

Computerized Clinical Decision Support: Contributions from 2014

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Summary

Objective: To summarize recent research and propose a selection of best papers published in 2014 in the field of computerized clinical decision support for the Decision Support section of the IMIA yearbook.

Method: A literature review was performed by searching two bibliographic databases for papers related to clinical decision support systems (CDSSs) and computerized provider order entry systems in order to select a list of candidate best papers to be then peer-reviewed by external reviewers. A consensus meeting between the two section editors and the editorial team was finally organized to conclude on the selection of best papers.

Results: Among the 1,254 returned papers published in 2014, the full review process selected four best papers. The first one is an experimental contribution to a better understanding of unintended uses of CDSSs. The second paper describes the effective use of previously collected data to tailor and adapt a CDSS. The third paper presents an innovative application that uses pharmacogenomic information to support personalized medicine. The fourth paper reports on the long-term effect of the routine use of a CDSS for antibiotic therapy.

Conclusions: As health information technologies spread more and more meaningfully, CDSSs are improving to answer users' needs more accurately. The exploitation of previously collected data and the use of genomic data for decision support has started to materialize. However, more work is still needed to address issues related to the correct usage of such technologies, and to assess their effective impact in the long term.

Keywords

Medical informatics, International Medical Informatics Association, Yearbook, Clinical Decision Support Systems

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Introduction

Decision support in medicine has always been, and continues to be, a central theme in the biomedical domain as illustrated by the growing number of contributions published in the field every year. In the tradition of the IMIA Yearbook, the literature review performed for the Decision Support section was targeted to papers published in 2014 related to clinical decision support systems (CDSSs) and computerized provider order entry systems (CPOEs). Unlike the survey paper by Sacchi et al. [1] (contained in this Yearbook issue) where decision support literature is analyzed with a particular focus on patient-centered and personalized care, no particular focus was a priori adopted in our review. A first general observation that emerges from the review is that CDSSs, be they complex or just providing simple alerts, are still developed, implemented, and assessed in various domains and various contexts. However, four key points, or trends, in the field of decision support deserve to be mentioned as health information technologies (HIT) spread more and more:

1. The understanding of all the pitfalls that might deteriorate the potential of CDSSs and their expected benefits becomes crucial.
2. The trend, announced for years especially with the recent advent of "big data" [2], consisting in the exploitation of previously collected data for providing new decision support, seems now to materialize with applied objectives.
3. In a similar way, and also in strong relationship with big data issues, the inclusion of genomic information within routine DSS is currently considered in some real practice applications.

4. If CDSS evaluation studies demonstrate a positive impact on practices during the study, the assessment of the long-term effect of routinely used CDSSs has still to be explored.

Each of the four papers highlighted as best papers in 2014 illustrates one of these aspects. The next section presents the best paper selection process and quantitative features about the review. The last section describes more deeply the selected papers, emphasizes their contribution to the field of decision support, and reports other interesting publications spotted during the review process.

About the Paper Selection

A comprehensive literature search was performed according to the protocol that was applied the previous year [3]. The search was targeted on topics related to clinical decision support and CPOE. Queries were developed for two bibliographic databases, namely, PubMed/Medline (from NCBI, National Center for Biotechnology Information) and Web of Science® (from Thomson Reuters). However, two main modifications of last year's queries were performed. First, we excluded short papers published in conference proceedings, and kept only journal articles. Second, we also took into account the electronic publication date (at least in PubMed). The rationale for the first point relies on the fact that short papers (often less than 5 pages), though potentially interesting, would hardly provide enough details on the reported works to make them candidate best papers. The rationale for the second point is that many papers are currently first published

online, sometimes a long time before they get their print publication date. This later decision was collectively made by the Yearbook editorial committee at the end of 2014.

Databases were searched on January 12, 2015 for papers published in 2014. A total of 1,254 references were returned, 808 from PubMed, 803 from Web of Science®, 358 were common to both databases. All articles were separately reviewed by the two section editors who each assigned one of the following three statuses: kept, discarded, or pending. During the review process, articles were evaluated according to their contribution to one of the following categories of DSS research: application, methodology and design, evaluation studies or experiments including reviews, or DSS tools. Then, the two lists of references were merged, yielding 44 references that were classified as “kept” by at least one reviewer. These 44 references were then jointly reviewed by the two section editors to select a consensual list of 15 candidate best papers representative of all the above categories. Following the IMIA Yearbook best paper selection process, these 15 papers were then peer-reviewed by the Yearbook editors and external reviewers – at least four reviewers per paper. The four papers described below were finally selected as best papers (Table 1). A content summary of these selected papers can be found in the appendix of this synopsis.

Discussion and Outlook

The first paper by Goddard et al. [4] lies in the scope of unintended consequences of HIT. CDSSs are indeed expected to deliver the most appropriate personalized care recommendations for managing individual patients. Ideally, relying on CDSS advice should lead to positive outcomes. However, in some situations, and for various reasons, the CDSS advice might be incorrect, which, when followed by the user, can have serious consequences for the patient. In the paper, the authors proposed a controlled empirical framework to assess and quantify the phenomenon of “automation bias” (AB), when a user follows a DSS advice that is

Table 1 Best paper selection of articles for the IMIA Yearbook of Medical Informatics 2015 in the section ‘Decision Support’. The articles are listed in alphabetical order of the first author’s surname.

Section
Decision Support
<ul style="list-style-type: none"> ▪ Goddard K, Roudsari A, Wyatt JC. Automation bias: empirical results assessing influencing factors. <i>Int J Med Inform</i> 2014 May;83(5):368-75. ▪ Klann JG, Szolovits P, Downs SM, Schadow G. Decision support from local data: creating adaptive order menus from past clinician behavior. <i>J Biomed Inform</i> 2014 Apr;48:84-93. ▪ Miñarro-Giménez JA, Blagec K, Boyce RD, Adlassnig KP, Samwald M. An ontology-based, mobile-optimized system for pharmacogenomic decision support at the point-of-care. <i>PLoS One</i> 2014 May 2;9(5):e93769. ▪ Nachtigall I, Tafelski S, Deja M, Halle E, Grebe MC, Tamarkin A, Rothbart A, Uhrig A, Meyer E, Musial-Bright L, Wernecke KD, Spies C. Long-term effect of computer-assisted decision support for antibiotic treatment in critically ill patients: a prospective ‘before/after’ cohort study. <i>BMJ Open</i> 2014 Dec 22;4(12):e005370.

incorrect. Authors designed a simulated DSS, applied to drug prescription in general practice, for which the correctness of the advice was controlled. They built a number of validated clinical scenarios and prepared correct and incorrect recommendations according to guidelines and state of the art. In the experiment, they adopted a before/after design where a clinical case was presented to a general practitioner (GP) who had to propose a pre-advice prescription. Then, the simulated advice was presented to the GP who could modify his/her initial prescription to a new post-advice prescription. For each participant, 20 clinical cases were presented, with a reliability of the simulated decision support set to 70% – advices were randomly chosen incorrect in 6 cases. Authors measured the accuracy of pre- and post-advice prescriptions and the rate of decision switch according to four patterns: wrong-to-right, wrong-to-wrong, right-to-right, and right-to-wrong. The later pattern, or negative switch, corresponds to AB. With a panel of 26 participants, results demonstrated an improvement in prescription accuracy of 8%, from 50.4% pre-advice to 58.3% post-advice. Decision switch was observed in 22.5% of the cases, including 13.1% of positive switches (wrong-to-right) and 5.2% of AB, explaining the global improvement rate of 8%. The correctness of the advice influenced significantly the direction of prescription switches. Trust in the DSS, decision confidence, and task difficulty were the main influencing factors for decision switching. Clinical experience of GPs was negatively correlated to the number of

decision switches, but not to the overall performance (pre- or post-advice). Age of user, DSS experience, and trust in CDSS were not linked to decision switching. This empirical study demonstrated that the AB phenomenon is likely to occur when GPs would use non-100% reliable CDSSs. Authors suggested that future research focuses on delivering highly reliable CDSSs.

However, beyond the quality and the accuracy of medical content, the reliability of a CDSS also depends on the way it is actually used. For instance, Nwulu et al. [5] studied physicians’ rationale for bypassing CDSS recommendations. In their study, in the domain of venous thromboembolism prophylaxis, alert overriding was measured at 9%, and, in 20% of such cases, CDSS alerts were considered inappropriate. McCoy et al. proposed a framework to better assess alert appropriateness [6]. Moreover, errors in patient data entry are also a source of inaccurate CDSS-generated advices in various domains, e.g. diagnosis of pulmonary embolus [7], or therapeutic management of breast cancer [8]. One reason cited by Gupta et al. [7] when examining CDS integrity would be intentional erroneous input to avoid intrusive computer alerts. This illustrates how clinicians adapt their practices to their computerized working environment. Thereby, Lee et al. [9] observed a reduction in prescription errors with an alert system, and modifications of prescription-order patterns. Similarly, shifts in imaging prescribing patterns were observed by Carnevale et al. [10] after the implementation of a CDSS though no reduction of imaging rates was recorded.

The work by Klann et al. [11] described in the second best paper lies in the emerging trend of using previously collected data to tailor and adapt a CDSS. The authors used a machine learning approach for generating adaptive, context-specific, treatment menus of a CDSS. The major innovation of the approach lies in the data that has been used for this purpose, i.e. local order entry data, and in the quite extensive evaluation that has been performed to account for different clinical settings (emergency care, intensive care, etc.). The goal was to complement the development of the CDS content with knowledge distilled in Electronic Medical Record data, in order to provide contextualized (i.e. both patient and situation-specific) treatment advices. This would lead to workload reduction in the development of a localized CDSS and, as a secondary effect, should facilitate the analysis of local practice patterns. The study provided interesting findings and demonstrated an overall good system performance, but a high variability on individual orders, both across and within considered settings, was observed. Notably, some orders were displayed within the menus exactly where they should be, while others appeared at the bottom of long menus. In addition, quite common (short item) orders were ranked higher at the time they were ordered than prior to ordering. Despite the assumption that average patterns in the data may represent reasonably good care for future patients, and represent as such “crowd wisdom”, as well as the limitation of the modeling used which did not account for important factors such as test outcomes and physiologic changes, this study provided a relevant framework for the construction of clinical knowledge-abstraction systems. Interestingly, the principle of using local data has also been chosen by Rodriguez-Maresca et al. [12] to improve the appropriateness of antibiotic therapy.

The third best paper is authored by Miñarro-Giménez et al. [13]. It is a remarkable work first because it is an attempt to actually take into account pharmacogenomics data for clinical decision support and personalized medicine at large, and second because it implements an innovative combination of latest information technologies. While the perspective of adopting pharmacogenomics

information for decision support has been elaborated by other researchers as well [14], the so-called Medicine Safety Code (MSC) considers important practical aspects in order to make this idea a solid potential. In particular, MSC proposes a solution to represent and interpret pharmacogenomics data through semantic technologies, in order to offer therapeutic guidance and predict drug response. MSC enables patients to carry their pharmacogenomics data at the point-of-care in a convenient and unobtrusive way by encoding the relevant information into an anonymous QR (Quick Response) code. QR codes can be easily decoded by current smartphones (via a barcode reader application) to yield tailored recommendations of pharmacotherapy based on an individual's genetic profile. In the MSC prototype implementation, decision support rules were obtained from drug label approvals, and clinical guidelines by pharmacogenomics working groups/consortia. Besides, the study illustrated the development of an open infrastructure for pharmacogenomics data sharing and decision support. Notably, this development is available as open source, and proposes a new paradigm for pursuing personalized medicine in practice.

Most evaluation studies of CDSS impact, whatever the study design, rely on a comparison of indicators in two groups, one using the CDSS for its assessment, and a second without CDSS use (intervention studies). However, beyond the duration of the study, the long-term effect of implementing CDSSs is often not evaluated. In the fourth best paper, Nachtigall et al. [15] assessed the effect in the long term of a guideline-based CDSS applied to the prescription of antibiotics for critically ill patients. Quality of care was measured by means of guideline adherence in five intensive care units (ICUs) of a same University Hospital, before the CDSS was implemented, and at 3 time points after: directly after the CDSS introduction, 2, and 3 years after, respectively. The study adopted a before/after interventional design within a 5-year time span. Outcome measurements were the percentage of days with antibiotic guideline adherence, the number of antibiotic-free days, and all-cause mortality. About 13,000 ICU days, corresponding to 1,316 patients, were analyzed. Results showed that

antibiotic guideline adherence measured at 61% in the pre-intervention period increased to 92% after the intervention, then decreased to 76% two years later, and stabilized at 71% three years after. The difference between the pre-intervention rate and the 3-year post-intervention rate is still significant. Noticeably, the number of antibiotic-free days increased with time, and high guideline adherence was associated with reduced mortality. Authors concluded that the CDSS maintained a positive effect in the long term. Authors mentioned limitations of their work, hampering the generalization of their findings. In particular, such results were obtained in an intent-to-treat analysis, which is positive since it corresponds to real-life situations, but clues about actual CDSS usage would have added insightful information on the role of the CDSS. Nevertheless, this work contributes to a better knowledge of CDSS impact during long periods of time. In the future, measuring and reporting on the effect of CDSSs in the long term should be encouraged. In a similar way, McCullough et al. [16] analyzed a US National Survey Database of a representative sample of clinicians on a 5-year period to identify the effect of using a CDSS on antibiotic prescription for acute bronchitis and upper respiratory tract infection. Their results show that CDSS users constantly prescribe less antibiotics than non-users, but that nonetheless a secular increasing trend is observed for both user categories.

Among the 1,254 reviewed papers for the Decision Support section in the 2015 edition of the IMIA Yearbook, several contributions brought to light some interesting results and developments and deserve to be cited in this synopsis. From a design and development perspective, Bellos et al. [17] presented an intelligent system for the analysis and the real-time evaluation of chronic obstructive pulmonary disease (COPD) episodes. The system relies on a hybrid classifier combining a support vector machine, a random forest, and a rule-based component to provide categorization scheme for early and real-time characterization of identified episodes. Based on a severity estimation algorithm, the system triggers alerts to guide/inform patients/supervisors, respectively. Being part of the CHRONIOUS wearable integrated platform, the system achieved a

classification accuracy of 94%. Eccher et al. [18] presented an Asbru-based DSS for the adjuvant treatment of breast cancer. The system executes breast cancer protocols by accessing data from an oncological electronic health record (EHR). With a special focus on decision support for adjuvant pharmaceutical treatment of patients in an early stage of invasive breast cancer, the system is evaluated based on the comparison of the system's recommendations and decisions issued by the multidisciplinary panel held weekly in the hospital. Brodin et al. [19] focused also on cancer (Hodgkin lymphoma) and presented an interactive tool allowing for quantitative estimation and visualization of the risk of various relevant normal tissue endpoints to support the comparison of treatment plans and clinical decision making in radiation therapy planning. To this end, the tool displays dose-response relationships published in the literature for a number of relevant side effects directly visualizing the trade-off between endpoints, supplementing this way the clinical judgment of radiation oncologists when comparing different radiation therapy options. Simpao et al. [20] explored the power of visual analytics to optimize drug-drug interaction alert rules in a pediatric hospital's EHR system. Bell et al. [14] presented an approach for active clinical decision via preemptive pharmacogenomics. In particular, decision support was delivered through an EHR that aims at facilitating gene-based drug prescription as well as other applications of genomics to patient care. Anani et al. [21] worked on the assessment of compliance with practice guidelines for acute stroke care. The study uses the openEHR's Guideline Definition Language (GDL) as a mean to address the lack of commonly shared EHR models and terminology bindings, hampering CDS content sharing among different organizations. The study concluded with the successful representation of 14 out of 19 clinical rules on contraindications for thrombolysis and other aspects of acute stroke care by employing 80 GDL rules, and a complete match between manual and automated compliance results. In terms of applied systems, a number of studies focused on quite complex clinical conditions, such as the early recognition of sepsis [22-24], the prediction of periventricular

leukomalacia in neonates after heart surgery [25], the detection of cervical intraepithelial neoplasia [26], and even the support for transcatheter aortic valve implantation [27].

In conclusion, as HIT spread more and more meaningfully and inevitably, CDSSs are being developed, aligned with users' needs. The literature analysis attested that announced developments, like the exploitation of previously collected data and the use of genomic data for decision support, have started to materialize. However, research on applied DSS should continue to address issues related to the correct usage of such technologies and to help assess their effective impact in the long term.

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Appendix: Content Summaries of Selected Best Papers for the 2015 IMIA Yearbook, Section Decision Support

Goddard K, Roudsari A, Wyatt JC

Automation bias: empirical results assessing influencing factors

Int J Med Inform 2014 May;83(5):368-75

Automation bias (AB) is defined as the propensity of people to over-rely on automated advice. In the healthcare domain, this effect could lead to inaccurate decisions when the generated advice is not 100% correct and, therefore, to potentially serious consequences for patients. This issue is of great concern for CDSSs which main objective is to improve

medical practices and health care. The authors present an empirical experimental framework for quantifying AB and investigating influencing factors in the context of drug prescription by general practitioners (GPs). The experiment material is made of 20 simulated patient cases requiring a prescription, for which both correct and incorrect advices have been prepared. The study adopts a before/after design. Each case is presented to a GP, who has first to prescribe without any decision support, then receives an advice as decision support, and prescribes again, changing or not his/her initial prescription. On the 20 presented cases, incorrect advice was delivered for 6 patient cases. The authors measured GPs' prescription accuracy pre- and post-advice, and the switches in prescriptions according to four patterns: wrong-to-right, wrong-to-wrong, right-to-right, and right-to-wrong. The later pattern, or negative switching, corresponds to AB. Factors considered to influence AB were: task difficulty, task experience, CDSS familiarity, decision confidence, and trust in CDSSs.

Prescriptions accuracy increased after the provision of decision support by 8%, from 50.4% pre-advice to 58.3% post-advice. However, decision switching was observed in 22.5% of the cases, including 13.1% of positive switches and 5.2% of AB. The correctness of the given advice influenced significantly the direction of prescription switches. Among other factors, trust in the specific DSS, decision confidence, and task difficulty influenced the rate of decision switching. GPs' seniority was negatively correlated to the number of decision switches, but not to the overall performance (pre- or post-advice). Age, DSS experience, and trust in CDSS were not associated with decision switching. In controlled, simulated situations, this empirical study demonstrates that AB is likely to occur when GPs would use non-100% reliable CDSSs. Authors also suggest that influencing factors should be taken into account when implementing CDSSs in routine use. Future research should focus on delivering highly reliable CDSSs.

Klann JG, Szolovits P, Downs SM, Schadow G
Decision support from local data: creating adaptive order menus from past clinician behavior

J Biomed Inform 2014 Apr;48:84-93

Driven by the potential of the “wisdom of the crowd” in the development of CDSSs, Klann et al. presented a Bayesian Network (BN) learning approach for generating adaptive, context-specific, treatment menus based on local order-entry data. Given that computable clinical decision support content (as a mean to reduce care variability) is expensive and time-consuming to create, maintain, and contextualize, the study relies on the exploitation of local data to generate such content. In essence, the goal was to complement content development with the knowledge distilled in Electronic Medical Record data, but also to propose a methodology to produce adaptive, patient-tailored, and situation-specific treatment advices from order-entry data. This approach could be applicable for workload reduction in developing localized CDS, or as a method to quickly analyze local practice patterns. More specifically, the Greedy Equivalence Search algorithm was used to learn four 50-node domain-specific BNs, according to the typical successions of orders made by clinicians in various situations. Induced BNs represent the probabilistic relationships among orders and diagnoses, which were in turn used to build a recommendation system capable of suggesting the most common next orders based on what had been ordered and diagnosed previously. The authors instantiated the variables corresponding to specific order actions in the BN, and revised the probabilities for other orders in the BN to the posterior probability that they would be placed conditioned on the previous actions. This allowed for ranking remaining orders according to their probability of occurrence to suggest treatment, without presenting the diagnoses on the order menus (an action left to the clinician). In terms of evaluation, four settings were considered to illustrate the different aspects of medicine, namely, inpatients, emergency department, urgent visit clinic, and intensive care unit. In addition, the system was compared with an ARM (association rule mining) method. The obtained results showed a quite strong overall performance. In particular, treatment suggestion menus correctly suggested common orders in a short list (between 3.91-5.83 order items) as well as high average AUC (Area Under the Receiver-Operator Curve) value (74-84%),

indicating that common orders were ranked higher at the time they were ordered than prior to ordering. However, there was a high variability in the performance of the approach on individual orders (AUC 0.5–0.99), both across and within the considered domains. The ARM method was not able to detect less common associations, while the proposed BN-based approach appeared more efficient. Overall, this study illustrated a significant development towards adaptive clinical knowledge-based systems.

Miñarro-Giménez JA, Blagec K, Boyce RD, Adlassnig KP, Samwald M

An ontology-based, mobile-optimized system for pharmacogenomic decision support at the point-of-care

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Despite the potential of personalized medicine to adapt healthcare to individual patients, the rather limited training of clinicians in personalized medicine hampers its inclusion in actual clinical settings. Miñarro-Giménez et al. proposed to introduce pharmacogenomics data in clinical practice through a decision support system, the “Medicine Safety Code” (MSC). The objective of MSC is to provide a way to represent pharmacogenomics data in a computable form to offer guidance at the point-of-care. In this respect, the requirements that MSC aimed to address involved parsing genetic data to identify relevant genetic variations, representing pharmacogenomics knowledge in a formal way, and facilitating access to the inferred genetic markers and drug dosage recommendations. At the same time, MSC should conform to security and privacy issues and demonstrate the necessary efficiency to be deployed in routine clinical practice. The development of MSC was based on formal ontologies, semantic technologies, and automated reasoning. The idea was that a reduction of the large and complex data yielded by genotyping into more manageable, higher-level characteristics such as alleles, haplotypes, phenotypes, or other

classifications could facilitate drug response prediction. An interesting development practice adopted in MSC was the encoding of a patient’s genetic profile into an anonymous QR (Quick Response) code. QR codes are a 2D standard barcode representation, quite popular in mobile computing applications. This feature enables patients to carry their pharmacogenomics data at the point-of-care, in a convenient and unobtrusive way. On the other hand, MSC is capable of analyzing the genotype profile from the QR code to provide decision support messages based on the patient’s genotype. This functionality was based on a reasoner, which inferred matching clinical decision support recommendations by using an ontology that contained basic genetic markers as well as inferred treatment recommendations. The ontology was populated with data for 58 genes and 385 polymorphisms, while decision support rules were built from drug label approvals, and clinical guidelines by pharmacogenomics working groups/consortia. The study illustrated the development of an open infrastructure for pharmacogenomics data sharing and decision support with very limited dedicated infrastructure. Authors mention some limitations of their work, like the current unavailability of pharmacogenomics testing for most patients, the data capacity of QR codes, as well as important challenges that need to be addressed, such as the synthesis of pharmacogenomics findings with other patient parameters, and (to some extent) performance issues. Despite these limitations, MSC can be seen as a paradigm to develop personalized medicine in practice.

Nachtigall I, Tafelski S, Deja M, Halle E, Grebe MC, Tamarkin A, Rothbart A, Uhrig A, Meyer E, Musial-Bright L, Wernecke KD, Spies C

Long-term effect of computer-assisted decision support for antibiotic treatment in critically ill patients: a prospective ‘before/after’ cohort study

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The adequate management of antibiotics is of primary importance in medicine with implications on morbidity and mortality, healthcare costs, and future pathogen resistance. Guideline-based CDSSs are considered effective tools to support the implementation of best antimicrobial treatment strategies, but their long-term effect is not yet known. This study aimed at evaluating such effect in the framework of a prospective before/after design within a 5-year period. The intervention consisted in the implementation for routine use of a CDSS based on local guidelines that advises on antibiotic therapy in intensive care units (ICUs). The study included 1,316 patients, corresponding to nearly 13,000 ICU days, in 5 ICUs of one University Hospital. The outcome measures were the percentage of days with guideline adherence, number of antibiotic-free days, and all-cause mortality. Guideline adherence was considered high, when greater than 70%. Measures were performed in the pre-interventional period (pre), immediately after intervention (post1), 2 years after (post2), and 3 years after (post3). Results showed that overall guideline adherence increased from 61% in the pre-interventional period to 92% directly after CDSS implementation (post1), decreased to 76% two years later (post2), and then stabilized three years after to 71% (post3). The 10% difference between the pre and post3 periods was still significant, illustrating a remaining long-term effect of the CDSS. The number of antibiotic-free days significantly increased during the study timespan. Whatever the period, high guideline adherence was statistically associated with reduced mortality. The authors discussed the limitations of the study (especially concerning the design) but argued that, for assessing interventions in routine use, implementing more powerful study designs is hardly feasible. One key point of the study is that guideline adherence was measured at several times after CDSS implementation, until three years, and not only just after as it is often the case in most studies.