS. We think the presence of a CDSS is even more important in a context of limited resources. In this context, as an interpretation of the basic principle of Evidence Based Medicine, a contribution of this paper is to highlight an extension of the definition of ASP team that includes all the physicians of the hospital.

From the user point of view, we highlight some of the functionalities not previously mentioned in other research articles on CDSS but which form part of the current development of WASPSS:

- Multidisciplinary: current CDSSs only consider one type of user, while the ASP is a multidisciplinary approach by definition. Different experts should be able to introduce their knowledge into the system and to have a customized view of the information.
- Continuous: WASPSS focuses not on only one stage of the treatment of infections, but considers an integral view of the management of patient and information. In this way, we can follow up the patients and increase patient safety, helping to solve the ethical dilemma for the physician.
- Modular: WASPSS allows knowledge modules to be created for the disciplines in such a way that it can be shared between different settings.
- Shareable: the knowledge modules can be shared between different instances of WASPSS in different hospitals.
- Adaptive: the knowledge modules can be customized to the current context of the hospital. They also allow the integration of clinical guidelines and local protocols.
- Interoperable: although WASPSS can work standalone, we are integrating it with the current EHR system of the hospital.
- Accurate: we aim to avoid false positive alarms with more personalized rules in subgroup of patients.
- Communicative: WASPSS does not focus only on reporting or launching alarms, but it also promotes the bidirectional communication between the different clinical specialists and the ASP team.
- Documental: WASPSS provides a way of documenting both plans and decisions on patient management. It is essential during night, shift changes, and weekends where different physicians with probably less knowledge on specific patients are on duty.
- Educational: WASPSS allows the identification of specific points to be included in the educational program of the hospital. What is more, it can be used as a teaching platform.

ACKNOWLEDGEMENTS

This work was partially funded by the Spanish Ministry of Economy and Competitiveness under the WASPSS project (Ref: TIN2013-45491-R) and by European Fund for Regional Development (EFRD).

REFERENCES

CDC, 2013. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States. Available from: www.cdc.gov/drugresistance/threat-report-2013/.

ECDC, 2009. European Centre for Disease Prevention and Control. The bacterial challenge: time to react;. Available from: www.ecdc.europa.eu/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf.

Doron S, Davidson LE, 2011. Antimicrobial stewardship. *Mayo Clin Proc.*; 86(11): 1113-23.

Nathan C, Cars O, 2014. Antibiotic Resistance - Problems, Progress, and Prospects. *N Engl J Med.*; 371:1761-3.

Carling P, Fung T, Killion A, Terrin N, Barza M, 2003. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infect Control Hosp Epidemiol*; 24:699-706.

Blumenthal D, Tavenner M, 2010. The "Meaningful Use" Regulation for Electronic Health Records. *N Engl J Med.*; 363 (6): 501–504.

Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al, 2007. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin. Infect. Dis*; 44: 159 – 177.

CDC, 2012. Institute for Healthcare Improvement. CDC/IHI Antibiotic Stewardship Driver Diagram and Change Package. Available from: http://www.cdc.gov/getsmart/healthcare/implementation.html.

Schulz L, Osterby K, Fox B, 2013. The use of best practice alerts with the development of an antimicrobial stewardship navigator to promote antibiotic de-escalation in the electronic medical record. *Infect Control Hosp Epidemiol*; 34(12): 1259-65.

Buchanan BG, Shortliffe EH. 1984. *Rule Based Expert Systems: The Mycin Experiments of the Stanford Heuristic Programming Project (The Addison-Wesley Series in Artificial Intelligence)*. Addison-Wesley Longman Publishing Co., Inc., Boston, MA, USA.

Evans RS, Pestotnik SL, Classen DC, Clemmer TP, Weaver LK, Orme JF Jr, et al, 1998. A computer-assisted management program for antibiotics and other antiinfective agents. *N Engl J Med*; 338(4):232-8.

Nachtigall I, Tafelski S, Deja M, Halle E, Grebe MC, Tamarkin A, et al, 2014. Long-term effect of computer-assisted decision support for antibiotic treatment in critically ill patients: a prospective 'before/after' cohort study. *BMJ Open*;4(12):e005370.

Pestotnik SL, 2005. Expert clinical decision support systems to enhance antimicrobial stewardship programs: insights from the society of infectious diseases pharmacists; *Pharmacotherapy;* 25(8):1116-25.

Forrest GN, Van Schooneveld TC, Kullar R, Schulz LT, Duong P, and Postelnick M, 2014. Use of Electronic Health Records and Clinical Decision Support Systems for Antimicrobial Stewardship. *Clin Infect Dis*; 59 (suppl 3): S122-S133.

Calloway S, Akilo HA, Bierman K, 2013 Impact of a clinical decision support system on pharmacy clinical interventions, documentation efforts, and costs. *Hosp Pharm*.; 48(9):744-52.

Avdic E, Carroll KC, 2014. The Role of the Microbiology Laboratory in Antimicrobial Stewardship Programs, *Infectious Disease Clinics of North America* ; 28(2):215-235.

Leclercq R, Cantón R, Brown DF, Giske CG, Heisig P, MacGowan AP, et al, 2013. EUCAST expert rules in antimicrobial susceptibility testing. *Clin Microbiol Infect*; 19(2):141-60.

Cosgrove SE, Patel A, Song X, Miller RE, Speck K, Banowetz A, et al., 2007. Impact of different methods of feedback to clinicians after postprescription antimicrobial review based on the Centers For Disease Control and Prevention's 12 Steps to Prevent Antimicrobial Resistance Among Hospitalized Adults. *Infect Control Hosp Epidemiol.*; 28(6):641-6.