Development of an Arden Syntax Clinical Foundation Framework for Event Monitoring in Intensive Care Units

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Abstract

The creation of clinical decision support systems has received a strong impulse over the last years, but their integration into clinical routine has lagged behind, partly due to lack of interoperability and also lack of trust by physicians. We report on the implementation of a clinical foundation framework in Arden Syntax, comprising knowledge units for (a) preprocessing raw clinical data, (b) the determination of single clinical concepts; and further (c) more complex medical knowledge can be modeled through the composition and configuration of knowledge units in this framework. It can thus be tailored to clinical institutions or patient caregivers. In this version, we integrated knowledge units for several infection-related clinical concepts in the framework, and developed a clinical event monitoring system on top of the framework that employs three different scenarios for monitoring clinical signs of blood stream infection. The clinical event monitoring system was tested using data from intensive care units at Vienna General Hospital, Austria.

Keywords:
Decision Support Systems, Clinical; Knowledge Bases; Infection Control.

Introduction

Recognition of the benefits and potentialities of information and communication technology in healthcare (eHealth) [1-3] led to the political support of healthcare digitization, providing financial incentives to healthcare institutions to adopt and make “meaningful use” of electronic health records (EHRs) [4]. Although the definition of meaningful use is quite broad, it includes the development and use of clinical decision support systems (CDSSs). CDSSs are eHealth systems designed to assist health professionals in clinical decision-making tasks at the point of care.

Clinical event monitors are CDSSs specialized in information delivery; a clinical event monitor delivers information to healthcare providers where and when they need it [5]. In general, a clinical event monitor performs one or more of the following tasks [5]: (a) it warns about adverse events such as potentially harmful drug-drug interactions or treatment complications, (b) it interprets medical findings, such as laboratory test results, (c) it provides reminders for immediate or future diagnostic or therapeutic steps, (d) it proposes (alternative) diagnoses or treatment options, and (e) it coordinates complex clinical protocols or workflows.

A substantial number of clinical event monitoring systems have effectively addressed one or many of the aforementioned tasks for a variety of healthcare settings. In the field of infection control there have been many studies on (semi-) automated systems for the detection and monitoring of healthcare-associated infections [6-8]. Similarly, computerized adverse drug event detection and computerized physician order entry have also been widely researched [9, 10]. The performance of the large majority of systems has been good or excellent. The systems, when measured, proved to be an improvement over traditional or manual methods.

Despite the success of these systems, their use and integration have been limited to their local development setting. This is a multifactorial problem. In the present report, we focus on technical and psychological aspects. From a technical point of view, most systems were developed for a specific hospital information system and specific EHRs. Furthermore, they might not always be implemented with established communication standards. As a result, the systems lack interoperability, and the effort of porting or recreating the systems outweigh their potential benefits. From a psychological point of view, many systems have only been internally verified, i.e., tested on data from a single healthcare institution. Without external validation, the generalizability of the results is unproven. Moreover, even if a system is externally verified, acceptance by third parties is not guaranteed because the adoption of the system might be perceived as a loss of autonomy [11]; this is especially true of illnesses and adverse events that are not yet fully understood, or for which there is no consensus on their definition or method of detection.

From the discussion above, it follows that the acceptance and dissemination of the system could be improved by providing an interoperable, configurable system. Such a system would use established standards for communication and knowledge representation, thus improving interoperability. A widely known standard for computerized knowledge representation and processing is Arden Syntax [12]. The latter is a programming language for the collection, description, and
exchange of medical knowledge in a machine-executable format. Indeed, many of the tasks performed by clinical monitoring systems have already been modeled in Arden Syntax [13-16]. To improve its acceptance among clinicians, a knowledge base would have to be configurable to fit the user’s clinical knowledge and experience.

In our view, clinical event monitors are systems that can be composed from standardized configurable building blocks. As such, a limited set of standardized medical knowledge units, the clinical foundation framework, should be available. Based on these, event systems can be constructed and configured to the wishes of clinical institutions or patient caregivers. These basic blocks of knowledge would be used for preprocessing raw clinical data and determining less complex, clearly defined clinical concepts that are directly measured from objective data and laboratory results. Based on this clinical foundation framework, more complex medical knowledge can then be modeled through the composition and configuration of these basic knowledge blocks.

In the present study, we report results following the implementation of a clinical foundation framework. We created a clinical event monitoring system that monitors several infection-related clinical concepts based on definitions from internationally respected institutions, such as Centers for Disease Control and Prevention (CDC), Atlanta, USA, and the European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden. For each of these concepts, we constructed rules in Arden Syntax and integrated them into the clinical foundation framework. Based on data from the intensive care units (ICUs) of the Vienna General Hospital (VGH), Austria, we show that, using knowledge units in the clinical foundation framework, more complex medical knowledge can then be modeled through the composition and configuration of these basic knowledge blocks.

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Methods

Clinical background

We discuss six infection-related clinical concepts included in the clinical foundation framework. These clinical concepts are well-known signs of infection, and are used in existing surveillance definitions for infections from the CDC and ECDC. These concepts are fever, leukopenia, leukocytosis, elevated C-reactive protein (CRP), shock, and drop in blood pressure. The definitions for fever, leukopenia and leukocytosis were taken from the “ECDC European surveillance of healthcare-associated infections for intensive care units" protocol, version 1.02 [17]. The definition of elevated CRP was obtained from the CDC National Healthcare Safety Network surveillance definitions for specific types of infections [18].

Definitions of the remaining concepts were constructed by clinical experts. The respective definitions are listed in Table 1.

Study design, setting, and participants

We conducted a single-center retrospective cohort study on prospectively collected and validated data. The study was performed at the Vienna General Hospital (VGH), Austria, a 1,933-bed tertiary-care and teaching hospital. Data were collected from patients admitted between 1 January and 31 March 2013 in one or more of VGH’s ICUs. All adult patients (age ≥ 18 years) admitted for at least 24 hours were eligible for the study.

### Table 1 – Definitions for clinical concepts modeled in the clinical foundation framework.

<table>
<thead>
<tr>
<th>Clinical concept</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Body temperature &gt; 38 °C</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>&lt;4,000 WBC/mm³ blood</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>≥ 12,000 WBC/mm³ blood</td>
</tr>
<tr>
<td>Elevated CRP</td>
<td>CRP &gt;10 mg/dl blood</td>
</tr>
<tr>
<td>Shock</td>
<td>Systolic blood pressure &lt;1</td>
</tr>
<tr>
<td>Drop in BP</td>
<td>BP value in the 37.5% percentile of all averages between systolic and diastolic BP over the last 3 days</td>
</tr>
</tbody>
</table>

Note: WBC, white blood cell; CRP, C-reactive protein; BP, blood pressure.

Data management and sample size

Demographic patient data as well as clinical and laboratory values were obtained through systematic interrogation of the Philips IntelliSpace Critical Care and Anesthesia (ICCA) information system, which is in operation at ICUs in the VGH. Interrogation of the data sources using the selection criteria mentioned earlier yielded a total of 984 patient stays.

Knowledge base and data processing

For this project, we reimplemented a part of the knowledge base of Moni (Monitoring of Nosocomial Infections), a fully automated knowledge-based surveillance tool for the identification, monitoring, and reporting of nosocomial (hospital-acquired) infections in ICUs [19].

We used Arden Syntax to implement rules for the clinical infection-related concepts listed in Table 1, as well as rules for data preprocessing and feature extraction. Arden Syntax is a programming language used for representing, processing, and sharing medical knowledge, employed in an executable format by CDSSs to generate alerts, reminders, interpretations, as well as manage messages to clinicians [20]. In an Arden Syntax knowledge base, medical knowledge is divided into medical logic modules (MLMs) [13]; each MLM contains instructions and logic to support at least a single medical decision.

In the clinical foundation framework, MLMs perform one of three types of processing tasks:

- Raw data processing, which deals with importing and processing of raw data directly from the structured data source, here the Philips ICCA system.
- Data-to-symbol conversion, which deals with data preprocessing (such as handling of missing or contradictory values), and feature extraction (such as calculating mean values or intermediate scores).
- Symbol calculation, which deals with the calculation of basic clinical concepts (e.g., medical symptoms and signs).

In all, 17 MLMs were created; seven for raw data import and processing, four for preprocessing and feature extraction, and six for symbol calculation. Table 2 lists these MLMs with a brief description of their task(s).

We used the ARDENSUITE integrated development and test environment (IDE) for the implementation, management, and testing of MLMs in the clinical foundation framework. For the execution of MLMs, we used the ARDENSUITE server [21],
The youngest was 18 years old, the oldest 92 years.

Results

DropInBP
Shock
CRPElev
Leukocytosis
Leukopenia
TempElev
Symbol calculation
BPProfile
CRPMax
LeukoMax
TempMax
Data-to-symbol conversion
HeartRate
DiastBP
SystBP
HeartRate
DiastBP
SystBP
CRP
Leuko
ThermoReg
Data
HeartRate
DiastBP
SystBP
CRP
Leuko
ThermoReg
Temp
HeartRate
DiastBP
SystBP
CRP
Leuko
ThermoReg
Temp

Task description
Imports body temperatures in °C over the last 24 hours
Imports explicit indications of thermoregulation in the last 24 hours, which is performed to cool the patient
Imports leukocyte concentrations in G/l
Imports CRP values in mg/dl
Imports systolic blood pressure measurements over the last 24 hours
Imports diastolic blood pressure measurements over the last 24 hours
Imports heart rate measurements over the last 24 hours
Imports the daily maximum body temperature in °C
Imports the daily maximum leukocyte concentration in G/l
Imports the daily maximum CRP in mg/dl
Imports the blood pressure profile with data over the last 6 hours

Note: MLM, medical logic module; CRP, C-reactive protein; BP, blood pressure.

We developed three scenarios, which we model with the clinical foundation framework:

1. ClinSignsV1: A straightforward definition of the concept “clinical signs of bloodstream infection” as defined by the ECDC in [17], involving only the clinical concepts elevated body temperature, leukopenia, and leukocytosis.

2. ClinSignsV2: A more complex definition that uses a more comprehensive modeling of the clinical concept fever. In this case, the presence of fever is not only derived from the patient’s body temperature, but also from clinical interventions that indirectly indicate the presence of fever, here the use of cooling packs or blankets (cf., ThermoReg in Table 2).

3. ClinSignsV3: A definition that extends the ClinSignsV2 definition by involving known markers of infection such as elevated CRP and hypotension. In this scenario, hypotension is modeled with the clinical concepts shock and drop in blood pressure.

Table 3 shows the logical definitions of the clinical concepts used in each scenario. A graphical depiction of the knowledge base for these clinical concepts (including the clinical foundation framework) is shown in Figure 1. Finally, Table 4 presents the respective logical rules.

<table>
<thead>
<tr>
<th>MLM name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario 1</td>
<td>ClinSignsV1</td>
</tr>
<tr>
<td>Scenario 2</td>
<td>Fever</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>ClinSignsV3</td>
</tr>
</tbody>
</table>

Note: MLM, medical logic module; BP, blood pressure; CRP, C-reactive protein.

Table 4 – Symbolic calculation and the resulting number of symptom and scenario events.

<table>
<thead>
<tr>
<th>MLM name</th>
<th>#Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical foundation framework</td>
<td>1,394</td>
</tr>
<tr>
<td>TempElev</td>
<td>4,527</td>
</tr>
<tr>
<td>ThermoReg</td>
<td>270</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>2,214</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>3,606</td>
</tr>
<tr>
<td>CRPElev</td>
<td>2,968</td>
</tr>
<tr>
<td>Shock</td>
<td>3,217</td>
</tr>
<tr>
<td>DropInBP</td>
<td>3,268</td>
</tr>
<tr>
<td>Scenario 1</td>
<td></td>
</tr>
<tr>
<td>ClinSignsV1</td>
<td>5,154</td>
</tr>
<tr>
<td>Scenario 2</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>5,760</td>
</tr>
<tr>
<td>ClinSignsV2</td>
<td></td>
</tr>
<tr>
<td>Scenario 3</td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>6,835</td>
</tr>
<tr>
<td>ClinSignsV3</td>
<td></td>
</tr>
</tbody>
</table>

Note: MLM, medical logic module; BP, blood pressure; CRP, C-reactive protein.

To be executed through service-oriented access for client applications.

Presentation of results

We show how different versions of a system for the detection of clinical signs of infection can be constructed and configured, using basic building blocks from the clinical foundation framework. Moreover, we show how different setups lead to different detection results using the study data collected from the ICUs at VGH.

Results

Of the 984 patients included in this study, 417 were female (42.4%). The youngest was 18 years old, the oldest 92 years; the median age was 61 years, with an interquartile range (IQR) of 24 years. In all, 7,573 patient days were recorded in the study period. The length of the hospital stay ranged between two and 93 days, median 4 days and an IQR of 6 days.
shows the number of events that were registered for relevant clinical concepts and infection symptoms in the clinical foundation framework, and for the clinical concepts in the three scenarios mentioned earlier.

**Discussion**

We presented the implementation of a clinical foundation framework in Arden Syntax. The calculation of standardized lower-level clinical concepts directly related to raw clinical data is pre-implemented in a framework of this nature. Consequently, the calculation of more complex, semantically richer concepts can be done by combining elements from the framework with custom implementations. This permits easier and more rapid construction of CDSSs.

The scenarios presented in the Results section all yielded different results. Using the clinical foundation framework, we were able to create different versions of the same clinical concept. This may be useful when the system needs to be implemented for different goals or different stages of the problem. For example, ClinSignsV1 would be more suited for prospective clinical alerting due to its relatively low number of occurrences, while the more complex ClinSignsV2 would be more suited for retrospective detection of healthcare-associated infections. Scenario ClinSignsV3 inspects a wider range of infection criteria and is therefore more suited for screening purposes, such as screening patients for potential infections at the time of admission to the hospital.

The limitations of the study are worthy of mention. First, as the clinical foundation framework is still in its pilot phase, not many MLMs have been implemented so far. Second, we still need to reimplement the systems integrated at VGH in order to test the framework in clinical routine. Finally, new systems need to be created and composed in order to assess the ease of construction and improve framework performance and interfaces.

Several CDSSs have been implemented with Arden Syntax and integrated into clinical routine at VGH, in a variety of clinical specialties, such as nephrology, oncology, and infection control [22]. Inspection of these systems revealed that most of the MLMs in these CDSSs have processing duties performed by the clinical foundation framework, such as raw data processing, data-to-symbol conversion, or symbol calculation. As such, implementation and configuration of these and similar systems could be simplified by the clinical foundation framework. Furthermore, as the clinical foundation framework grows, extension of these systems and more complex modeling of symptoms, signs, interpretations of laboratory test results, clinical findings, diseases, therapies, adverse events, quality measures, etc. will become easier.

**Conclusion**

We created a clinical foundation framework, based on which clinical event monitoring systems can be constructed through combination and configuration. Using the framework, CDSSs can be created more rapidly, and configured to the particular needs of healthcare institutions and patient caregivers.

![Figure 1 – Graphical depiction of the clinical event monitoring system’s architecture. The picture shows the medical logic modules (MLMs) integrated in the clinical foundation framework, and custom-built MLMs for the detection of additional symptoms and infection signs constructed above it. Arrows depict data dependencies between MLMs, or MLM collections. Note: CRP, C-reactive protein; BP, blood pressure.](image-url)
References


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