Evaluation of the Guideline Definition Language (GDL) in the clinical area of severe sepsis and septic shock

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Abstract

Background: The currently existing Guideline Representation Models (GRM) present limitations which hinder the adoption of guideline oriented Clinical Decision Support Systems (CDSS). To overcome these limitations and allow a successful adoption of guideline oriented CDSS standardized GRMs, which can express Clinical Practice Guidelines (CPGs) as Clinical Decision Support (CDS) rules, are needed. Therefore the two standardized GRMs GELLO and GDL have emerged. Even though GDL is currently evaluated in different clinical areas further evaluation is needed to improve and verify its design.

Objectives: The aim is to assess if GDL can be used to successfully represent CPGs as CDS rules in an EHR and to unveil any similarities between the specifications of GELLO and GDL.

Methods: A small part of a severe sepsis and septic shock guideline was modeled using GDL which was then applied to mock patient data to validate GDL. Furthermore the specification of GELLO and GDL were compared against certain criteria to unveil any similarities.

Results: Four GDL guides were produced for the detection and management of severe sepsis and septic shock. Results from the validation of GDL were in line with the mock patient data and results from the comparison of GELLO and GDL revealed two similarities.

Conclusion: The validation indicates that GDL can support the criteria for modeling guidelines in the clinical area of severe sepsis and septic shock; due to limitations this finding cannot be generalized. The comparison of GELLO and GDL revealed similarities regarding the use of the OO approach for their design and the use of a local term binded to an external terminology.

Keywords: Guideline representation models, GDL, GELLO, Clinical decision support systems, HL7, openEHR.
Acknowledgements

First and foremost I would like to thank my supervisor Nadim Anani for the support and guidance he provided me throughout the entire thesis period. It has been a pleasure working with you and thanks to your guidance and patience I was able to feel more secure about myself and greatly improve my skills as a health informatician. Thanks again for making this project a smooth sailing for me.

I also would like to thank Rong Chen for being my Co-Supervisor, for the support and the valuable feedback for the thesis. Your expertise with openEHR and the archetypes has been an inspiration for me ever since you used the term “Lego bricks” to describe the archetypes. Thank you for giving me the opportunity to work with you!

Furthermore I would like to thank Per Furness for using a part of his precious time in order to review the graphical model of the guidelines and provide me with valuable feedback regarding the management of severe sepsis and septic shock.

I would also like to thank my cousin Eirini Kalliamvakou and Marianthi Svinterikou for using their valuable time to repeatedly and critically read the thesis and provide me with valuable feedback.

Finally I would like to thank my family and my sambo for their love and support and for believing in me.
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<th>Full Form</th>
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<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical</td>
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<tr>
<td>CDS</td>
<td>Clinical Decision Support</td>
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<td>CDSS</td>
<td>Clinical Decision Support System</td>
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<td>CIGs</td>
<td>Computer-Interpretable Clinical Practice Guidelines</td>
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<td>CPGs</td>
<td>Clinical Practice Guidelines</td>
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<td>GDL</td>
<td>Guideline Definition Language</td>
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<td>GRM</td>
<td>Guideline Representation Model</td>
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<td>ICD</td>
<td>International Classification Of Diseases</td>
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<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
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<td>MAP</td>
<td>Mean Arterial Pressure</td>
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<td>OCL</td>
<td>Object Constraint Language</td>
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<td>OO</td>
<td>Object-Oriented</td>
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<td>RIM</td>
<td>Reference Information Model</td>
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<td>RISSC</td>
<td>Risk Of Infection To Severe Sepsis Shock Score</td>
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<td>SIRS</td>
<td>Systemic Inflammatory Response Syndrome</td>
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<td>SSC</td>
<td>Surviving Sepsis Campaign</td>
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<td>vMR</td>
<td>Virtual Medical Record</td>
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<td>VUE</td>
<td>Visual Understanding Environment</td>
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1. Introduction

1.1. Background

Efforts to create a clinical decision support system (CDSS) which would contribute in the improvement of safety and efficiency in health care began as early as 1960 [1]. Since then many definitions have been introduced in order to describe what clinical decision support (CDS) is, but in a simplistic way CDS can be seen as a computer system developed to assist clinicians in their decision making [2,3]. The effects of CDS most commonly in the form of reminder systems or dosing systems on the quality of healthcare have been continuously recognized throughout the years and perhaps its strongest benefit is that it can increase adherence to clinical practice guidelines (CPGs) and evidence based protocols [1,4,5].

CPGs as defined in 1990 by the Institute of Medicine are “systematically developed statements that can be used to assess the appropriateness of specific health care decisions, services, and outcomes” [6]. The purposes of CPGs are “to improve the quality of patient care and health care outcomes, to summarize research findings and make clinical decisions more transparent, to reduce inappropriate variation in practice, to promote efficient use of resources, to identify gaps in knowledge and prioritize research activities, to provide guidance for consumers and inform and empower patients, to inform public policy, and to support quality control, including audits of clinicians’ or hospitals’ practices” [7].

Due to the possibilities that CPGs offer and the reputation that evidence based medicine holds today, use of computer-interpretable clinical practice guidelines (CIGs) in the form of guideline-oriented CDS has gained a lot of interest as the underlying rules are developed according to evidence based best practices [1]. Computer-interpretable clinical practice guidelines are text-based clinical guidelines which have been converted to machine executable CDS rules through the use of a guideline representation model (GRM).

GRMs can be described in general as “clinical guideline representation languages and frameworks...for modeling guidelines and protocols in a computer interpretable and executable format” [8]. Thus, GRMs allow the development of formal computer-interpretable
representations of CPGs and the dissemination and implementation of medical knowledge in the form of electronic applications that can be used in order to create recommendations or actions for clinical decision support. Perhaps the most well-known example of GRMs is the Arden Syntax developed by the University of Columbia, which is a rule-based language that allows the conversion of individual clinical rules in Medical Logic Modules or else known as MLMs [9]. Other known examples of GRMs are shown in Table 1.

Table 1. Examples of known guideline representation models

<table>
<thead>
<tr>
<th>Name</th>
<th>Developer</th>
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<tr>
<td>Asbru</td>
<td>• Ben Curion University</td>
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<td></td>
<td>• Vienna University of Technology</td>
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<tr>
<td>EON</td>
<td>• Stanford University</td>
<td><a href="http://www.openclinical.org/gmm_eon.html">http://www.openclinical.org/gmm_eon.html</a></td>
</tr>
<tr>
<td>GEM</td>
<td>• Yale Center for Medical Informatics</td>
<td><a href="http://www.openclinical.org/gmm_gem.html">http://www.openclinical.org/gmm_gem.html</a></td>
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<tr>
<td>GLIF</td>
<td>• Columbia University</td>
<td><a href="http://www.openclinical.org/gmm_glif.html">http://www.openclinical.org/gmm_glif.html</a></td>
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<td></td>
<td>• Stanford University</td>
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<td></td>
<td>• Harvard University</td>
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</tr>
<tr>
<td>GUIDE</td>
<td>• University of Pavia</td>
<td><a href="http://www.openclinical.org/gmm_guide.html">http://www.openclinical.org/gmm_guide.html</a></td>
</tr>
<tr>
<td>PRODIGY</td>
<td>• Newcastle University</td>
<td><a href="http://www.openclinical.org/gmm_prodigy.html">http://www.openclinical.org/gmm_prodigy.html</a></td>
</tr>
<tr>
<td>PROforma</td>
<td>• Advanced Computation Laboratory of Cancer Research in United Kingdom</td>
<td><a href="http://www.openclinical.org/gmm_proforma.html">http://www.openclinical.org/gmm_proforma.html</a></td>
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<td>• Stanford Medical Informatics</td>
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<td>• IDX Systems Corporation</td>
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<td>• University of Nebraska Medical Center</td>
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Although the above GRMs have been designed for the same purpose and they contain several common components (such as in the plan organization, the expression language, the conceptual medical record model, the medical concept model and the data abstractions) they present certain fundamental differences in the underlying decision model, goal representation, use of scenarios and structured medical actions [8,10].

As described above there are numerous examples of GRMs which can contribute to the development of guideline-oriented CDSSs and to the wide adoption of CPGs, thus promoting
consequently the use of evidence based medicine. However due to the above mentioned differences and in connection with certain limitations, guideline-oriented CDSSs and consequently CDS haven’t been able to realize their full potential, therefore hampering their widespread implementation.

1.1.1. Limitations of guideline representation models

Fifty-three years after the first efforts to introduce a CDS system as part of medical practice, CDS hasn’t been able to maximize its potential to the health care. Despite the numerous examples of guideline representation models that support the development and implementation of guideline-oriented CDS systems, their adoption is impeded due to several limitations of the GRMs.

None of the above mentioned tools are able to aid in all major parts during the process of converting guidelines to computer-interpretable CDS rules (Figure 1). This is also the reason why there are so many implementations of GRMs, as each of them is using different approaches and can only assist with certain parts of the process. As a consequence, it is complicated and costly to maintain more than one GRM over time [8].

![Figure 1. Major processes for rule authoring. Source: Zhou L et al. [8]](image-url)
Another limitation of the GRMs is that they are isolated and not connected to a central knowledge repository. As a result, they are not able to be fully integrated with electronic health records (Figure 2) and this can lead to overlapping or conflict of rules as they can be implemented in different systems across a health care institution [8].

Figure 2. The missing link between the GRMs and EHR systems. Source: Anandi N. [11]

Aside from their isolation GRMs are also not capable of sharing the rules contained within them, with other systems or health care institutions. This results to an unneeded complexity and a lot of effort when trying to implement a successful CDS system from one health care institution to another, thus further increasing the isolation of these tools. Perhaps the most well-known example of the inability of the GRMs to share the rules among different systems is the “curly braces problem”. In Arden Syntax each rule’s data section contains information which indicates how the various data elements should be retrieved from a specific information system. This information is specified within curly braces, indicating that it is not part of the general rule but system-specific. This generates a disadvantage as data enclosed within the curly braces have to be redefined according to the local protocols of each health care institution, which poses many difficulties to the ability to share MLMs across different institutions [1,8].
In addition to their inability to be shared among different systems and health care institutions, most of the rules developed by each GRM are based on local terminologies and non-standardized knowledge representations. This lack of terminology standardization consequently serves to further enhance their lack of sharability [8].

A final limitation that the GRMs described in Table 1 present, is their difficulty in extending their structure in order to support the future complexity of knowledge representation. These tools were developed to support the current specifications for CDS rules and as such they are less likely to manage future needs for more complex CDS rules [8].

As a result of the previously described limitations, there is a need for a common guideline representation model that will be built upon current standards and have the ability to be semantic interoperable across different systems or health care institutions as well as share the various rules between them. Additionally, this common guideline representation model must offer the flexibility that is needed in order to adapt to future CDS needs and to support the use of standardized external terminology systems. [8,11–14].

1.1.2. GELLO and GDL

Current efforts to meet the previously described requirements for a standard GRM have led to the creation of GELLO, an expression language for decision support developed by HL7. GELLO is built upon the HL7 version 3 Reference Information Model (RIM)ii and is a class-based, Object-Oriented (OO) language that is built on existing standards. GELLO includes both query and expression sublanguages, and is based on the Object Constraint Language (OCL), developed by the Object Management Group. Relevant components of OCL have been selected and integrated into the GELLO query and expression languages to provide a suitable framework for manipulation of clinical data for decision support in health care [15].

An alternative to GELLO is the Guideline Definition Language (GDL)iii, which is a lightweight language for expressing CDS rules. It is built on top of the openEHR Reference

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i http://www.hl7.org/
ii http://www.hl7.org/implement/standards/rim.cfm
iii http://www.openehr.org/news_events/releases/20130311
Model\(^1\) and Archetypes\(^2\) in order to share CDS rules across different electronic health record systems. A CDS rule in GDL format is neutral to natural languages, reference terminologies and technical implementations [16]. At the moment GDL is still developing and it is under evaluation in clinical areas such as stroke care and atrial fibrillation which have certain desirable characteristics for CDS such as their complexity and critical conditions [17]. Regardless of that, evaluation in other clinical domains is essential for further improvement and verification of the design of GDL. The same complexity and critical conditions, also apply in the clinical area of severe sepsis and septic shock [18].

1.1.3. Severe Sepsis and Septic Shock

Sepsis is a harmful systemic inflammatory condition as a response to a severe infection, mostly caused by a bacterial infection, which can progress to severe sepsis or septic shock. Severe sepsis is defined as “*sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion*” [18]. Septic Shock is defined as “*severe sepsis combined with persistently low blood pressure even after the administration of intravenous fluids*” [18]. Severe sepsis or septic shock and its symptoms are the most common cause of death at the Intensive Care Units (ICU). Examples of symptoms are, systemic inflammatory response syndrome (SIRS), low blood pressure, high or very low temperature, and rapid heart rate [19].

Due to the variety of definitions which describe what septic shock is it has been difficult to evaluate the effects of it in the population [20]. Two studies published in 2002 presented an overall hospital mortality for patients with severe sepsis of 20 to 30% in Sweden and an average cost for an ICU treated survivor of 79 600 € and for a non-survivor 51 400 €. Both studies also reported that the mortality rose with the age [21,22]. Another study published in 2007 reported an increase by two fold in the hospitalization rate for severe sepsis and a two thirds increase in the mortality rate of septic shock in the United States from 1993 to 2003 [23].

Due to the increasing mortality and the significant costs for the health care organizations septic shock is considered a major healthcare problem. Early detection of severe sepsis is crucial to the survival of the patient, as it can allow the management of severe sepsis and

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\(^1\) http://www.openehr.org/wiki/display/spec/openEHR+1.0.2+UML+resources
\(^2\) http://www.openehr.org/wiki/display/healthmod/Introduction+to+Archetypes+and+Archetype+classes
septic shock to begin early, thus increasing significantly the chances for preventing septic shock which can be deadly to the patient [18].

All these characteristics make severe sepsis and septic shock a desirable area, which can be used as an example to evaluate a standardized GRM, since a future guideline-oriented CDS could potentially assist in the early detection of patients suspected to progress in severe sepsis, and in the management of severe sepsis and septic shock (either at the patient level or as a compliance checking).

1.2. Aim and Objectives

The primary aim of the study is to assess if GDL can satisfy the criteria of representing clinical knowledge in the form of CPGs as CDS rules in an EHR. The secondary aim is to unveil any similarities between the specifications of GELLO and GDL.

The reason that GELLO is not part of the primary aim is due to certain financial, accessibility and scope reasons which limit its use throughout this study. However an assessment of the specifications of the two GRMs is possible.

Consequently the main objective of this study is to evaluate GDL through the example of the severe sepsis and septic shock clinical area, thus part of the work will be to create a computer-interpretable model in GDL of a severe sepsis and septic shock guideline. The secondary objective is to compare the specifications of GDL with its counterpart GELLO in accordance to specific requirements.

1.3. Research Questions

The specific research questions addressed in this study are:

- Can GDL satisfy the requirements of modeling guidelines in the detection of severe sepsis and the management of severe sepsis and septic shock?
- Does GDL present any similarities in terms of specifications in comparison to its pre-existing alternative (GELLO)?
2. Methods

As described earlier the aims of this study is to assess if GDL can satisfy the criteria of modeling guidelines as CDS rules in an EHR and to expose any similarities between the specifications of GELLO and GDL. Consequently the design used in this study is evaluation using a mixed-methods approach. The data for this study were collected using a literature review, analysis and modeling. Furthermore the data were analyzed using validation by applying the created GDL guides on mock patient data for the first part and a comparison against certain criteria for the second part. Finally the study framework of this study is given in Figure 3.

2.1. Study Design

A study design is a systematic plan which defines a series of steps that need to be taken in order to answer a specific research question. Generally a study design can be historical, descriptive, correlational, comparative, experimental, simulation, evaluation, action or ethnological. Each of these study designs encompasses a range of methods or techniques that are used in order to collect and analyze the data that are generated during a study, and the choice of each design depends on the nature of the problem described in the aim [24].

Evaluation in general is a study design which can be used in order to examine a system from a certain point of view or under certain criteria and draw conclusions about the current state of...
that system. More specifically Ammenwerth et al. define evaluation as “the act of measuring or exploring properties of a health information system (in planning, development, implementation, or operation), the result of which informs a decision to be made concerning that system in a specific context” [25].

Taking these facts into account and according to the aims set in the previous chapter, the evaluation study design suits the needs of this project as it can provide answers regarding the capabilities of GDL.

2.2. Study approach

The two main approaches of a study design are quantitative and qualitative. The quantitative approach focuses on the collection and analysis of numerical data in order to provide answers to questions such as how much? How many? In a more simplistic way the quantitative approach refers to counts and measures of things.

Alternatively the qualitative approach focuses on the collection, analysis and interpretation of data by observing a certain phenomenon and provides answers to questions such as what? or why? Therefore the qualitative approach constitutes meanings, concepts, characteristics, or descriptions of things.

Regardless of that, another approach that has gained popularity over the past years is the mixed-methods approach. This approach is situated between the quantitative and qualitative approach and it allows the combination of both quantitative and qualitative methods. More accurately according to Johnson and Onwuegbuzie “Mixed-methods research is formally defined as the class of research where the researcher mixes or combines quantitative and qualitative research techniques, methods, approaches, concepts or language into a single study” [26].

Taking into consideration the objectives and the aims of this study, in the first part a quantitative approach is more appropriate to provide the answer needed, whereas in the second part a qualitative approach is better suited for the comparison of GELLO and GDL.
Thus, mixed-methods approach was selected for this study as it allowed the use of quantitative methods and qualitative methods.

2.3. Data collection and analysis

As shown in Figure 3 the first step of the study involved the selection of guidelines and the detection tools for the identification of severe sepsis and septic shock. For the purposes of this a literature review was performed by searching throughout scientific databases such as PubMed and the online university library of Karolinska Institutet and search engines such as Google and Google Scholar. The following keywords and MeSh Terms were used during the search:

- Guidelines/Practice guidelines
- Standards
- Protocols
- Sepsis
- Sepsis, Severe
- Shock, Septic
- Systemic Inflammatory Response Syndrome
- Diagnosis/Early diagnosis
- Detection/Detection tool/Early detection

The returned guidelines were furthermore analyzed according to certain criteria set in regard to the needs of this study. The criteria that were used are the following:

- The guidelines must have been written within the past five years as this will facilitate better future research work.
- They must be international or national in order to allow the generalization of the results.
- They must be in the English language.
- There must be sufficient amount of evidence regarding each recommendation within the guidelines.
The detection tools were analyzed according to the following criteria:

- They must be available to public.
- They must be in the English language.
- They must contain most of the criteria for diagnosis of severe sepsis and septic shock defined in the guidelines.
- They must be from an acceptable scientific source.
- There must be sufficient information regarding each element used within the detection tool.

The second step of the study included the elicitation of text-based rules from the selected guidelines. In order to collect the appropriate rules a secondary analysis was performed according to the strength of evidence supporting each recommendation and according to the extent of each of the recommendations in the selected guidelines.

As described in the introduction GDL is built upon the openEHR Reference Model and Archetypes and as such it requires the use of archetypes in order to operate. Furthermore as GDL is using local terminology codes binded to external terminology systems the use of external terminology codes is necessary. Therefore, in the third step of the study the necessary openEHR archetypes and terminology codes were elicited. To facilitate this process a graphical representation of the selected text-based rules was used which will is presented later in the results section.

According to the created graphical model, the International Repository of Archetypes \(^1\) was reviewed in order to locate the required archetypes. Moreover the online version of the International Classification of Diseases (ICD)\(^2\) the SnomedCT (see section 2.4 Software tools) and the Anatomical Therapeutic Chemical (ATC)\(^3\) databases were searched in order to locate the necessary external terminology codes.

\(^1\)http://openehr.org/ckm/
\(^2\)http://apps.who.int/classifications/icd10/browse/2010/en
\(^3\)http://www.whocc.no/atc_ddd_index/
Finally the created graphical model was used in order to communicate and obtain expert feedback from a specialized nurse so that possible gaps between the rules and the clinical practice, which could reduce the accuracy of the model, would be identified before proceeding to the specification of rules as computer interpretable CDS rules.

The fourth step of the study involved the conversion of the text-based rules to computer-interpretable CDS rules expressed in GDL. The GDL models or guides\(^1\) produced were later used on the final step of the study.

The fifth step included the selection of the specifications of GELLO and GDL, and the collection of the criteria which were used to analyze the specifications. The specifications of GELLO and GDL were selected by searching through the HL7 and openEHR databases. Furthermore, in order to derive the criteria for the analysis a literature review was performed by searching throughout scientific databases such as PubMed and the online university library of Karolinska Institutet and search engines such as Google and Google Scholar. The following keywords were used during the search:

- Guideline representation models
- Computer-interpretable guidelines
- Computer-interpretable guideline models
- Rule authoring environments
- Knowledge authoring tool
- Rule-based decision support
- Guideline based decision support

In the final step of the study GDL was evaluated using a validation and a comparison of the specifications of GELLO and GDL. In this study validation is used as it is defined in ISO 9000-3 “the process of evaluating software to ensure compliance with specified requirements”. In a more simplified meaning validation is used to answer questions such as “Is it doing what it is supposed to do?” [25]. Therefore, the created GDL guides were applied on mock patient data (see appendix B) in order to validate the automatic compliance through a comparison with a manual check. The validation was performed in two parts; on the first

\(^1\) Creators of GDL have replaced the word guide with guideline in order to describe a GDL model. However due to the risk of confusion, throughout this thesis the old term is kept.
part the detection guides were assessed and on the second part the management guides were assessed. This was chosen due to the fact that the RISSC are older and not part of the SSC guidelines. For the purposes of this 10 mock patients were created for each part (a total of 20) which were assigned random values according to the specified rules. Additionally certain patients were assigned extreme values or values close to the decision criteria in order to assess how GDL manages these types of values. Specifically to the second part, different external terminology codes were used for the local term of sepsis in order to assess the ability of GDL to use different external terminology codes binded on the same local term.

Finally, the specifications of GELLO and GDL were compared according to how each language was set to fulfill each of the requirements for a standardized guideline representation model.

2.4. Software tools

Throughout the study the following software tools were used:

1. Visual Understanding Environment\(^1\) (VUE) - Open Source project based at Tufts University. The VUE project is focused on creating flexible tools for managing and integrating digital resources in support of teaching, learning and research. VUE provides a flexible visual environment for structuring, presenting, and sharing digital information. It was used in order to produce a graphical representation of the elicited rules from the severe sepsis and septic shock guidelines as well as a means to communicate in order to gather expert feedback.

2. Ocean Archetype Editor\(^2\) developed by Ocean Informatics – supports the authoring of archetypes as part of the openEHR initiative and the CEN EHR standardisations. It was used for the creation of new archetypes or modification of existing archetypes.

3. Ocean Template Designer\(^3\) developed by Ocean Informatics – allows users to compose a set of archetypes into a collection called a template. This can be used for

\(^1\) [http://vue.tufts.edu/](http://vue.tufts.edu/)
\(^2\) [https://wiki.oceaninformatics.com/confluence/display/TTL/Archetype+Editor](https://wiki.oceaninformatics.com/confluence/display/TTL/Archetype+Editor)
\(^3\) [https://wiki.oceaninformatics.com/confluence/display/TTL/Template+Designer](https://wiki.oceaninformatics.com/confluence/display/TTL/Template+Designer)
data entry, as the basis for a form or for creating a data schema for bringing data into the openEHR environment. The user can use those archetypes and features of archetypes that are required as well as setting default values, limiting choices, naming fields, removing unwanted fields etc. as required for a particular use environment. It was used in order to further enable the specialization of certain archetypes.

4. CliniClue® Xplore\textsuperscript{1} – freeware browser for SNOMED Clinical Terms. It was used in order to extract SNOMED-CT terminology codes.

5. GDL Editor developed by Cambio Healthcare Systems – open-source multiplatform desktop application that allows users to create, edit and run GDL files. It provides a testing environment capable of generating forms based on the archetype elements defined in the GDL. These forms can be used to capture data from the user and trigger the rules. This tool was used in order to create the GDL guides used in the evaluation of GDL.

6. CDS Workbench developed by Cambio Healthcare Systems – an application which allows the execution of CDS rules in the form of GDL guides on EHR patients. It was used in order apply the produced GDL guides on the mock patient data.

2.5. Ethical consideration

No real patient data were used during the course of this study, thus there are no ethical considerations regarding confidentiality and patient integrity.

Furthermore no financial aid was given from any organization for the conduct of this study thus, there is no conflict of interest regarding the material discussed throughout the study.

It should also be mentioned that the co-supervisor of the dissertation is a developer of GDL. His role, however, has been to provide guidance and feedback on the study and dissertation relating to openEHR and archetypes, and to make sure that the research and scientific protocol

\textsuperscript{1}http://www.cliniclue.com/
followed is correct. As a result, there are no ethical concerns arising from his involvement with GDL or any threats to the study's reliability.

Finally, any information used regarding the specifications of GELLO and GDL was used strictly for academic purposes in order to provide answers to a specific research question set in this study and not for any other purposes.

3. Results

In the following sections the results from the different steps of the study are presented. The first section presents the results from the comparison between GELLO and GDL specifications while, the rest of the sections describe the results from the assessment of GDL in the clinical area of severe sepsis and septic shock. Although the comparison of GELLO and GDL is the second part of this study, the results from the comparison are presented first as the details contained within these results helps in understanding certain choices that were made during the first part of the study.

3.1 Results from the comparison of the specifications of GDL and GELLO

In order for a GRM to be able to meet the various challenges and withstand future developments it needs to have certain characteristics such as to be built upon current standards, to be able to support multiple terminologies, to be semantically interoperable and extensible, as well as having the ability to share the rules among different systems.

Exploring the designing requirements that each of the developers has set for each of the languages revealed certain similarities and differences which assisted in gaining a better understanding of the specifications of each language.
Developers of GELLO have specified the following design requirements in their documentation [27]:

- Vendor-independent
- Platform-independent
- Object-oriented and compatible with the HL7 RIM
- Side-effect free
- Extensible
- Flexible
- Easy to read/write

Whereas developers of GDL have defined the following design requirements [16]:

- It should be straight-forward to convert the CDS rules to main-stream general-purpose rule languages for execution.
- It must be reference terminology-agnostic so different terminologies can be used to support reasoning.
- It must be natural language-agnostic and able to support multiple language translations without changing the rule definitions.
- It must be possible to express CDS rules using archetypes both as input and output for the rule execution.
- There must be sufficient meta-information about the CDS rules, e.g. authorship, purpose, versions and relevant references.
- It must be possible to reuse the CDS rules in different clinical contexts.
- It should be possible to group a set of related CDS rules in order to support complex decision making.

It can be observed that both languages seem to place a focus on using standards such as the HL7 RIM and the openEHR Reference Model and Archetypes. Technology independency and the ability to share the different rules on various platforms, as well as the ability for the users to be able to easily work and create the rules using those languages are also other areas focused upon.

However, certain differences can also be observed. Regarding the use of terminology GELLO does not specify it within its design requirements whereas GDL contains it as an important feature to support reasoning during decision making. Moreover, the use of meta-information in the CDS rules is also an area where they differ as GELLO does not specify any requirements. The use of meta-information can assist the sharability of CDS rules and enables the ability to build upon existing work.

The following table is summarizing how the specifications of Gello and GDL were designed to meet the previously mentioned characteristics.
Table 2. Results from the comparison of GELLO and GDL

<table>
<thead>
<tr>
<th>Standardization</th>
<th>GELLO[27]</th>
<th>GDL[16]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of the virtual medical record (vMR) a limited view of the multiple classes existing within the HL7 RIM.</td>
<td>• Use of the virtual medical record (vMR) a limited view of the multiple classes existing within the HL7 RIM.</td>
<td>• Developed on top of openEHR reference model and the archetype model.</td>
</tr>
<tr>
<td>Incorporates most of the features included (certain features have been kept out as Gello is designed to be an expression language and not a constrained language) in the object constrained language (OCL).</td>
<td>• Incorporates most of the features included (certain features have been kept out as Gello is designed to be an expression language and not a constrained language) in the object constrained language (OCL).</td>
<td>• Use of archetypes as input or output during rules execution. Each variable contained within a CDS rule is bound to a specific data element defined by an archetype. After the variable is bound, it can be used in a statement as input or output.</td>
</tr>
<tr>
<td>Created according to a standard guideline execution model which contains a series of steps: actions, decisions, patient-state, branches and synchronization.</td>
<td>• Created according to a standard guideline execution model which contains a series of steps: actions, decisions, patient-state, branches and synchronization.</td>
<td></td>
</tr>
</tbody>
</table>

| Semantic Interoperability                                                                 | The OO design of GELLO allows it to interact with any HL7 RIM-based OO data model.                                                                                                                                                                         | The Guide Object Model allows GDL to interact with any OO data model based on the openEHR Reference Model.                                                                                             |
|                                                                                      | • The UML ITS which is part of OCL, implements the semantic of the HL7 abstract data types by mapping the HL7 data types into the core UML and OCL kernel data types, thus enabling GELLO to reference instances of patient-specific data free of platform, vendor or data model. | • Archetype data have the same meaning no matter what context it is used within the EHR and, similarly, no matter which EHR system it is used or what language is used. |

| Sharability                                                                 | Contains basic built-in data types and the required tools to manipulate an OO data model compatible with the HL7 RIM. This gives the ability to access all the associated data model and methods, which further enables the rule expressions to support different data models in as many classes and relationships as possible. | Archetypes as input or output in GDL enable it to share the various rules and definitions with other systems. A main characteristic of the openEHR archetypes is their ability to be shared and reused among platforms based on the openEHR Reference Model. |
|                                                                                      | • The OO approach enables it as well to share the decision logic and other computer expressions instances of patient-specific data free of platform, vendor or data model.                                                                                       |                                                                                                                                                                                                          |
One similarity that can be observed concerns the selection of the object-oriented approach as the underpinning design in order to develop GELLO and GDL, as well as to support the extensibility that both languages require.

Another similarity is the ability of both languages to bind an external terminology code to a local code in order to facilitate the support of existing terminologies systems and the sharability of rules.

3.2. Selection of guidelines and detection tool

According to the criteria described in the methods section the “International Guidelines for Management of Severe Sepsis and Septic Shock: 2012”, developed by the organization “Survive Sepsis Campaign (SSC)” published in February 2013 where selected as the source for extracting rules regarding the management of severe sepsis and septic shock [18]. The guidelines are a result of the joint collaboration of the European Society of Intensive Care Medicine, the Society of Critical Care Medicine, and the International Sepsis Forum launched at the European Society of Intensive Care Medicine's annual congress in Barcelona in 2002. In 2004 the initial guidelines were published and since then two more revisions have been

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1 http://www.survivingsepsis.org
published in 2008 and 2013. Finally the guidelines contain 84 recommendations without the pediatric considerations regarding the management of severe sepsis and septic shock.

As described earlier in the introduction an important factor to the management of severe sepsis and septic shock is the early detection of it. Due to the fact that the SSC guidelines are quite new a tool for early identification based on the SSC 2012 guidelines was set to be released at mid to late April 2013. Due to time limitations an alternative detection tool for severe sepsis and septic shock was chosen based on the criteria set in the methods.

Consequently, the “Risk of Infection to Severe Sepsis and Shock Score (RISSC)” developed by Alberti et.al was selected in order to extract rules regarding the early identification of severe sepsis. The RISSC is based on the total sum of 12 variables including 7 physiologic variables and 5 variables related to infection characteristics (see Table 2). According to how high the RISSC is the greater the risk to progress to severe sepsis and septic shock [28].

3.3. Selection of text-based rules

The SSC guidelines have graded each recommendation according to the strength of evidence that supports it. Recommendations that were marked as ungraded (UG) were excluded from this study as the strength of evidence was not strong. According to the secondary analysis the following rules regarding the fluid resuscitation, the administration of vassopressors and the administration of inotropes were selected for the management of severe sepsis and septic shock:

1. “Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L).”
2. “Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock.”
3. “Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock.”
4. “Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids.”
5. “Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients.”

6. “Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg.”

7. “Norepinephrine as the first choice vasopressor.”

8. “Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure.”

9. “Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia).”

10. “Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low or (c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target.”

11. “A trial of dobutamine infusion up to 20 micrograms/kg/min be administered or added to vasopressor (if in use) in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or (b) ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate MAP.”

12. “Not using a strategy to increase cardiac index to predetermined supranormal levels.”

In addition to the previous rules Tables 3 and 4 were adapted from the RISSC document in order to extract the rules for the RISSC scale.

**Table 3. The RISSC scale**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Finding</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>&lt;= 120 per minute</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 120 per minute</td>
<td>3</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>&gt;=110mmHG</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt;110mmHG</td>
<td>4</td>
</tr>
<tr>
<td>Body temperature</td>
<td>&lt;= 38.2°C</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt; 38.2°C</td>
<td>5</td>
</tr>
<tr>
<td>Parameter</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------</td>
<td>------</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>6.5</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Peritonitis</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Primary bacteremia</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Serum total bilirubin &lt;= 30 μmol/L</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Serum Sodium &lt;= 145 mmol/L</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Platelet count &gt;= 150,000 per μL</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Gram-positive Cocci</td>
<td>2.5</td>
<td>0</td>
</tr>
<tr>
<td>Aerobic Gram-negative bacilli</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total Score</td>
<td>SUM (points for all 12 parameters)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 4. Risk of progression from sepsis to severe sepsis and septic shock according to the RISSC.**

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Risk Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 8</td>
<td>Low</td>
</tr>
<tr>
<td>8.1 to 16</td>
<td>Moderate</td>
</tr>
<tr>
<td>16.1 to 24</td>
<td>High</td>
</tr>
<tr>
<td>&gt;24</td>
<td>Very high</td>
</tr>
</tbody>
</table>
3.4. Elicitation of openEHR archetypes and terminology

In order to ease the extraction of the archetypes from the International Repository of Archetypes and to gather the necessary external terminology codes a graphical representation of selected parts from the guidelines was made using the tool Visual Understanding Environment (VUE) (Figure 4) in accordance to Anani et al., 2012 [29].

Figure 4: Graphical representation of the fluid resuscitation and the administration of vasopressors and inotropes
Each node represents a clinical knowledge element that would be contained within an openEHR observation, action, instruction or evaluation archetypes. The arrows between each node contain a condition or a relationship representing the connection between nodes and subnodes. The chronological order of activities is set from left to right. The two distinct areas surrounding the nodes represent the time recommendation for their completion as stated in the SSC guidelines. It must be noted that the activities that need to be done within 3 hours and 6 hours do not take place sequential but in parallel. Finally the green highlighted areas were modeled using GDL.

The graphical representation was also used as a means to communicate with a specialized nurse in the management of septic patients in order to assist with the verification of the selected rules and the detection of possible clinical gaps in the guidelines. The feedback that was received assisted in the clarification of the initial fluid challenge process and it was incorporated on the previous model.

3.4.1. openEHR archetypes

According to the graphical model that was described earlier the following archetypes were selected and were able to be reused in this study without any changes:

- openEHR-EHR-EVALUATION.problem_diagnosis.v1
- openEHR-EHR-EVALUATION.risk.v1
- openEHR-EHR-INSTRUCTION.intravenous_fluid_order.v1
- openEHR-EHR-ITEM_TREE.intravenous_fluids.v1
- openEHR-EHR-INSTRUCTION.medication.v1
- openEHR-EHR-ITEM_TREE.medication.v1
- openEHR-EHR-OBSERVATION.pulse.v1
- openEHR-EHR-OBSERVATION.blood_pressure.v1
- openEHR-EHR-OBSERVATION.body_temperature.v1
- openEHR-EHR-OBSERVATION.body_weight.v1
- openEHR-EHR-OBSERVATION.lab_test.v1
- openEHR-EHR-OBSERVATION.lab_test-microbiology.v1
- openEHR-EHR-OBSERVATION.lab_test-urea_and_electrolytes.v1
Three archetypes were modified for the needs of this study:

- openEHR-EHR-OBSERVATION.lab_test-full_blood_count.v1: /μL units were added to the units of the element Platelet count
- openEHR-EHR-OBSERVATION.lab_test-total_bilirubin.v1: This is a specialization of the archetype openEHR-EHR-OBSERVATION.lab_test.v1 which has been modified in order to record the quantity of the serum total bilirubin.
- openEHR-EHR-OBSERVATION.lab_test-blood_lactate.v1: This is a specialization of the archetype openEHR-EHR-OBSERVATION.lab_test.v1 which has been modified in order to record the quantity of the lactate.

Two new archetypes were created for this study:

- openEHR-EHR-ACTION.mechanical_ventilation.v1: This archetype is used in order to record the use of mechanical ventilation on patients.
- openEHR-EHR-OBSERVATION.rissc_score.v1: This archetypes is used in order to record all the elements and the total score of the RISSC (Figure 5).

Figure 5: The archetype for recording the RISSC
3.4.2. Terminologies

The following terminology codes were selected in order to detect relevant diagnosis from an EHR:

**ICD 10**
- Pneumonia: J12, J14, J13, J16, J15, J17, J18, P23
- Peritonitis: K65
- Primary Bacteremia: A499
- Sepsis: A40, A41

**SNOMED-CT**
- Sepsis: 151276018, 151281010
- Hypoperfusion: 393004013
- Gram-positive Cocci: 1788076012, 7980230013, 1788077015, 98367014
- Aerobic Gram-negative Bacilli: 144550011, 829590011, 1235204010

**ATC**
- Crystalloids: Due to the absence of a terminology code for crystalloids the code for isotonic solutions B05DA was used instead as the current crystalloids used in the management of severe sepsis and septic shock are isotonic solutions.
- Albumin: B05AA01

3.5. Specification of GDL rules

According to the needs of this study four GDL guides were created, the RISSC score calculation guide, the RISSC risk group calculation, the Initial fluid challenge guide and the Monitoring of sepsis-induced hypoperfusion guide. A complete list of all the rules specified within these guides is provided at Appendix “A”

**RISSC score calculation and RISSC risk group calculation guide**

The RISSC score calculation guide evaluates certain patient’s physiologic and infection variables from the EHR as input and derives a total score as the output (Figure 6).
The RISSC risk group calculation evaluates the total score that derived from the RISSC score calculation guide as input and estimates the risk of progressing to severe sepsis or septic shock as output (Figure 7).

Figure 6: The RISSC score calculation

Figure 7: The RISSC risk group
Monitoring of sepsis-induced hypoperfusion and Initial fluid challenge guide

The monitoring of sepsis-induced hypoperfusion guide is used in order to detect the patients that are developing sepsis-induced hypoperfusion according to certain critical variables as defined in the SSC guidelines (Figure 8). Due to the absence of a terminology code for the sepsis-induced hypoperfusion the coexistence of sepsis and hypoperfusion was evaluated instead. A precondition was set that evaluates the patient’s diagnosis if sepsis is present. Only when sepsis is present the rule will trigger and set the diagnosis to hypoperfusion according to the critical variables. Consequently the SNOMED-CT terminology for hypoperfusion was used.

The initial fluid challenge guide is used in order to calculate the amount of fluid that a patient who has been diagnosed with sepsis-induced hypoperfusion needs to receive according to his weight, and to set the type of the fluid to receive as well as the form of therapy according to the guidelines (Figure 9). Due to the absence of a terminology code for the crystalloids the terminology code for isotonic solutions was used instead. Furthermore the form of therapy is set to intermittent infusion as the initial fluid challenge is an emergency administration under which a big amount of fluid is administered for a short period of time. Finally, similar to the monitoring of sepsis-induced hypoperfusion guide the patient’s diagnosis is also evaluated according to the coexistence of Sepsis and hypoperfusion.

Figure 8: The monitoring of sepsis-induced hypoperfusion guide
3.6. Validation using mock patient data

In order to validate the design of GDL the created guides were applied to mock patient data using the tool CDS workbench and the automatic compliance was compared against a manual check. The validation was executed in two parts, on the first part the detection guides (RISSC score calculation and RISSC risk group calculation) were assessed and on the second part the management guides were assessed (Monitoring of sepsis-induced hypoperfusion and Initial fluid challenge). The two groups of guides were assessed separately due to the fact that the detection tool used in this study is older than the SSC guidelines and also not part of them.

3.6.1. Detection of severe sepsis and septic shock

In this part GDL was assessed according to how many patients the total score was correctly calculated as well as estimating the correct risk for progressing to severe sepsis and septic shock according to the total score. Other areas that were also assessed were whether GDL manages extreme values as well as values that are very close to the decision criteria, and the ability of using the output of a guide as an input to another guide. Figure 10 presents the results of applying the GDL rules in the mock patient data as produced from the CDS workbench.
In the total number of 10 patients, two patients were correctly classified as having a low risk, 3 patients as having moderate risk, 3 patients high risk and two patients as having very high risk to progress to severe sepsis and septic shock. The results for each variable and the execution log for each patient are included in appendix C.

### 3.6.2. Management of severe sepsis and septic shock

In this part, GDL was assessed according to how many patients were correctly identified as having hypoperfusion as well as calculating the correct amount of fluid to be administered according to the weight of each patient. Similar to the previous part, GDL was also assessed whether it can manage extreme values and values close to the decision criteria as well as using the output of a guide as an input to another guide. Finally, another area that GDL was also assessed was in how many patients sepsis was correctly identified when two external terminologies are bounded under the same local term for sepsis. The following figures summarize the results after applying the GDL rules to the mock patient data.
Figure 11. Amount of patients that the rule for sepsis-induced hypoperfusion was fired on and not fired on. n=10, mock patients with sepsis and hypoperfusion =6

Figure 12. Amount of patients that the rule for the initial fluid challenge was fired on and not fired on. n=10, mock patients in need for initial fluid challenge =6
From Figure 11 in can be observed that the rule for sepsis-induced hypoperfusion was fired correctly for all 6 patients that had sepsis and hypoperfusion. Moreover in Figure 12 it can be observed that the rule for the initial fluid challenge was also fired correctly for all 6 patients that needed an initial fluid challenge to be administered. As observed from Figure 13 in all 6 patients the correct amount of fluid (element “Volume”) and type of therapy (element “Form of therapy”) and fluid (element “Fluid type”) were calculated. Finally sepsis was correctly identified regardless of the external terminology code used.

Figure 13. The execution log as generated by CDS workbench after applying the GDL rules on the patient data.
4. Discussion

In accordance to the objectives described for this study a computer interpretable model of GDL, based on the SSC guidelines was created which was then applied on mock patient data in order to validate the automatic compliance of GDL. The process of creating the GDL model involved several steps according to which a set of guidelines and a detection tool was selected from which several text-based rules where elicited. Moreover, the extracted rules were presented using a graphical representation which was then used to extract the necessary archetypes and external terminology codes and to receive expert feedback. Additionally the rules where then converted to 4 GDL guides which were then applied to mock patient data. Lastly in parallel with this, the design specification of GELLO and GDL were compared against certain characteristics in order to reveal certain similarities which would assist in understanding the results from the validation of GDL. Throughout these steps several general and specific to GDL findings emerged.

4.1. Discussion of GDL aspects

A first finding that is supported by the results of this study is that **GDL can enhance the sharability of rules across different organizations**. As described earlier in the introduction a major challenge of the guideline representation models is that they are based on local non-standardized terminologies [8]. As shown during the validation of the management GDL guides, more than one standard external terminology was assigned to a local term for sepsis and the patients were correctly identified for having sepsis regardless of the terminology code used. This gives the ability to GDL rules to be shared among different institutions and organizations regardless the terminology system they are using thus, providing a very good solution to the sharability issues due to terminology challenges.

Another finding is that **the use of archetypes as input and output supports the reusability of openEHR archetypes**. This is supported by the fact that most of the clinical elements needed for the purposes of this study were able to be matched with existing archetypes and only two archetypes had to be created from scratch. The reusability of archetypes further enhances the standardization and sharability of the CDS rules.
On the other hand using archetypes as input and output presents also a weakness. Limitations within the archetypes will inevitably extend to GDL. This is supported by the fact that the design of the RISSC scale archetype had to deviate from the normal way that scale archetypes are designed. Scale archetypes usually are designed using classes of DV_Ordinals for each element and a class of DV_Count for the element of total score. However DV_Ordinals do not support the use of decimal values which are contained in the RISSC scale (Mechanical ventilation, gram-positive Cocci). Therefore DV_Quantity was chosen for these elements as well as for the total score since the result can contain decimals. This option though created certain stability issues in GDL due to the fact that DV_Quantity elements must have a unit even though the total score does not require any units. In order to overcome this issue and since units do not play any part in the calculation of the total score, the “kg” units were chosen since they allow the use of decimals and didn’t present any stability issues.

Finally one more finding is the flexibility that GDL offers. During the modeling of the management guides no external terminology code was found for sepsis-induced hypoperfusion. However it was possible to check the coexistence of sepsis and hypoperfusion as an alternative solution either by setting a pre-condition that would assess the presence of sepsis on a patient before executing the rule for the evaluation of hypoperfusion, or either by evaluating the coexistence of both diagnoses.

4.2. Discussion of general findings

In the second part of the study the design specifications of GELLO and GDL were compared in order to reveal any similarities between the two languages. A first similarity that was found is that both languages use an underpinning class based model in order to support the ability of being extensible. Extensibility is a well know property of the object-oriented approach and as such it provides a good solution to the challenges described in the introduction regarding the ability of the GRM to withstand future complexity [8].

Another similarity between the two languages was that the use of a local term binded to an external terminology. This property provides a good solution to sharability issues such as the
“curly braces” problem and also enhances the semantic interoperability between two systems as CDS rules are bounded to standardized external terminologies.

One more finding that relates to the process of converting guidelines to computer-interpretable rules is the necessity of the graphical representation as part of the process. In this study a graphical representation of the extracted text based rules was created. The model was proved very useful at simplifying the process of extracting the necessary openEHR archetypes as well as revealing gaps in the knowledge of the guidelines. Furthermore the model was also very useful at communicating with an expert in order to receive a better understanding of the initial fluid challenge process. This finding is similar to the findings described by Anani et.al which also elaborate about the benefits of using a graphical representation model as an intermediate step before specifying the computer-interpretable rules [29].

Additionally the use of expert feedback as part of the process is very important to the accuracy of the CDS rules. Although there are logical grounds that support this, surprisingly no literature exists which supports the importance of having expert feedback as means to verify the knowledge content of the rules.

Finally, another finding is the need to create a new archetype for the initial fluid challenge. Although for the needs of this study the initial fluid challenge was covered by the archetype “openEHR-EHR-INSTRUCTION.intravenous_fluid_order.v1” the diagnosis aspect of it is not covered by this archetype. The initial fluid challenge except for treatment purposes is also used in order to define whether the patient is progressing to severe sepsis or not. In this case, a new archetype should be created which will contain the necessary elements for the initial fluid challenge.

4.3. Limitations

The primary limitation of this study was the time frame under which it had to be accomplished. Due to the fact that the guidelines used in this study were recently released it was not possible to obtain a detection tool in accordance to the recommendations of the 2012 guidelines, as it was set to be released in mid to late April 2013. As a result GDL was
validated in two parts for the detection and management of severe sepsis and septic shock, since RISSC was older and not part of the SSC guidelines. Consequently, there was a risk that it would be unclear to define any possible inconsistencies in the results after using all 4 guides together, as a consequence of the previous mentioned issues or of GDL limitations. Additionally GDL was not able to be assessed for compliance checking as the guideline compliance criteria according to the SSC guidelines 2012 were set for a release on the same date. Furthermore due to the time limitations it was not possible to model all the recommendations from the guidelines but only the most critical parts in the management of severe sepsis and septic shock. In addition to this, it was not possible to obtain feedback from an expert physician regarding vasopressor and inotrope therapy; therefore only part of the graphical-representation was specified as CDS rules.

A second limitation was the financial capability of this study. Due to the absence of financial aid it was not possible to obtain the software packages for GELLO in order to allow for a more extensive comparison of the two GRMs. Moreover, another limitation regarding the comparison of GELLO and GDL was the quality of documentation of each language. Although GELLO has been introduced for almost 10 years, obtaining a detailed documentation of each specification is not possible. Most of the information provided in the documentation of GELLO has been constructed in a marketing purpose and as such it was not possible to acquire more details on certain areas. On the other hand the documentation of GDL provides several details about its design, however since it is still under beta the information contained is susceptible to near future changes.

### 4.4. Strength and weaknesses of the study

The use of a multi-method approach in a study enables the collection of richer information on different characteristics of a researched object [26]. Therefore the strength of this study relies on the qualitative information that was collected in order to provide a more comprehensive understanding of GDL.

On the other hand, during a comparison certain reliability issues can be presented in regard to the presence of bias in defined criteria. In order to overcome this weakness an extensive literature review was done in order to select the criteria which were used to compare GELLO
and GDL. Furthermore another weakness of this study is the extent of the limitations which limit the generalization of the results.

**Alternative method consideration**

An alternative design that could be used for this study is the comparative evaluation which is a form of research that an evaluation and the findings of the evaluation process are set in a comparative framework [30]. During the process of the comparative evaluation two well defined objects are compared under the same criteria. The extent of the criteria as well as the depth of the comparison determines the quality of the results. This research design was not selected due to financial reasons, as it would require the modeling of the same guidelines in GELLO and GDL format and compare them according to the criteria for modeling CDS rules in severe sepsis and septic shock.

**4.5. Future research**

In order to overcome the limitations of this study and in order to produce more reliable and generalizable results a larger study needs to be performed using both GELLO and GDL in order to model the whole extent of the SSC guidelines. Additionally by the time this study will be completed a detection tool for severe sepsis and septic shock based on the 2012 guidelines will have been released, which could also be used in the same study and allow the assessment of both languages under the same protocol, from detection to the management of severe sepsis and septic shock. Lastly the languages would be assessed against real patient data in order to produce more reliable results.

Finally, another study could focus on assessing whether GDL can be used in order to assess guideline compliance of the SSC guidelines in an organization. Guideline compliance is an important factor to the successful implementation of the SSC guidelines and as such it provides an interesting area for further evaluation of GDL. By the time this study will be completed the criteria for guideline compliance will have been released according to the 2012 SSC guidelines.
5. Conclusions

This study aimed at evaluating whether GDL could satisfy the criteria for modeling guidelines through the example of the clinical area of severe sepsis and septic shock. Additionally, the detection of similarities between GELLO and GDL was also an aim.

The validation of GDL gives an indication that GDL can support the criteria for modeling guidelines in the clinical area of severe sepsis and septic shock; however due to certain limitations this finding cannot be generalized.

The comparison of GELLO and GDL revealed certain similarities regarding the use of the OO approach for their design in order to allow their extensibility and the use of a local term binded to an external terminology in order to facilitate semantic interoperability and sharability of the CDS rules.

In conclusion, this study produced important results that can contribute to the overall understanding of the process of converting guidelines to CDS rules, as well as the limitations that challenge this process and the adoption of the produced CDS rules.
References


17. Chen R. Chief Medical Informatics Officer Cambio Healthcare Systems. Personal communication. 7th February 2013.


Appendix A – GDL Rules

RiSSC score calculation

GUIDE DETAILS

Description: The Risk of Infection to Severe Sepsis and Shock Score (RiSSC)
Purpose: Calculates the risk of septic patients to progress to severe sepsis and septic shock.
Use: Calculates the risk of septic patients to progress to severe sepsis and septic shock.


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KEYWORDS

Septic, Severe Sepsis, Septic Shock, RiSSC

RULE LIST

Rule Pneumonia absent
When
Element Pneumonia does not exist
Then
Set element Pneumonia to absent

Rule Pneumonia present
When
Element Problem/Diagnosis is a Pneumonia
Then
Set element Pneumonia to present

Rule Peritonitis absent
When
Element Peritonitis does not exist
Then
Set element Peritonitis to absent

Rule Peritonitis present
When
Element Problem/Diagnosis is a Peritonitis
Then
Set element Peritonitis to present

Rule Primary bacteremia absent
When
Element Primary Bacteremia does not exist
Then
Set element Primary Bacteremia to absent

Rule Primary bacteremia present
When
Element Problem/Diagnosis is a Primary Bacteremia
Then
Set element Primary Bacteremia to present

Rule Mechanical ventilation absent
When
Element Type of ventilator/respirator does not exist
Then
Set element Mechanical Ventilation to 0 %
### Appendix A – GDL Rules

<table>
<thead>
<tr>
<th>Rule</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rule Mechanical ventilation present</td>
<td>When Element Type of ventilator/respirator exists&lt;br&gt;Then Set element Mechanical Ventilation to 0.5 %</td>
</tr>
<tr>
<td>Rule Heart rate below/equal to 120/min</td>
<td>When Element Rate is less than or equals to 120 /min&lt;br&gt;Then Set element Heart Rate to Below or equal to 120/min</td>
</tr>
<tr>
<td>Rule Heart rate above 120/min</td>
<td>When Element Rate is greater than 120 /min&lt;br&gt;Then Set element Heart Rate to Above 120</td>
</tr>
<tr>
<td>Rule Systolic blood pressure above/equal to 110mmHg</td>
<td>When Element Systolic is greater than or equals to 110 mm[Hg]&lt;br&gt;Then Set element Systolic Blood Pressure to Above or equal 110mmHg</td>
</tr>
<tr>
<td>Rule Systolic blood pressure below 110mmHg</td>
<td>When Element Systolic is less than 110 mm[Hg]&lt;br&gt;Then Set element Systolic Blood Pressure to Below 110mmHg</td>
</tr>
<tr>
<td>Rule Body temperature below/equal to 38.2</td>
<td>When Element Temperature is less than or equals to 38.2 °C&lt;br&gt;Then Set element Body Temperature to Below or equal to 38.2</td>
</tr>
<tr>
<td>Rule Body temperature above 38.2</td>
<td>When Element Temperature is greater than 38.2 °C&lt;br&gt;Then Set element Body Temperature to Above 38.2</td>
</tr>
<tr>
<td>Rule Serum total Bilirubin below/equal to 30</td>
<td>When Element Total Bilirubin is less than or equals to 30 μmol/l&lt;br&gt;Then Set element Serum Total Bilirubin to Below or equal to 30</td>
</tr>
<tr>
<td>Rule Serum total Bilirubin above 30</td>
<td>When Element Total Bilirubin is greater than 30 μmol/l&lt;br&gt;Then Set element Serum Total Bilirubin to Above 30</td>
</tr>
<tr>
<td>Rule Serum Sodium below/equal to 145mmol/L</td>
<td>When Element Sodium is less than or equals to 145 mmol/l&lt;br&gt;Then Set element Serum sodium to below or equal to 145mmol/L</td>
</tr>
<tr>
<td>Rule Serum Sodium above 145mmol/L</td>
<td>When Element Sodium is greater than 145 mmol/l&lt;br&gt;Then Set element Serum sodium to above 145</td>
</tr>
<tr>
<td>Rule Platelet count above/equal to 150000</td>
<td>When Element Platelet count is greater than or equals to 150000 /μL&lt;br&gt;Then Set element Platelet count to above or equal to 150000</td>
</tr>
</tbody>
</table>
Appendix A – GDL Rules

<table>
<thead>
<tr>
<th>Rule</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count below 150000</td>
<td>Element Platelet count is less than 150000 /μL. Then set element Platelet count to below 150000</td>
</tr>
<tr>
<td>Gram-positive cocci absent</td>
<td>Element Gram-Positive Cocci does not exist. Then set element Gram-Positive Cocci to 0%</td>
</tr>
<tr>
<td>Gram-positive cocci present</td>
<td>Element Result is a Gram-positive Cocci. Then set element Gram-Positive Cocci to 2.5%</td>
</tr>
<tr>
<td>Aerobic Gram-negative Bacilli absent</td>
<td>Element Aerobic Gram-Negative Bacilli does not exist. Then set element Aerobic Gram-Negative Bacilli to absent</td>
</tr>
<tr>
<td>Aerobic Gram-negative Bacilli present</td>
<td>Element Result is a Aerobic Gram-negative Bacilli. Then set element Aerobic Gram-Negative Bacilli to present</td>
</tr>
</tbody>
</table>

RISSC risk group calculation

GUIDE DETAILS

Description: Severe sepsis or septic shock risk estimation based on RISSC score
Purpose: To estimate the risk of a patient to progress to severe sepsis or septic shock based on the RISSC score
Use:
Milestone:

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KEYWORDS
Severe, Severe Sepsis, Septic Shock, RISSC

RULE LIST

Rule Low risk
When
Element Total Score is less than or equal to 8 kg
Then
Set element Rationale to "RISSC total score less or equal to 8" Set element Index condition to "Severe Sepsis or Septic Shock" Set element Significance of risk to Not significant
Appendix A – GDL Rules

Rule Moderate Risk
When
- Element Total Score is greater than or equals to 8.1 kg
- Element Total Score is less than or equals to 10 kg
Then
  - Set element Rationale to "RISSC total score between 8.1 and 16"
  - Set element Index condition to "Severe Sepsis or Septic Shock"
  - Set element Significance of risk to Minimal significance

Rule High risk
When
- Element Total Score is less than or equals to 24 kg
- Element Total Score is greater than or equals to 16.1 kg
Then
  - Set element Rationale to "RISSC total score between 16.1 and 24"
  - Set element Index condition to "Severe Sepsis or Septic Shock"
  - Set element Significance of risk to Significant

Rule Very high risk
When
- Element Total Score is greater than 24 kg
Then
  - Set element Rationale to "RISSC total score above 24"
  - Set element Index condition to "Severe Sepsis or Septic Shock"
  - Set element Significance of risk to Highly significant

Monitoring of sepsis-induced hypoperfusion

GUIDE DETAILS
Description: Monitoring of septic patients for sepsis-induced hypoperfusion according to the critical criteria set in the Surviving Sepsis Campaign (SSC) guidelines of 2022
Purpose: To monitor septic patients for sepsis-induced hypoperfusion according to the critical criteria set in the Surviving Sepsis Campaign (SSC) guidelines of 2012. In the future more criteria will be added according to the SSC severe sepsis detection tool which is planned to be published around late April or early May 2018
Use:
Misuse:

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KEYWORDS
Sepsis, Severe Sepsis, Septic Shock, Hypoperfusion, Sepsis-induced hypoperfusion

PRECONDITIONS
Element Problem/Diagnosis is a Sepsis

RULE LIST
Rule Sepsis-induced hypoperfusion
When
- Element Lactic Acid/Lactate is greater than or equals to 4 mmol/l
  or
  - Element Systolic is less than 90 mm[Hg]
  or
  - Element Mean Arterial Pressure is less than 65 mm[Hg]
Then
  - Set element Problem/Diagnosis to 8910004013
Appendix A – GDL Rules

Initial fluid challenge

GUIDE DETAILS

Description: Calculates the amount of fluid to be given in patients with sepsis-induced hypoperfusion according to the instructions set in the Surviving Sepsis Campaign (SSC) guidelines of 2012.

Purpose: To calculate the amount and type of fluid to be given in patients with sepsis-induced hypoperfusion according to the instructions set in the Surviving Sepsis Campaign (SSC) guidelines of 2012.

Use:

Mistake:


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Copyright:

KEYWORDS

Sepsis, Severe Sepsis, Septic Shock, Hypoperfusion, Sepsis-induced hypoperfusion, Fluid challenge

RULE LIST

Rule: Initial Fluid Challenge

When:

- Element Problem/Diagnosis is a Hypoperfusion
- Element Problem/Diagnosis is a Sepsis

Then:

- Set element Form of therapy to Intermittent infusion
- Set element Fluid type to Isotonic solutions
- Set element “Volume_meas” to “ml”
- Set element “Volume_awaited” to (30 * Weight)
## Appendix B – Mock Patient Data

### Table 4. Mock patients for the detection of severe sepsis and septic shock

| N/o Patient | Heart Rate /m | SBP mmHg | Body Temperature °C | Mechanical Ventilation | Pneumonia | Peritonitis | Primary Bacteremia | Serum total bilirubin μmol/L | Serum sodium mmol/L | Platelet count /μL | Gram-positive cocci | Aerobic gram-negative bacilli | Total Score | Risk Group |
|-------------|---------------|----------|---------------------|------------------------|-----------|-------------|-------------------|---------------------------|---------------------|-----------------|---------------------|------------------|-----------------------------|-------------|------------|
| 1           | 200           | 60       | 41                  | Yes                    | Yes       | Yes         | Yes               | 70                        | 200                 | 50000          | Yes                 | Yes              | 49                          | Very High   |
| 2           | 80            | 120      | 36                  | No                     | No        | No          | No                | 6                         | 50                  | 500000         | No                  | No               | 0                           | Low         |
| 3           | 121           | 110      | 38.3                | Yes                    | No        | No          | Yes               | 31                        | 145                 | 149999         | No                  | Yes              | 30.5                        | Very High   |
| 4           | 100           | 80       | 34                  | No                     | No        | No          | No                | 15                        | 164                 | 151000         | Yes                 | Yes              | 13.5                        | Moderate    |
| 5           | 110           | 130      | 37.8                | Yes                    | Yes       | No          | No                | 30                        | 135                 | 150000         | No                  | No               | 10.5                        | Moderate    |
| 6           | 90            | 100      | 39                  | No                     | No        | Yes         | No                | 50                        | 130                 | 180000         | Yes                 | No               | 18.5                        | High        |
| 7           | 150           | 70       | 37                  | No                     | No        | No          | Yes               | 20                        | 136                 | 158542         | No                  | No               | 13                          | Moderate    |
| 8           | 120           | 109      | 38                  | No                     | Yes       | No          | Yes               | 25                        | 140                 | 134562         | No                  | Yes              | 21                          | High        |
| 9           | 60            | 205      | 36.5                | No                     | No        | No          | No                | 30                        | 150                 | 148654         | No                  | No               | 8                           | Low         |
| 10          | 105           | 103      | 38.7                | No                     | No        | Yes         | No                | 60                        | 135                 | 56549          | No                  | No               | 20                          | High        |

### Table 5. Mock patients for the management of severe sepsis and septic shock

<table>
<thead>
<tr>
<th>N/o Patient</th>
<th>Sepsis</th>
<th>Sepsis code</th>
<th>SBP mmHg</th>
<th>MAP mmHg</th>
<th>Lactate mmol/L</th>
<th>Hypoperfusion</th>
<th>Weight kg</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>A40</td>
<td>40</td>
<td>20</td>
<td>10</td>
<td>Yes</td>
<td>49</td>
<td>1470</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>A41</td>
<td>200</td>
<td>120</td>
<td>1</td>
<td>No</td>
<td>38</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>-</td>
<td>110</td>
<td>60</td>
<td>3</td>
<td>No</td>
<td>63</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>151276018</td>
<td>80</td>
<td>75</td>
<td>2</td>
<td>Yes</td>
<td>79</td>
<td>2370</td>
</tr>
<tr>
<td>5</td>
<td>No</td>
<td>-</td>
<td>120</td>
<td>75</td>
<td>2</td>
<td>No</td>
<td>82</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>151281010</td>
<td>90</td>
<td>65</td>
<td>4</td>
<td>Yes</td>
<td>120</td>
<td>3600</td>
</tr>
<tr>
<td>7</td>
<td>No</td>
<td>-</td>
<td>100</td>
<td>30</td>
<td>2</td>
<td>No</td>
<td>101</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>Yes</td>
<td>A40</td>
<td>60</td>
<td>70</td>
<td>1</td>
<td>Yes</td>
<td>71</td>
<td>2130</td>
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<tr>
<td>9</td>
<td>Yes</td>
<td>A41</td>
<td>130</td>
<td>80</td>
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<td>Yes</td>
<td>61</td>
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<tr>
<td>10</td>
<td>Yes</td>
<td>151276018</td>
<td>89</td>
<td>64</td>
<td>2</td>
<td>Yes</td>
<td>57</td>
<td>1710</td>
</tr>
</tbody>
</table>
Appendix C – Execution Logs

Log for patient 'Patient 1':
- RISSC score calculation @b0002 => Pneumonia = DV_ORDINAL,0 (local: 0014) [absent]
- RISSC score calculation @b0004 => Pneumonia = DV_ORDINAL,4 (local: 0015) [present]
- RISSC score calculation @b0007 => Peritonitis = DV_ORDINAL,0 (local: 0017) [absent]
- RISSC score calculation @b0009 => Pententoto = DV_ORDINAL,4 (local: 0018) [present]
- RISSC score calculation @b0011 => Primary Bacteremia = DV_ORDINAL,0 (local: 0020) [absent]
- RISSC score calculation @b0013 => Primary Bacteremia = DV_ORDINAL,8 (local: 0021) [present]
- RISSC score calculation @b0018 => Mechanical Ventilation = DV_QUANTITY,8.5% [present]
- RISSC score calculation @b0023 => Heart Rate = DV_ORDINAL,3 (local: 0026) [Above 120]
- RISSC score calculation @b0027 => Systolic Blood Pressure = DV_ORDINAL,4 (local: 0028) [Below 110mmHg]
- RISSC score calculation @b0031 => Body Temperature = DV_ORDINAL,5 (local: 0032) [Above 38.2]
- RISSC score calculation @b0035 => Serum Total Bilirubin = DV_ORDINAL,3 (local: 0024) [Above 30]
- RISSC score calculation @b0039 => Serum sodium = DV_ORDINAL,4 (local: 0039) [Above 145]
- RISSC score calculation @b0048 => Platelet count = DV_ORDINAL,4 (local: 0027) [Below 150000]
- RISSC score calculation @b0040 => Gram-Positive Cocci = DV_QUANTITY,0 [%]
- RISSC score calculation @b0042 => Gram-Positive Cocci = DV_QUANTITY,2.5 [%
- RISSC score calculation @b0049 => Aerobic Gram-Negative Bacilli = DV_ORDINAL,0 (local: 0034) [absent]
- RISSC score calculation @b0051 => Aerobic Gram-Negative Bacilli = DV_ORDINAL,3 (local: 0035) [present]
-RISK score calculation @b0008 => Rationale = DV_TEXT, RISSC total score above 24
- RISK risk group calculation @b0008 => Index condition = DV_TEXT, Severe Sepsis or Septic Shock
- RISK risk group calculation @b0008 => Significance of risk = DV_CODED_TEXT, local: 0009 [Highly significant]
- RISK score calculation @b0051 => Aerobic Gram-Negative Bacilli = DV_ORDINAL,3 (local: 0035) [present]
- RISK score calculation @b0001 => Total Score = DV_QUANTITY,46.0 kg
- RISK score calculation @b0001 => Total Score = DV_QUANTITY,46.0 kg
- RISK score calculation @b001 => Total Score = DV_QUANTITY,49.0 kg
- RISK risk group calculation @b0008 => Rationale = DV_TEXT, RISSC total score above 24
- RISK risk group calculation @b0008 => Index condition = DV_TEXT, Severe Sepsis or Septic Shock
- RISK risk group calculation @b0008 => Significance of risk = DV_CODED_TEXT, local: 0009 [Highly significant]

Log for patient 'Patient 2':
- RISSC score calculation @b0002 => Pneumonia = DV_ORDINAL,0 (local: 0014) [absent]
- RISSC score calculation @b0007 => Peritonitis = DV_ORDINAL,0 (local: 0017) [absent]
- RISSC score calculation @b0011 => Primary Bacteremia = DV_ORDINAL,0 (local: 0020) [absent]
- RISSC score calculation @b0018 => Mechanical Ventilation = DV_QUANTITY,0.0%
- RISSC score calculation @b0020 => Heart Rate = DV_ORDINAL,0 (local: 0020) [Below or equal to 120/min]
- RISSC score calculation @b0024 => Systolic Blood Pressure = DV_ORDINAL,0 (local: 0026) [Above or equal 110mmHg]
- RISSC score calculation @b0028 => Body Temperature = DV_ORDINAL,0 (local: 0011) [Below or equal to 38.2]
- RISSC score calculation @b0032 => Serum Total Bilirubin = DV_ORDINAL,0 (local: 0024) [Below or equal to 30]
- RISSC score calculation @b0039 => Serum sodium = DV_ORDINAL,0 (local: 0039) [Below or equal to 145mmol/L]
- RISSC score calculation @b0045 => Platelet count = DV_ORDINAL,0 (local: 0027) [Above or equal to 150000]
- RISSC score calculation @b0040 => Gram-Positive Cocci = DV_QUANTITY,0.0%
- RISSC score calculation @b0049 => Aerobic Gram-Negative Bacilli = DV_ORDINAL,0 (local: 0034) [absent]
- RISSC score calculation @b0051 => Aerobic Gram-Negative Bacilli = DV_ORDINAL,3 (local: 0035) [present]
- RISK score calculation @b0001 => Total Score = DV_QUANTITY,10.0 kg
- RISK score calculation @b0001 => Total Score = DV_QUANTITY,10.0 kg
- RISK score calculation @b001 => Total Score = DV_QUANTITY,10.0 kg
- RISK risk group calculation @b0001 => Rationale = DV_TEXT, total score less or equal to 8
- RISK risk group calculation @b0001 => Index condition = DV_TEXT, Severe Sepsis or Septic Shock, Significance of risk = DV_CODED_TEXT, local: 0009 [Not significant]
Appendix C – Execution Logs

Log for patient Patient 3:
RASSC score calculation g0002 >= Pneumonia = DV_ORDINAL,0 [local:a0014][absent]
RASSC score calculation g0007 >= Peritonitis = DV_ORDINAL,0 [local:a0017][absent]
RASSC score calculation g0011 >= Primary Bacteraemia = DV_ORDINAL,0 [local:a0020][absent]
RASSC score calculation g0013 >= Primary Bacteraemia = DV_ORDINAL,0 [local:a0021][present]
RASSC score calculation g0018 >= Mechanical Ventilation = DV_QUANTITY,8.5%
RASSC score calculation g0023 >= Heart Rate = DV_ORDINAL,3 [local:a0006][above 120]
RASSC score calculation g0024 >= Systolic Blood Pressure = DV_ORDINAL,0 [local:a0008][above or equal 110mmHg]
RASSC score calculation g0031 >= Body Temperature = DV_ORDINAL,5 [local:a0012][above 38.2]
RASSC score calculation g0035 >= Serum Total Bilirubin = DV_ORDINAL,3 [local:a0024][above 30]
RASSC score calculation g0036 >= Serum sodium = DV_ORDINAL,0 [local:a0003][below or equal to 145mmol/L]
RASSC score calculation g0049 >= Platelet count = DV_ORDINAL,4 [local:a0027][below or equal to 150000]
RASSC score calculation g0040 >= Gram-Positive Cocci = DV_QUANTITY,2%
RASSC score calculation g0049 >= Aerobic Gram-Negative Bacilli = DV_ORDINAL,0 [local:a0034][absent]
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,10.0kg
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,27.5kg
RASSC risk group calculation g0001 >= Rationale = DV_TEXT, Risk Group Score above 24
RASSC risk group calculation g0001 >= Rationale = DV_TEXT, Severe Sepsis or Septic Shock
RASSC risk group calculation g0001 >= Significance of risk = DV_CODED_TEXT [local:a0003][highly significant]
RASSC score calculation g0051 >= Aerobic Gram-Negative Bacilli = DV_ORDINAL,3 [local:a0035][present]
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,27.5kg
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,30.5kg
RASSC risk group calculation g0008 >= Rationale = DV_TEXT, Risk Group Score above 24
RASSC risk group calculation g0008 >= Significance of risk = DV_CODED_TEXT [local:a0003][highly significant]

Log for patient Patient 4:
RASSC score calculation g0002 >= Pneumonia = DV_ORDINAL,0 [local:a0014][absent]
RASSC score calculation g0007 >= Peritonitis = DV_ORDINAL,0 [local:a0017][absent]
RASSC score calculation g0011 >= Primary Bacteraemia = DV_ORDINAL,0 [local:a0020][absent]
RASSC score calculation g0013 >= Primary Bacteraemia = DV_ORDINAL,0 [local:a0021][present]
RASSC score calculation g0020 >= Heart Rate = DV_ORDINAL,2 [local:a0005][below or equal to 120mmHg]
RASSC score calculation g0022 >= Systolic Blood Pressure = DV_ORDINAL,4 [local:a0009][below 110mmHg]
RASSC score calculation g0026 >= Body Temperature = DV_ORDINAL,0 [local:a0011][below or equal to 38.2]
RASSC score calculation g0032 >= Serum Total Bilirubin = DV_ORDINAL,0 [local:a0023][below or equal to 30]
RASSC score calculation g0039 >= Serum sodium = DV_ORDINAL,4 [local:a0003][above 145]
RASSC score calculation g0045 >= Platelet count = DV_ORDINAL,0 [local:a0026][above or equal to 150000]
RASSC score calculation g0040 >= Gram-Positive Cocci = DV_QUANTITY,2%
RASSC score calculation g0049 >= Aerobic Gram-Negative Bacilli = DV_ORDINAL,0 [local:a0034][absent]
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,10.0kg
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,10.5kg
RASSC risk group calculation g0006 >= Rationale = DV_TEXT, Risk Group Score between 8.1 and 16
RASSC risk group calculation g0006 >= Index condition = DV_TEXT, Severe Sepsis or Septic Shock
RASSC risk group calculation g0006 >= Significance of risk = DV_CODED_TEXT [local:a0007][Minimal significance]
RASSC score calculation g0051 >= Aerobic Gram-Negative Bacilli = DV_ORDINAL,3 [local:a0035][present]
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,10.5kg
RASSC score calculation g0001 >= Total Score = DV_QUANTITY,13.5kg
RASSC risk group calculation g0006 >= Rationale = DV_TEXT, Risk Group Score between 8.1 and 16
RASSC risk group calculation g0006 >= Index condition = DV_TEXT, Severe Sepsis or Septic Shock
RASSC risk group calculation g0006 >= Significance of risk = DV_CODED_TEXT [local:a0007][Minimal significance]
Appendix C – Execution Logs

Log for patient Patient B:
RISC score calculation: RISC score calculation: Patient B:
Pneumonia  = DV_ORDINAL, [local: st00014/absent]
Pneumonia  = DV_ORDINAL, [local: st00015/present]
RISC score calculation: RISC score calculation: Patient B:
Platelets  = DV_ORDINAL, [local: st00017/absent]
Primary Bacteremia  = DV_ORDINAL, [local: st00020/absent]
Mechanical Ventilation  = DV_QUANTITY, 0,5
RISC score calculation: RISC score calculation: Patient B:
Heart Rate  = DV_ORDINAL, [local: st0003/below or equal to 120/m]
Systolic Blood Pressure  = DV_ORDINAL, [local: st0004/above or equal to 110/mmHg]
Body Temperature  = DV_ORDINAL, [local: st0011/below or equal to 36,2]
RISC score calculation: RISC score calculation: Patient B:
Serum Total Bilirubin  = DV_ORDINAL, [local: st0020/below or equal to 145/mg/dl]
Serum sodium  = DV_ORDINAL, [local: st0023/below or equal to 145/mmol/L]
Platelet count  = DV_ORDINAL, [local: st0026/above or equal to 150,000/mm3]
Gram-Positive Cocci  = DV_QUANTITY, 0,5
RISC score calculation: RISC score calculation: Patient B:
Aerobic Gram-Negative Bacilli  = DV_ORDINAL, [local: st0034/absent]
Total Score  = DV_QUANTITY, 10,0 kg
Total Score  = DV_QUANTITY, 10,5 kg
Total Score  = DV_QUANTITY, 10,5 kg
Total Score  = DV_QUANTITY, 10,5 kg
RISC risk group calculation: RISC risk group calculation: Patient B:
Rationale  = DV_TEXT, RISC total score between 6,1 and 16
Index condition  = DV_TEXT, Severe Sepsis or Septic Shock
Significance of risk  = DV_CCODED_TEXT, [local: st0007/Minimal significance]

Log for patient Patient B:
RISC score calculation: RISC score calculation: Patient B:
Pneumonia  = DV_ORDINAL, [local: st00014/absent]
Platelets  = DV_ORDINAL, [local: st0017/absent]
Primary Bacteremia  = DV_ORDINAL, [local: st0020/absent]
Mechanical Ventilation  = DV_QUANTITY, 0,5
RISC score calculation: RISC score calculation: Patient B:
Heart Rate  = DV_ORDINAL, [local: st0003/above or equal to 120/m]
Systolic Blood Pressure  = DV_ORDINAL, [local: st0004/above or equal to 145/mmHg]
Body Temperature  = DV_ORDINAL, [local: st0011/below or equal to 36,2]
RISC score calculation: RISC score calculation: Patient B:
Serum Total Bilirubin  = DV_ORDINAL, [local: st0020/above or equal to 145/mg/dl]
Serum sodium  = DV_ORDINAL, [local: st0023/above or equal to 145/mmol/L]
Platelet count  = DV_ORDINAL, [local: st0026/above or equal to 150,000/mm3]
Gram-Positive Cocci  = DV_QUANTITY, 0,5
RISC score calculation: RISC score calculation: Patient B:
Aerobic Gram-Negative Bacilli  = DV_ORDINAL, [local: st0034/absent]
Total Score  = DV_QUANTITY, 10,0 kg
Total Score  = DV_QUANTITY, 10,5 kg
Total Score  = DV_QUANTITY, 10,5 kg
Total Score  = DV_QUANTITY, 10,5 kg
RISC risk group calculation: RISC risk group calculation: Patient B:
Rationale  = DV_TEXT, RISC total score between 6,1 and 16
Index condition  = DV_TEXT, Severe Sepsis or Septic Shock
Significance of risk  = DV_CCODED_TEXT, [local: st0007/Minimal significance]
Appendix C – Execution Logs

Log for patient Patient 7:
RISSC score calculation 0002 -> Pneumonia = DV_ORDINAL(0|local:at0014|absent)
RISSC score calculation 0007 -> Pneumonia = DV_ORDINAL(0|local:at0017|absent)
RISSC score calculation 0011 -> Primary Bacteraemia = DV_ORDINAL(0|local:at0020|absent)
RISSC score calculation 0013 -> Primary Bacteraemia = DV_ORDINAL(0|local:at0021|present)
RISSC score calculation 0015 -> Mechanical Ventilation = DV_QUANTITY(0.5 %)
RISSC score calculation 0023 -> Heart Rate = DV_ORDINAL(3|local:at0005|Above 120)
RISSC score calculation 0027 -> Systolic Blood Pressure = DV_ORDINAL(0|local:at0009|Below 110mmHg)
RISSC score calculation 0028 -> Body Temperature = DV_ORDINAL(0|local:at0011|Below or equal to 38.2)
RISSC score calculation 0032 -> Serum Total Bilirubin = DV_ORDINAL(0|local:at0023|Below or equal to 30)
RISSC score calculation 0036 -> Serum sodium = DV_ORDINAL(0|local:at0038|below or equal to 145mmol/L)
RISSC score calculation 0045 -> Platelet count = DV_ORDINAL(0|local:at0025|above or equal to 150000)
RISSC score calculation 0046 -> Gram Positive Cocci = DV_QUANTITY(0 %)
RISSC score calculation 0048 -> Aerobic Gram-Negative Bacilli = DV_ORDINAL(0|local:at0034|absent)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(10.0 kg)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(10.0 kg)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(13.0 kg)
RISSC risk group calculation 0006 -> Rationale = DV_TEXT(RISSC total score between 8.1 and 16)
RISSC risk group calculation 0006 -> Index Condition = DV_TEXT(Severe Sepsis or Septic Shock)
RISSC risk group calculation 0006 -> Significance of Risk = DV_CODED_TEXT(local:at0007|Minimal significance)

Log for patient Patient 8:
RISSC score calculation 0002 -> Pneumonia = DV_ORDINAL(0|local:at0014|absent)
RISSC score calculation 0004 -> Pneumonia = DV_ORDINAL(4|local:at0015|present)
RISSC score calculation 0007 -> Pneumonia = DV_ORDINAL(0|local:at0017|absent)
RISSC score calculation 0011 -> Primary Bacteraemia = DV_ORDINAL(0|local:at0020|absent)
RISSC score calculation 0013 -> Primary Bacteraemia = DV_ORDINAL(0|local:at0021|present)
RISSC score calculation 0015 -> Mechanical Ventilation = DV_QUANTITY(0 %)
RISSC score calculation 0023 -> Heart Rate = DV_ORDINAL(0|local:at0005|Below or equal to 120)
RISSC score calculation 0027 -> Systolic Blood Pressure = DV_ORDINAL(4|local:at0009|Below 110mmHg)
RISSC score calculation 0028 -> Body Temperature = DV_ORDINAL(0|local:at0011|Below or equal to 38.2)
RISSC score calculation 0032 -> Serum Total Bilirubin = DV_ORDINAL(0|local:at0023|Below or equal to 30)
RISSC score calculation 0036 -> Serum sodium = DV_ORDINAL(4|local:at0038|below or equal to 145mmol/L)
RISSC score calculation 0045 -> Platelet count = DV_ORDINAL(0|local:at0025|above or equal to 150000)
RISSC score calculation 0046 -> Gram Positive Cocci = DV_QUANTITY(0 %)
RISSC score calculation 0048 -> Aerobic Gram-Negative Bacilli = DV_ORDINAL(0|local:at0034|absent)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(10.0 kg)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(10.0 kg)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(18.0 kg)
RISSC risk group calculation 0007 -> Rationale = DV_TEXT(RISSC total score between 16.1 and 24)
RISSC risk group calculation 0007 -> Index Condition = DV_TEXT(Severe Sepsis or Septic Shock)
RISSC risk group calculation 0007 -> Significance of Risk = DV_CODED_TEXT(local:at0008|Significant)
RISSC score calculation 0061 -> Aerobic Gram-Negative Bacilli = DV_ORDINAL(3|local:at0035|present)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(18.0 kg)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(18.0 kg)
RISSC score calculation 0001 -> Total Score = DV_QUANTITY(21.0 kg)
RISSC risk group calculation 0007 -> Rationale = DV_TEXT(RISSC total score between 16.1 and 24)
RISSC risk group calculation 0007 -> Index Condition = DV_TEXT(Severe Sepsis or Septic Shock)
RISSC risk group calculation 0007 -> Significance of Risk = DV_CODED_TEXT(local:at0008|Significant)
Appendix C – Execution Logs

Log for patient 'Patient 5':
RISSC score calculation(0002) => Pneumonia = DV_ORDINAL_0 [local: 0001] [absent]
RISSC score calculation(0007) => Peritonitis = DV_ORDINAL_0 [local: 0017] [absent]
RISSC score calculation(0011) => Primary Bacteremia = DV_ORDINAL_0 [local: 0020] [absent]
RISSC score calculation(0015) => Mechanical Ventilation = DV_QUANTITY_0, 0%
RISSC score calculation(0020) => Heart Rate = DV_ORDINAL_0 [local: 0003] [below or equal to 120/1][m]
RISSC score calculation(0024) => Systolic Blood Pressure = DV_ORDINAL_0 [local: 0008] [above or equal to 110/mmHg]
RISSC score calculation(0026) => Body Temperature = DV_ORDINAL_0 [local: 0011] [below or equal to 36.2]
RISSC score calculation(0032) => Serum Total Bilirubin = DV_ORDINAL_0 [local: 0023] [below or equal to 30]
RISSC score calculation(0034) => Serum sodium = DV_ORDINAL_4 [local: 0030] [above 145]
RISSC score calculation(0040) => Platelet count = DV_ORDINAL_4 [local: 0027] [below 150000]
RISSC score calculation(0040) => Gram-Positive Cocci = DV_QUANTITY_0, 0%
RISSC score calculation(0040) => Aerobic Gram-Negative Bacilli = DV_ORDINAL_0 [local: 0034] [absent]
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC risk group calculation(0001) => Rationale = DV_TEXT, RISSC total score less or equal to 8
RISSC risk group calculation(0001) => Index condition = DV_TEXT, Severe Sepsis or Septic Shock
RISSC risk group calculation(0001) => Significance of risk = DV_CODED_TEXT, local: 0008 [Not significant]

Log for patient 'Patient 10':
RISSC score calculation(0002) => Pneumonia = DV_ORDINAL_0 [local: 0001] [absent]
RISSC score calculation(0007) => Peritonitis = DV_ORDINAL_0 [local: 0017] [absent]
RISSC score calculation(0009) => Mechanical Ventilation = DV_ORDINAL_0 [local: 0015] [present]
RISSC score calculation(0011) => Primary Bacteremia = DV_ORDINAL_0 [local: 0020] [absent]
RISSC score calculation(0015) => Mechanical Ventilation = DV_QUANTITY_0, 0%
RISSC score calculation(0020) => Heart Rate = DV_ORDINAL_0 [local: 0003] [below or equal to 120/1][m]
RISSC score calculation(0024) => Systolic Blood Pressure = DV_ORDINAL_4 [local: 0008] [below or equal to 110/mmHg]
RISSC score calculation(0031) => Body Temperature = DV_ORDINAL_5 [local: 0012] [above 38.2]
RISSC score calculation(0035) => Serum Total Bilirubin = DV_ORDINAL_3 [local: 0024] [above 30]
RISSC score calculation(0036) => Serum sodium = DV_ORDINAL_0 [local: 0030] [below or equal to 145/mmHg]
RISSC score calculation(0040) => Platelet count = DV_ORDINAL_4 [local: 0027] [below 150000]
RISSC score calculation(0040) => Gram-Positive Cocci = DV_QUANTITY_0, 0%
RISSC score calculation(0040) => Aerobic Gram-Negative Bacilli = DV_ORDINAL_0 [local: 0034] [absent]
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC score calculation(0040) => Total Score = DV_QUANTITY_10, 0 kg
RISSC risk group calculation(0001) => Rationale = DV_TEXT, RISSC total score between 18.1 and 24
RISSC risk group calculation(0007) => Index condition = DV_TEXT, Severe Sepsis or Septic Shock
RISSC risk group calculation(0007) => Significance of risk = DV_CODED_TEXT, local: 0008 [Significant]
Appendix D – Time Frame of Study

<table>
<thead>
<tr>
<th>Task Name</th>
<th>Duration</th>
<th>Start</th>
<th>Finish</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Project Plan</strong></td>
<td>25 days</td>
<td>Tue 2/22/13</td>
<td>Fri 2/15/13</td>
</tr>
<tr>
<td>Send project plan to supervisor</td>
<td>8 days</td>
<td>Tue 3/22/13</td>
<td>Tue 3/29/13</td>
</tr>
<tr>
<td>Apply feedback changes to Project Plan and send to supervisor for approval</td>
<td>6 days</td>
<td>Fri 2/1/13</td>
<td>Wed 2/6/13</td>
</tr>
<tr>
<td>Deadline to upload Project Plan</td>
<td>1 day</td>
<td>Fri 2/8/13</td>
<td>Fri 2/8/13</td>
</tr>
<tr>
<td>Mandatory Project Plan Discussions</td>
<td>5 days</td>
<td>Mon 2/11/13</td>
<td>Fri 2/15/13</td>
</tr>
<tr>
<td><strong>Data Collection</strong></td>
<td>8 days</td>
<td>Sat 2/24/13</td>
<td>Wed 4/24/13</td>
</tr>
<tr>
<td>Selecting Guideline(s)</td>
<td>10 days</td>
<td>Thu 2/28/13</td>
<td>Thu 2/28/13</td>
</tr>
<tr>
<td>Check point</td>
<td>1 day</td>
<td>Thu 2/28/13</td>
<td>Thu 2/28/13</td>
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<tr>
<td>Extraction of rules from guidelines</td>
<td>10 days</td>
<td>Fri 3/1/13</td>
<td>Sun 3/10/13</td>
</tr>
<tr>
<td>Graphical representation of rules</td>
<td>7 days</td>
<td>Mon 3/11/13</td>
<td>Sun 3/17/13</td>
</tr>
<tr>
<td>Collection/Modification of Archetypes</td>
<td>8 days</td>
<td>Mon 3/18/13</td>
<td>Mon 3/25/13</td>
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<tr>
<td>Computation of rules with ODL Editor</td>
<td>22 days</td>
<td>Tue 3/26/13</td>
<td>Tue 4/18/13</td>
</tr>
<tr>
<td>Creation of mock patient data</td>
<td>8 days</td>
<td>Wed 4/17/13</td>
<td>Wed 4/24/13</td>
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<tr>
<td>Deadline to upload progress report</td>
<td>1 day</td>
<td>Mon 4/15/13</td>
<td>Mon 4/15/13</td>
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<tr>
<td>Mandatory Progress report discussions</td>
<td>4 days</td>
<td>Mon 4/15/13</td>
<td>Mon 4/15/13</td>
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<tr>
<td><strong>Data Analysis</strong></td>
<td>23 days</td>
<td>Sat 4/20/13</td>
<td>Sun 5/12/13</td>
</tr>
<tr>
<td>Application of rules in CDS workbench</td>
<td>5 days</td>
<td>Wed 4/24/13</td>
<td>Wed 4/24/13</td>
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<tr>
<td>Selection of criteria for the comparison</td>
<td>5 days</td>
<td>Thu 4/25/13</td>
<td>Mon 4/29/13</td>
</tr>
<tr>
<td>Comparison of automatic compliance check with manual check (criteria)</td>
<td>8 days</td>
<td>Tue 5/7/13</td>
<td>Tue 5/7/13</td>
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<tr>
<td>Comparison with Gielo</td>
<td>5 days</td>
<td>Wed 5/8/13</td>
<td>Sun 5/12/13</td>
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<tr>
<td><strong>Composition of Theses</strong></td>
<td>16 days</td>
<td>Mon 5/13/13</td>
<td>Tue 5/28/13</td>
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<tr>
<td>Structuring of preliminary thesis report</td>
<td>4 days</td>
<td>Mon 5/13/13</td>
<td>Thu 5/16/13</td>
</tr>
<tr>
<td>Deadline to upload preliminary thesis report</td>
<td>1 day</td>
<td>Fri 5/17/13</td>
<td>Fri 5/17/13</td>
</tr>
<tr>
<td>Continue work with the composition of the final Thesis</td>
<td>4 days</td>
<td>Sat 5/18/13</td>
<td>Tue 5/21/13</td>
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<tr>
<td>Preparatory seminar</td>
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<td>Wed 5/22/13</td>
<td>Wed 5/22/13</td>
</tr>
<tr>
<td>Apply feedback from seminar</td>
<td>5 days</td>
<td>Thu 5/23/13</td>
<td>Mon 5/27/13</td>
</tr>
<tr>
<td>Deadline to upload final thesis report</td>
<td>1 day</td>
<td>Tue 5/28/13</td>
<td>Tue 5/28/13</td>
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