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An Arden-Syntax-Based Clinical Decision Support Framework for Medical Guidelines —Lyme Borreliosis as an Example

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Abstract. Medicine is evolving at a very fast pace. The overwhelming quantity of new data compels the practician to be consistently informed about the most recent scientific advances. While medical guidelines have proven to be an acceptable tool for bringing new medical knowledge into clinical practice and also support medical personnel, reading them may be rather time-consuming. Clinical decision support systems have been developed to simplify this process. However, the implementation or adaptation of such systems for individual guidelines involves substantial effort. This paper introduces a clinical decision support platform that uses Arden Syntax to implement medical guidelines using client−server architecture. It provides a means of implementing different guidelines without the need for adapting the system's source code. To implement a prototype, three Lyme borreliosis guidelines were aggregated and a knowledge base created. The prototype employs transfer objects to represent any text-based medical guideline. As part of the implementation, we show how Fuzzy Arden Syntax can improve the overall usability of a clinical decision support system.

Keywords. Clinical decision support system, Arden Syntax, fuzzy logic, Lyme borreliosis.

1. Introduction

Evidence-based medical guidelines are being developed to support clinicians and assist in decision-making. These guidelines usually summarize and evaluate the evidence and most recent information on prevention, diagnosis, prognosis, therapy, risk/benefit, and cost-effectiveness with reference to a specific medical issue. Even in their simplest form—as plain documents—guidelines serve clinicians by providing the most recent medical knowledge in a procedural form that can be applied in clinical routine.

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Regrettably, paper-based guidelines are still time-consuming to read and difficult to update. Furthermore, several guidelines exist for one and the same subject, recommending diverse diagnostic and treatment procedures and thus increasing ambiguity.

Computerized guidelines, e.g., special forms, dialog systems, or wizards, used to guide clinicians through a decision-making process eliminate the need to read entire text-based documents. By providing relevant medical knowledge, these systems are able to reduce the time needed for transferring new medical knowledge into clinical practice. However, one disadvantage is that any changes made to the knowledge base require its representation to be adapted as well.

Clinical decision support systems (CDSSs) try to solve this problem by separating medical knowledge implementation from technical implementation. Based on this consideration, we developed a platform for Arden-Syntax-based guidelines and a CDSS prototype for Lyme borreliosis. This platform gives medical professionals access to current clinical knowledge, stored on a central CDS server. By ensuring client–server independence, any text-based guideline may be implemented, provided the two key concepts explained in this paper are taken into account. Using the described platform, CDSS administrators (at least one clinical informatician and one medical expert) are able to add, manage, update, or remove guidelines on the server without changing a single line of the user interface or the server code. A patient database permits the representation of guidelines over longer periods of time, storing patient data over multiple sessions.

2. Methods

A first step when converting paper-based guidelines into computer-interpretable formats is to find a suitable formalism to represent clinical knowledge. Arden Syntax [1–3], a Health Level Seven (HL7) [4] standard for medical knowledge representation, has proven to be an effective language for this purpose. The latest version of Arden Syntax introduced fuzzy sets and logic, adding new concepts, data types and operators, to extend present methods for processing linguistic and propositional uncertainty (see Figure 1) [5].

Our platform employs a client–server architecture. The model describes the distribution of tasks and services within a network. An Arden Syntax server [6] is used for this purpose. It stores and processes the implemented knowledge of medical guidelines in the form of so-called medical logic modules (MLMs), and provides an interface for administrative and maintenance tasks. A hypertext preprocessor (PHP) [7] web client [8] is used to communicate with the Arden Syntax server via representational state transfer (REST) interfaces.

The implemented communication process is divided into four steps. First, the client retrieves all available patient data from a database established in the course of previous sessions. Second, it creates a connection with the Arden Syntax server, requesting the execution of a specific MLM and sending the retrieved patient data as payload. This payload is structured as an Arden Syntax list containing key–value pair objects. While the value may be of any type, each key has to be a string. The executed MLM uses received patient data as input to traverse the implemented decision tree. Whenever the decision tree checks for conditions, the parameter list is used to look up the required data. If the required data are available, the process continues and

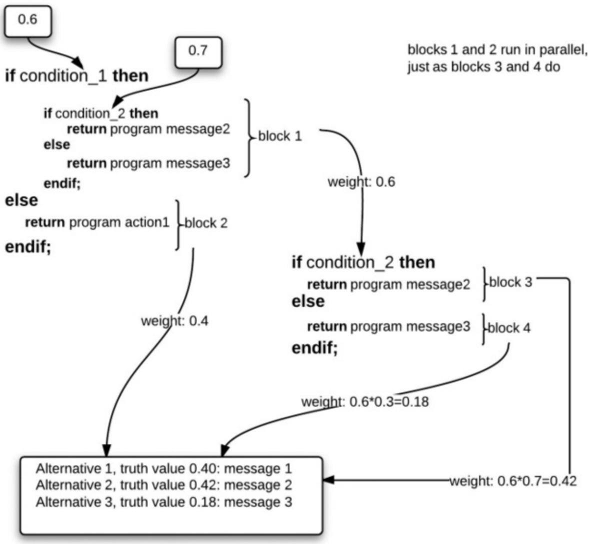

Figure 1. This figure describes how fuzziness is computed by the Arden Syntax engine. When evaluating an if-then-else statement for a proposition, which is neither true nor false, represented as a value greater than zero and less than one, the engine evaluates both branches simultaneously. This is done for every if-then-else statement in an MLM, resulting in multiple final outcomes, each with its own computed degree of compatibility. Combined propositional uncertainties (e.g., not, and, or) are calculated according to the HL7 Arden Syntax specification (which at this point is derived from fuzzy logic).

recommendations are generated. If the required data are not available, a question object asking for further information is generated, while the current execution of the MLM stops. In a third step, the Arden Syntax server sends the generated answer back to the client as a transfer object (see Figure 2) with a predefined structure.

The client generates the user interface utilizing this transfer object during a fourth step. In case of user interaction, all additional patient data provided during this interaction is stored in the database before the entire process is repeated. This permits the user to stop the decision support process at any time and resume whenever new data are available. Thus, the system is able to support guidelines spanning long periods of time, such as multiple patient consultations.

The client does not have to know anything about the executed MLM as long as the structure of the transfer object is known. The latter is kept simple and very general in order to permit the implementation of any medical guideline. The result list contains results and recommendations in text format, generated by the MLM during its previous execution, and can be displayed by the client in a straightforward manner. Question objects constitute data required to further traverse the implemented decision tree.

Transfer object
result: A list of strings containing recommendations generated by the CDSS.
next_questions: A list of question objects gathering more patient data.
q_label: Represents the actual question as a string (text).
q_type: Describes the type of a question (e.g., Boolean, fuzzy).
q_info: Additional information useful to answer the question.

Figure 2. Actual structure of the transfer object using JavaScript Object Notation [9], which is generated by an MLM, executed by the Arden Syntax server, and used to build the graphical user interface for the CDSS client, e.g., result{"Check patient for carditis"}, next_question{q_label{"Carditis"}, q_type{fuzzy}, q_info{"description of carditis"}}.

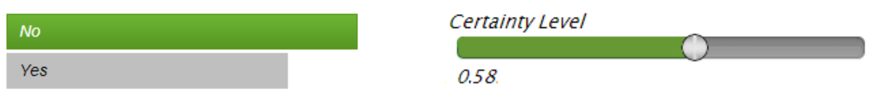

Figure 3. Graphical user interface elements: Buttons to represent the Boolean question type, anticipating either “yes” or “no” as the answer. Sliders represent the fuzzy question type, permitting clinicians to specify the degree to which signs presented by a patient match certain symptoms of a disease. The entire real unit interval [0,1] is available, with zero representing false and one representing true.

A question object contains a question type, a label, and explanatory details. With this information the client determines the appearance of the actual graphical user interface. Resolved results and recommendations are displayed and, if question objects exist, additional input fields are generated. Different layouts may be used in querying the question type (see Figure 3). The CDSS prototype employs two question types: Boolean and fuzzy. While Boolean describes a question for which only the answers “yes” or “no” are expected, fuzzy describes a question for which the user has to specify the degree of certainty to which specific situations or symptoms apply [10].

Using all these concepts, it is the MLM representation of a guideline that defines the client’s user interface and its elements for user interaction. Finally, if a guideline has to be updated, MLMs are the only elements affected by these changes.

3. Implementation

To demonstrate the proposed framework, we implemented a guideline for the diagnosis and treatment of Lyme borreliosis. Lyme borreliosis, also known as Lyme disease, is an illness transmitted by ticks. It is caused by the bacterium *Borrelia burgdorferi sensu lato*, and was discovered as an independent illness by Allen Steere et al. according to [11] in 1975. The main challenge in diagnosing Lyme borreliosis is that its signs and symptoms differ from person to person, and no composition of symptoms is pathognomonic [12]. The existence of several medical guidelines is another difficulty. These different guidelines focus on various aspects of the patient’s examination, diagnostic and therapeutic procedures. Despite their similar appearance the guidelines differ in terms of detail.

Three Lyme borreliosis guidelines, created by the German Society for Dermatology [13], the Swiss Society for Infectious Diseases [14], and an Austrian expert on Lyme borreliosis, were selected to serve as the starting point for the CDSS prototype. A single combined guideline was created. As a first step, all three guidelines were transformed into decision trees represented by flowcharts. Using this style of knowledge representation, we were able to identify ambiguities. Missing information in each guideline became manageable. The implementation promotes the comprehensibility of the represented decision-making process and clearly shows whether all of its parts are covered in sufficient detail or not covered at all. Besides facilitating the identification of ambiguities and contradictions within medical guidelines, the use of detailed flowcharts as intermediate representation was found to simplify the transformation of medical guidelines into computer-interpretable Arden Syntax. As a second step, these flowcharts were used to analyze similarities. This step disclosed contradictions in guideline statements. In case of contradictions, medical domain experts involved in the project discussed the problem and agreed on a decision. As a final step, all three guidelines were merged. The details of one guideline were used to fill gaps in others. The final Lyme borreliosis decision tree was used to implement corresponding MLMs.

The CDSS prototype also provides a range of predefined entry points for the clinician to choose from during the creation of a patient ID database entry. Since the medical guideline is implemented as a decision tree, it is necessary to provide a means of skipping parts of this tree which would be irrelevant for a specific case. The patient ID is used to save and retrieve relevant data for decision support with reference to a specific patient.

4. Results

The implemented CDSS prototype for Lyme borreliosis demonstrates the manual process of transforming text-based medical guidelines into Arden Syntax MLMs. These can be used in our developed platform without adapting a single line of the system code. Any MLM following the given transfer object specification works with the implemented system. The CDSS prototype (see Figure 4) can be accessed by any device capable of executing an internet browser.

Using the newest feature of Arden Syntax—data processing involving fuzzy logic—the Lyme borreliosis prototype allows clinicians to enter clinical data in a more natural way. Instead of merely processing sharply bounded "yes" or "no" answers, this platform is able to compute linguistic and propositional uncertainty, allowing clinicians

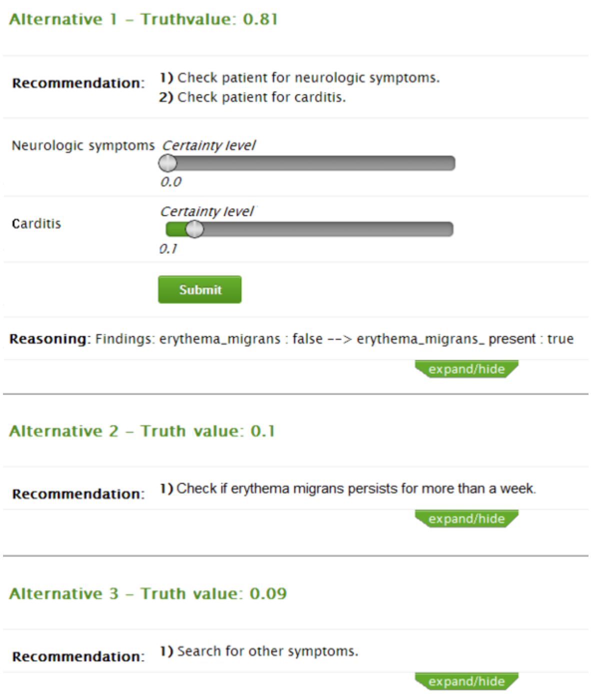

Figure 4. A graphical user interface generated using the transfer object which was returned by an MLM, executed by the Arden Syntax server. When a clinician provides fuzzy data as input, the Arden Syntax server returns all recommendations as alternatives which match entered patient data at least to some extent. However, each alternative is weighted according to how well it fits the provided data.

to select degrees of certainty as to which symptoms apply. In doing so, the system can take every possibility into account and is able to generate results according to the extent they match the provided patient data. Complex situations are no longer oversimplified by providing a single recommendation.

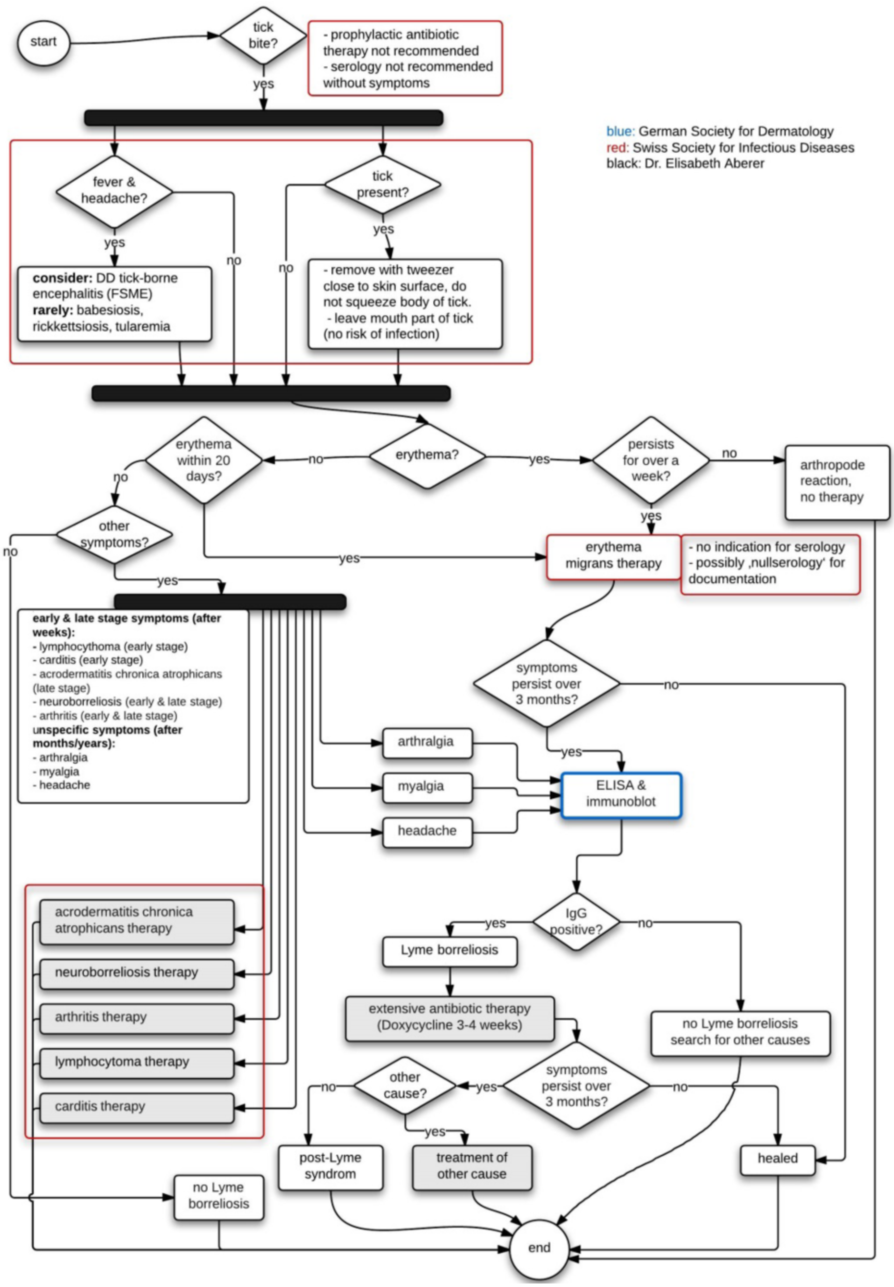

Figure 5. Excerpt of a Lyme borreliosis guideline created by analyzing and combining three guidelines [12, 14, 15], using their strengths to compensate their mutual weaknesses.

We also showed a method for manual transformation of multiple medical guidelines covering the same subject into a computer-interpretable language (e.g., Arden Syntax). Flowcharts were used to analyze each guideline individually and compare them with each other, subsequently merging the available medical knowledge into a single guideline. The combined Lyme borreliosis guideline (see Figure 5), encompassing medical knowledge provided by the three guidelines [12, 14, 15], is a detailed decision tree covering all aspects of the diagnosis and treatment of Lyme borreliosis. As many Lyme borreliosis guidelines focus on individual aspects of the disease, we found no guideline covering all aspects in adequate detail.

5. Discussion

CDSSs are by no means commonplace although they would certainly improve the quality of clinical practice. This is due to the absence of common medical standards, strict legal frameworks, and CDSSs not being well integrated into routine medical workflows. Current CDSSs have to be linked tightly to specific clinical information systems in order to exploit their full potential [15]. Sharing such CDSSs with other institutions involves significant effort and resources.

Our clinical decision support platform permits the user to focus on managing medical knowledge rather than adapting the surrounding system to every change in the knowledge base. As Arden Syntax is an HL7 standard, institutions are able to share MLMs with one another and upload them to their Arden Syntax servers. Given adequate security measures, other institutions may be granted access to the web interface via the internet. Additionally, its ability to access the hospital network from any location promotes smooth integration into clinical routine, making decision support available when it is needed. Moreover, the clients are always up-to-date by default, as all medical knowledge is stored centrally on the Arden Syntax server.

Like SANDS [16], our platform is centralized and supports modularity. MLMs may be developed as self-contained modules. One MLM may also be called from another. Platform components are divided into front-end and back-end, and may be deployed on separate servers. Furthermore, the costs and risks of trying new decision support modules are reduced because MLMs can be uploaded to and deleted from the Arden Syntax server at any time. In contrast to SANDS, our platform uses Arden Syntax and provides decision support only on request, using the client interface to enter patient data manually in a stepwise manner. However, data can be read from local electronic health record system databases using Arden Syntax curly brace expressions. Further, the user can view decision support rules directly, which is not possible in SANDS.

Our Lyme borreliosis CDSS prototype is one of the few systems attempting to cover all aspects of the disease in adequate detail. Other systems [17, 18] or rule sets [19] cover individual parts. Unlike the Electronic Medical Record Support for Public Health platform [17], which analyzes electronic medical records provided by primary care providers for events of public health interest (e.g., Lyme borreliosis, diabetes), our platform is focused on individual patient care. Nevertheless, it is possible to implement MLMs analyzing patient data for events of public health interest by coupling the system to specific clinical information systems.

The workflow of the CDSS prototype was verified on six selected Lyme borreliosis cases. Some were provided by a dermatologist while others were compiled using data derived from the internet. An extensive clinical investigation will be needed to perform a comprehensive analysis of the effectiveness of the combined medical guideline as well as the usability and stability of the implemented framework.

References

[1] K.-P. Adlassnig, K. Fehre, Arden-Syntax zur Repräsentation und Verarbeitung medizinischen Wissens, *HL7-Mitteilungen* **30** (2012), 8–15.

[2] M. Samwald, K. Fehre, J. de Bruin, K.-P. Adlassnig, The Arden Syntax standard for clinical decision support: Experiences and directions, *Journal of Biomedical Informatics* **45**(4) (2012), 711–718.

[3] Health Level Seven International, Arden Syntax, http://wiki.hl7.org/index.php?title=Arden_FAQ#Q10, last access: 12.12.2013.

[4] Health Level Seven International, HL7 Standard, http://www.hl7.org/special/Committees/arden/products.cfm, last access: 19.12.2013.

[5] T. Vetterlein, H. Mandl, K.-P. Adlassnig, Fuzzy Arden Syntax: A fuzzy programming language for medicine, *Artificial Intelligence in Medicine* **49**(1) (2010), 1–10.

[6] K. Fehre, K.-P. Adlassnig, *Service-Oriented Arden-Syntax-Based Clinical Decision Support*, in: Proceedings of eHealth2011. Austrian Computer Society, Vienna, 2011. pp. 123–128.

[7] M. Achour, F. Betz, A. Dovgal, N. Lopes, H. Magnusson, G. Richter, D. Seguy, J. Vrana, et al., PHP Handbuch, http://www.php.net/manual/de/, last access: 2.12.2013.

[8] J. Duckett, *Beginning HTML, XHTML, CSS and JavaScript*, Wiley Publishing, Inc., Indianapolis, 2010.

[9] D. Crockford, Introducing JSON, http://www.json.org, last access: 26.8.2013.

[10] B. Kosko, Fuzziness vs. probability, *International Journal of General Systems* **17** (1990), 211–240.

[11] H. Prautzsch, P.R. Von Baehr, B. Wilderich, H. Bennefeld, W. Berghoff, U. Everth, H.-P. Gabel, N. El-Mahgary, W. Großmann, W. Heesch, D. Hillscher, P. Hopf-Seidel, B.-D. Huismans, W. Klemann, M. Krahl, B. Krone, J. Merkel, K.E. Müller, U. Neubert, C. Nicolaus, O. Nolte, D. Rosin, A. Schwarzbach, C. Uebermuth, B. Weitkus, Diagnostik und Therapie der Lyme-Borreliose − Leitlinien der Deutschen Borreliose-Gesellschaft, http://www.borreliose-gesellschaft.de/Texte/Leitlinien.pdf., last access: 10.12.2013.

[12] R. Nau, H.-J. Christen, H. Eiffert, Lyme disease – current state of knowledge, *Deutsches Ärzteblatt International* **106**(5) (2009), 72–82.

[13] H. Hofmann, E. Aberer, H. Bruckbauer, V. Fingerle, M. Mempel, R.R. Müllegger, A. Plettenberg, M. Simon, R. Wallich, Kutane Manifestationen der Lyme Borreliose, *Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften Leitlinien-Register* **1**(013/044) (February 2009), 1–12.

[14] J. Evision, C. Aebi, P. Francioli, O. Peter, S. Bassetti, A. Gervaix, S. Zimmerli, R. Weber, Abklärung und Therapie der Lyme-Borreliose bei Erwachsenen und Kindern. Empfehlung der Schweizerischen Gesellschaft für Infektiologie Teil 2: Klinik und Therapie, *Schweizerische Ärztezeitung* **86**(42) (2005), 2375–2384.

[15] K. Kawamoto, J. Jacobs, B.M. Welch, V. Huser, M.D. Paterno, G. Del Fiol, D. Shields, H.R. Strasberg, P.J. Haug, Z. Liu, R.A. Jenders, D.W. Rowed, D. Chertcoff, K. Fehre, K.-P. Adlassnig, A.C. Curtis, *Clinical Information System Services and Capabilities Desired for Scalable, Standards-Based, Service-oriented Decision Support: Consensus Assessment of the Health Level 7 Clinical Decision Support Work Group*, in: AMIA Annual Symposium Proceedings 2012, pp. 446–455.

[16] A. Wright, D.F. Sittig, SANDS: A service-oriented architecture for clinical decision support in a national health information network, *Journal of Biomedical Informatics* **41**(6) (2008), 962–981.

[17] M. Klompas, J. McVetta, R. Lazarus, E. Eggleston, G. Haney, B.A. Kruskal, W.K. Yih, P. Daly, P. Oppedisano, B. Beagan, M. Lee, C. Kirby, D. Heisey-Grove, A. DeMaria Jr, R. Platt, Integrating clinical practice and public health surveillance using electronic medical record systems, *American Journal of Preventive Medicine* **42**(6S2) (2012), 154–162.

[18] O.K. Hejlesen, K.G. Olesen, R. Dessau, I. Beltoft, M. Trangeled, Decision support for diagnosis of Lyme disease, *Studies in Health Technology and Informatics* **116** (2012), 205–210.

[19] K.A. Cohn, A.D. Thompson, S.S. Shah, E.M. Hines, T.W. Lyons, E.J. Welsh, L.E. Nigrovic, Validation of a clinical prediction rule to distinguish Lyme meningitis from aseptic meningitis, *Pediatrics* **129** (2011), e46–e53.