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Evaluation of a machine learning capability for a clinical decision support system to enhance antimicrobial stewardship programs

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ABSTRACT

Objective: Antimicrobial stewardship programs have been shown to limit the inappropriate use of antimicrobials. Hospitals are increasingly relying on clinical decision support systems to assist in the demanding prescription reviewing process. In previous work, we have reported on an emerging clinical decision support system for antimicrobial stewardship that can learn new rules supervised by user feedback. In this paper, we report on the evaluation of this system.
Methods: The evaluated system uses a knowledge base coupled with a supervised learning module that extracts classification rules for inappropriate antimicrobial prescriptions using past recommendations for dose and dosing frequency adjustments, discontinuation of therapy, early switch from intravenous to oral therapy, and redundant antimicrobial spectrum. Over five weeks, the learning module was deployed alongside the baseline system to prospectively evaluate its ability to discover rules that complement the existing knowledge base for identifying inappropriate prescriptions of piperacillin–tazobactam, a frequently used antimicrobial.
Results: The antimicrobial stewardship pharmacists reviewed 374 prescriptions, of which 209 (56% of 374) were identified as inappropriate leading to 43 recommendations to optimize prescriptions. The baseline system combined with the learning module triggered alerts in 270 prescriptions with a positive predictive value of identifying inappropriate prescriptions of 74%. Of these, 240 reviewed prescriptions were identified by the alerts of the baseline system with a positive predictive value of 82% and 105 reviewed prescriptions were identified by the alerts of the learning module with a positive predictive value of 62%. The combined system triggered alerts for all 43 recommendations, resulting in a rate of actionable alerts of 16% (43 recommendations of 270 reviewed alerts); the baseline system triggered alerts for 38 interventions, resulting in a rate of actionable alerts of 16% (38 of 240 reviewed alerts); and the learning module triggered alerts for 17 interventions, resulting in a rate of actionable alerts of 16% (17 of 105 reviewed alerts). The learning module triggered alerts for every inappropriate prescription missed by the knowledge base of the baseline system ($n = 5$).
Conclusions: The learning module was able to extract clinically relevant rules for multiple types of antimicrobial alerts. The learned rules were shown to extend the knowledge base of the baseline system by identifying pharmacist interventions that were missed by the baseline system. The learned rules identified inappropriate prescribing practices that were not supported by local experts and were missing from its knowledge base. However, combining the baseline system and the learning module increased the number of false positives.

1. Introduction

Inappropriate prescribing of antimicrobials is a major clinical problem as well as a financial burden in hospitals. It has been reported that as many as 50% of antimicrobial prescriptions are unnecessary, suboptimal or inappropriate [1,2]. The challenges of antimicrobial prescribing lie in selecting the right antimicrobial therapy for the suspected pathogen and adjusting the

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concentrations and dosing frequency of the antimicrobial agent with an appropriate route of administration to ensure that effective levels of medication reach the site of the infection. A "one size fits all" approach is not appropriate in antimicrobial selection [3] as several host factors must be taken into account in addition to the pathogenic agent, its location and susceptibility.

Inappropriate prescribing can range from selecting an antimicrobial while another significantly less expensive but equally effective and safe alternative is available, to selecting an antimicrobial to which the causative pathogen is resistant, making the treatment ineffective and endangering the life of the patient [4]. Moreover, a selected antimicrobial therapy will be valid over a finite period of time; after selecting an initial empirical treatment, the physician must review his earlier prescription to account for newly available information [3].

Antimicrobial stewardship has been shown to improve quality of care and patient health, and to reduce unnecessary costs, by reducing inappropriate antimicrobial use [1,5–8]. A core strategy of antimicrobial stewardship is prospective audit of antimicrobial use and feedback to the prescribing physician. However, this process is labor and time intensive when performed manually [5] as it requires the review of an overwhelming amount of clinical data, which proves to be an obstacle in the current context of limited health care resources. Therefore, hospitals are increasingly relying on clinical decision support systems to assist their antimicrobial management team in analyzing relevant data and identifying patients that require reviewing [5,8–11].

Many of these clinical decision support systems for antimicrobial stewardship use knowledge bases of rules derived from published guidelines and expert opinions to detect potentially inappropriate prescriptions and generate patient-specific recommendations. However, the development and maintenance of knowledge bases for these systems is a challenging and costly process [10,12]. It is difficult to model all variables that a prescribing physician will take into account, let alone model the decision-making process. Antimicrobial prescribing is a subjective process where physicians continually rely on their experience and clinical judgment to select an effective treatment and prevent adverse events. In addition to published guidelines, hospitals have their own local therapeutic practices [13], including practices based on local incidence of pathogens and antimicrobial susceptibility profiles. These local guidelines must be taken into account when customizing a system to a new location [14].

In previous work, we presented the antimicrobial prescription surveillance system (APSS), a clinical decision support system that assists antimicrobial stewardship pharmacists in identifying and reporting potentially inappropriate prescriptions [15]. We introduced an emerging machine learning capability to enable APSS to learn new rules for identifying inappropriate prescriptions supervised by user feedback. It uses a rule induction algorithm to discover classification rules that identify temporal episode sequences that belong to the inappropriate class [15,16]. The ultimate goal of this learning capability is to allow APSS to self-reconfigure to local practices after deployment and to self-improve its knowledge base over the long term. However, this automated learning capability has not been evaluated so far in a clinical setting. In this study, we fill this gap.

Over five weeks, the learning module was deployed alongside the baseline system to prospectively evaluate its performance of the identification of inappropriate piperacillin–tazobactam prescriptions. We evaluated the clinical relevance of the learned rules and measured the precision, accuracy, and rate of actionable alerts (reviewed alerts for which a recommendation was issued) of these systems. The learning module is expected to discover practical rules whose alerts extend those of the existing knowledge base and lead to interventions.

2. Study context

The study was performed at the Centre hospitalier universitaire de Sherbrooke (CHUS), a 677-bed Canadian secondary – and tertiary – care hospital located at two distinct sites. The APSS, the baseline system, has been deployed at the CHUS since 2010 where it assists hospital pharmacists and infectious diseases specialists in their antimicrobial stewardship activities. The system receives clinical data from the electronic health-record system of the CHUS: QuadraMed's computerized-patient record (QCPR) [17]. The APSS collects relevant demographic, clinical, pharmacy, and laboratory data from QCPR and verifies that ongoing antimicrobial therapies remain appropriate according to contraindications conveyed by rules in its knowledge base. It is used to monitor all adult patients admitted at the CHUS who receive antimicrobials.

During this study, we evaluated the combined system presented in [15] consisting of the baseline system APSS, which uses a traditional knowledge base implemented by experts, coupled to a supervised learning module, which extracts classification rules for alerts of inappropriate prescriptions using past recommendations for dose and dosing frequency adjustments, discontinuation of therapy, early switch from intravenous to oral therapy, and spectrum redundancy.

2.1. Supervised learning module

The supervised learning module of APSS uses the learning approach described in [15,16] based on a two-step process. In the first step, it uses temporal abstraction [18] to extract a high-level description of the patient history in the form of sequences of symbolic episodes over time intervals. In the second step, it discovers rules from a labeled set of episode sequences. We approach this problem as a binary classification task, where sequences are labeled *appropriate* and *inappropriate*, and use the temporal induction of classification models (TIM) algorithm to discover rules for inappropriate sequences. The supervised learning module then uses rule matching to classify unseen prescriptions and identify potentially inappropriate sequences.

2.1.1. Temporal abstraction

This process involves extracting a uniform and meaningful data representation from the raw clinical data of APSS. This data contains qualitative and quantitative attributes sampled with both time points (e.g., temperature) and time intervals (e.g., drug order). Quantitative thresholds are used to identify qualitative states that hold over a period of time, which we call episodes. It extracts a single sequence for each hospitalization. Within a hospitalization, the observation period is restricted to the ongoing antimicrobial of interest. It considers only data between the first (t_{min}) and last (t_{max}) administered dose. This in turn ensures a common time zero (t_{min}) between sequences. It used a temporal granularity of 1 h.

We included the following attributes that are pertinent for evaluating the appropriateness of antimicrobial prescriptions: age, absolute neutrophil count (ANC) and white blood cell count (WBC) as indicators of immune system status, body mass index, blood pressure category according to systolic and diastolic pressures and cardiac frequency, prediction of creatinine clearance using the Cockcroft–Gault equation [19] as an indicator of renal function, gender, respiratory rate, temperature, and patient location.

The temporal abstraction process also extracts episodes for medications that were administered during the hospitalization, including non-monitored medications. Prescriptions are described using their medication name and the three following attributes: dose, frequency, and route of administration. For example, a prescription of oral (PO) ciprofloxacin "750 mg q12h" would be described as: "ciprofloxacin route = PO", "ciprofloxacin dose = 750"