Evidence-Based Medical Recommendations for Personalized Medicine [1]

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Abstract: Medical consultants face increasing challenges in keeping up-to-date with the rapid development of new treatments and medications. Evidence-based medical guidelines (EBM) are provided by healthcare institutions to support consultants in clinical decision making. However, due to time constraints in their daily routine, consultants rarely find time to research and cross-check medical decisions with such guidelines. This paper presents an approach for personalized EBM recommendations, tailored to each particular patient, without any research effort by the consultant. It is available at the point-of-care and requires electronic health records (EHR) to be semantically linked with EBM guidelines.

1. Introduction

Due to the rapid development of new treatments and medications, along with heavy workloads and limiting time constraints in their daily schedule, medical consultants face the challenge of continuously keeping up-to-date with the latest advances in clinical practice. In addition, treatment methods quickly become obsolete, change or are replaced by newly developed protocols (Marchant and Lindor, 2013).

Personalized medicine aims to tailor medical decisions, practices, interventions or products to the individual patient based on their predicted response or risk of disease (Academy of Medical Sciences, 2015). Evidence-Based Medicine (EBM) is a way of evaluating treatment in clinical practice. It is used to get the best available research for diagnosis and treatment to improve decision making (Masic et al., 2008). This is done by various types of research methods like systematic reviews, randomized controlled trials, meta-analysis, case report or practice guideline analysis (Hung et al., 2015). Most existing clinical decision support systems focus on providing evidence-based medical information, guidelines and summaries, written by networks of medical experts. By constantly updating information, these guidelines and summaries present the current state of medical best practice (Antes et al., 1998). But

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consultants rarely have time to read and navigate through guidelines and such services. Also summaries and guidelines are sometimes written in a confusing way, which cost additional time and makes it more difficult to understand the required information (Obst et al., 2015).

This paper presents an approach for personalized EBM recommendations, tailored to each particular patient, without any research effort by the consultant. It is available at the point-of-care. This combines the advantages of personalized medicine and EBM, while alleviating the problems with current EBM solutions. We present the concept and prototypical implementation of a personalized EBM service which semantically links electronic health records (EHR) with published EBM guidelines. This service can be integrated into an EHR application as module of a Clinical Decision Support System (CDSS) (Kawamoto et al., 2005).

2. Problem Statement

Based on intense consultation with clinicians involved in the treatment of melanoma, and in accordance with Idelhauser et al. (2016), we have identified the following requirements for providing an EBM solution for CDSS:

1. **Functional Requirements**
   - 1.1. *EBM recommendations*: The consultant shall get evidenced-based medical recommendations for treating cancer patients.
   - 1.2. *Personalized*: The information provided shall be tailored to the medical condition of a particular patient, based on their EHR.
   - 1.3. *Pro-active*: The EBM recommendations shall offer information pro-actively without additional data entry by the consultant.
   - 1.4. *Easily comprehensible*: The EBM recommendation service shall provide information at the point of care and it should be possible to quickly retrieve more detailed information.
   - 1.5. *Non-interfering*: The EBM recommendations shall not interfere with the consultant's EHR workflow.

2. **Non-Functional Requirements**
   - *2.1. Usability:* The EBM recommendations shall be intuitive to use and self-explanatory.
   - 2.2. *Performance*: The application shall allow users to work in their own pace in a pleasant way; In particular, response times for all interactions with the EBM recommendations shall be less than 1s.
   - 2.3. *Maintenance*: Maintaining changes in EBM recommendations data shall induce only a small effort.
   - 2.4. *Extensibility*: The ongoing extension of the EBM recommendations with new information sources shall be facilitated with moderate implementation effort.

3. A Personalized EBM Recommendation Service

3.1. User Interaction Concept

We illustrate the user interaction concept of the personalized EBM recommendation service by means of an example in melanoma treatment. Fig. 1 shows anonymised summary data of a melanoma patient from an EHR application.

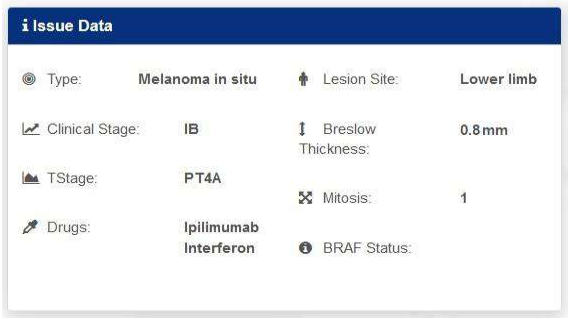

Figure 1: Patient-related issue data

In this example, the patient suffers from melanoma in situ at stage IB, with a Breslow thickness of 0.8 mm. Based on the EHR data, without interaction by the consultant, the relevant page of the NCCN EBM guideline (National Comprehensive Cancer Network, 2017) for melanoma treatment is retrieved (Fig. 2).

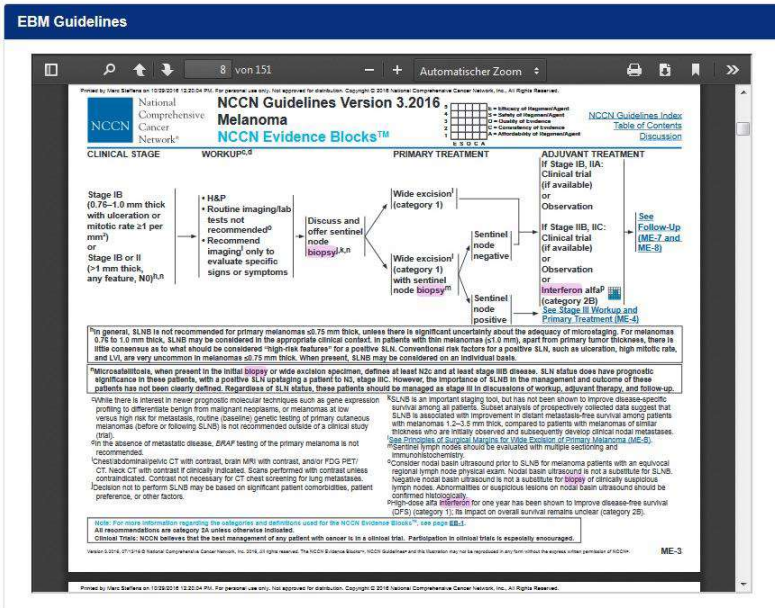

Figure 2: EBM recommendation

The guideline is structured as a decision tree with the relevant path (Stage IB, Breslow thickness 0.67 - 1.0 mm) displayed. Appropriate diagnosis and treatment procedures are recommended. Terms matching the EHR, e.g., interferon, are highlighted. The personalized EBM Guideline service is part of a CDSS which the consultant may or may not open when

working with the EHR. If interested, the consultant may read footnotes and follow hyperlinks for more details.

3.2. Information Sources

EBM recommendations are edited and published regularly by various organisations and companies. Tab. 1 gives an overview of prominent EBM information providers as a result of a survey we conducted.

Name	Description	API	Access	Volume
BMJ Best Practice	Evidence-based information to offer step-by-step guidance on diagnosis, prognosis, treatment and prevention.	yes	subscription	undisclosed
DynaMedPlus	Evidence-based clinical overviews and recommendations. Content updated daily. Also offers calculators, decision trees and unit and dose converters.	yes	subscription	> 3,200 topics and > 500 journals
EBMeDS	Platform-Independent web service CDSS with EBM module.	yes	commercial	undisclosed
Medscape / eMedicine	Largest clinical knowledge base available freely. Articles updated yearly. Also available as mobile application.	no	free, registration required	~6,800 articles
NCCN	Guidelines for treatment of cancer by site offering decision trees. Compiled by panels of experienced medicians.	no	free, registration required	~60 documents
Physician Data Query	Cancer database from the U. S. *National Cancer Institute*. Contains peer-reviewed information on cancer treatment in the form of summaries for patients and professionals.	no	public	Only cancer domain
UpToDate	Popular evidence-based POC tool for a wide range of disciplines but targeted on internal medicine. Extensive peer-review process to ensure accurate and precise recommendations	yes	subscription, some articles free	~8,500 topics

Table 1: EBM information providers

Some organizations like the US National Cancer Institute or the National Comprehensive Cancer Network provide guidelines for free. Commercial information providers like Wolters Kluwer (UpToDate) or EBSCO (DynaMedPlus) provide paid access to a large number of EBM guidelines published world-wide.

All information providers provide web access with full-text search. Some providers offer an application programmer's interface (API) for performing full-text search. However, to the best of our knowledge, no information provider offers an API for matching conditions, e.g., Breslow thickness 0.67-1.0 mm. Such conditional matching logic is required for the personalized EBM recommendation service.

3.3. Software Architecture

The personalized EBM recommendation service is part of a Clinical Decision Support System (CDSS), which is integrated into an EHR application. The application is organized as a three layer architecture where each layer consists of components that encapsulate logically separable units. See Fig. 3.

3.4. EHR Data Extraction

First, relevant the EHR data to be mapped to EBM guidelines are extracted from the EHR. In the melanoma example, this includes EHR attributes such as issue type, clinical stage, tumor stage, Breslow thickness, medication, ulceration, etc.

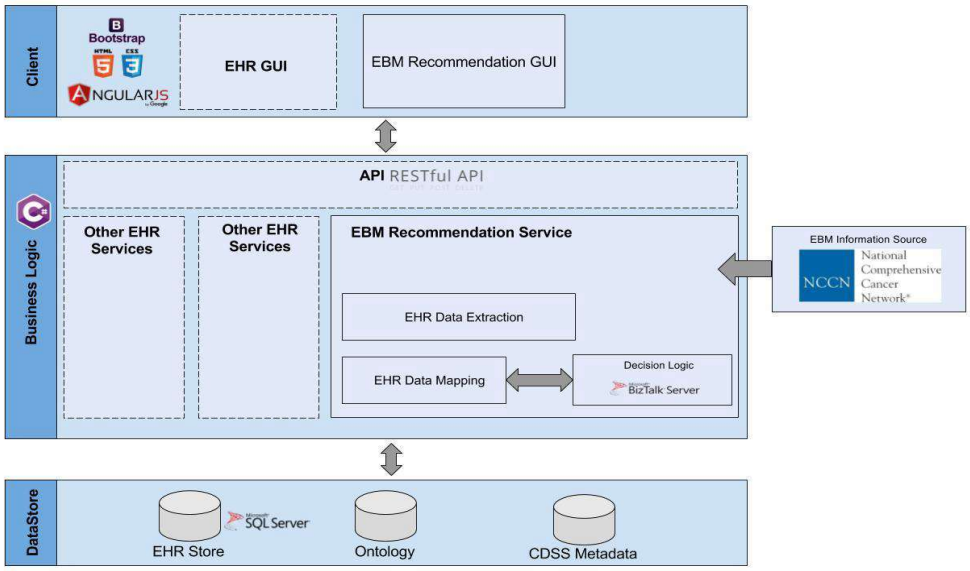

Figure 3: System architecture

3.5. Decision Logic

Identifying sections of EBM guidelines which are relevant for a particular patient under treatment requires more than full text search. Consider the example of Breslow thickness 0.8. Searching for the string “0.8” in the text of the NCCN guidelines will not match the relevant page ME-3, since on this page, the condition is formulated as “0.67-1.0 mm thick”. Therefore, some explicit decision logic is required for matching extracted EHR data to sections of the EBM guidelines. See Fig. 4 for an example rule.

Here, the following rule is shown: “If clinical stage is IB and Breslow thickness is between 0.76 - 1.0 mm, then section ME-3 on page 8 is relevant”. This rule is edited using a business rule composer (BRC), here MS BizTalk (Microsoft BizTalk, 2017).

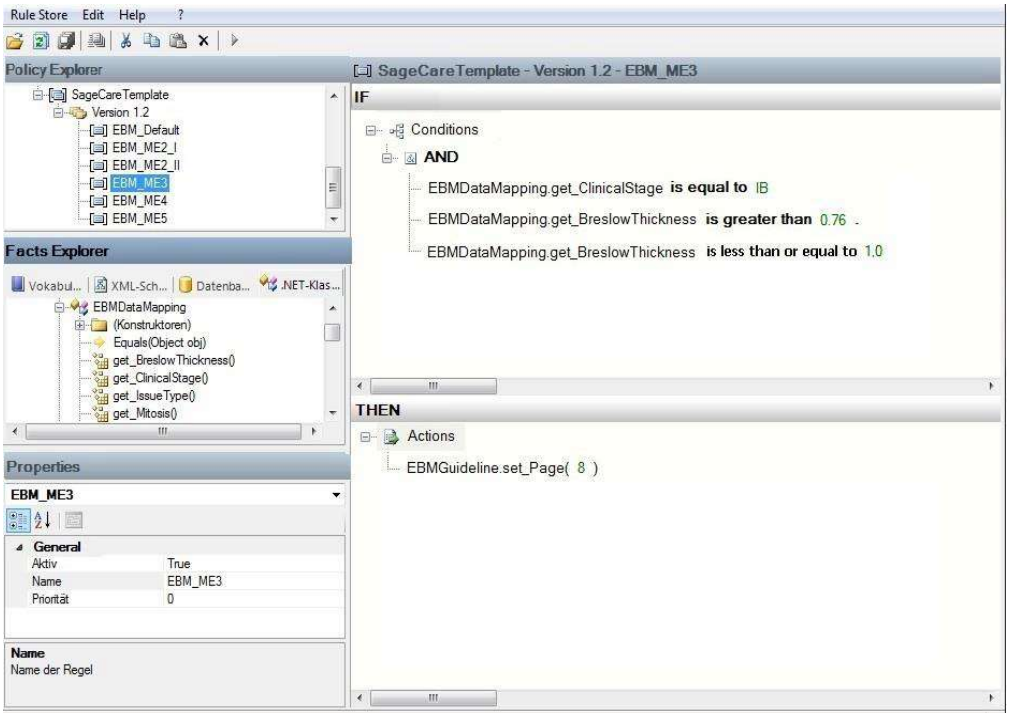

Figure 4: Example rule in business rule engine (MS Biztalk Server)

Applying the rules with the extracted EHR data as input in a business rule engine (BRE) will match the relevant section of the EBM guidelines which can then be displayed to the consultant in the CDSS GUI.

Using a BRC in combination with a BRE has advantages over coding the decision logic in a conventional programming language. It allows adding or modifying business rules by trained medical administrators whenever new or modified EBM guidelines are published.

3.6. Prototype Implementation

The EBM recommendation service has been implemented prototypically as part of an EHR application for melanoma treatment (Humm and Walsh, 2015; Beez et al., 2015; Idelhauser et al., 2016). The application is implemented in C# using .NET and MS SQL Server on the server side, and in HTML5 / CSS / JavaScript on the client side, using Bootstrap and AngularJS.

As a data source for the personalized EBM recommendation service, the NCCN guidelines have been selected. Microsoft BizTalk is as BRC / BRE. The HTML Inline Frame (Iframe) functionality for embedding documents is used to display the NCCN PDF files. Medical terms extracted from the EHR are highlighted in order to attract the consultant's attention.

4. Evaluation

In this section, we compare the concept and prototypical implementation of the personalized EBM service with the requirements from Section 2. As defined in Requirement 1.1, the physician receives evidence-based medical recommendations for the treatment of his patient. These recommendations are based on the clinical condition of the patient, as the

recommendation is selected by using the particular patient's specific EHR data. This makes the concept *personalized* (1.2).

When the consultant opens the patient's EHR, the service automatically displays the appropriate EBM recommendation in the CDSS, without requiring the consultant to enter additional data. This makes the service *pro-active* (1.3).

Requirement 1.4 (*easily comprehensible*) depends on the EBM guidelines selected. The NCCN guidelines provide step-by-step diagnosis and treatment instructions. Detail information may be obtained following hyperlinks. The consultant may or may not decide to open the CDSS GUI. So, he or she is not interrupted in his clinical workflow (1.5 *non-interfering*).
Freeing the consultant from the need to actively search for EBM recommendations also improves *usability* (2.1).

When opening a patient's EHR, the relevant EBM guideline is matched in the background. In the current implementation, this may take up to 5s. As soon as the consultant opens the CDSS GUI, all interactions such as scrolling or following hyperlinks have a response time of less than 300ms (tested with Mozilla Firefox performance analysis), clearly meeting Requirement 2.2 (*performance*).

The NCCN guidelines are updated regularly to always reflect state of the art. However, we expect modifications which actually affect whole sections of the EBM recommendations and, hence, decision logic rules, to be rare. If such a change is necessary, the *maintenance* effort is low (2.3) due to the use of a BRC.

Replacing the EBM information provider, respectively adding a new information provider like UpToDate (2.4 *extensibility*), requires programming. Due to the modular structure of the system architecture, only adaptors need to be implemented. Depending on the API to be integrated, the effort is estimated to be up to a few hundred lines of code. This could be considered moderate.

5. Related Work

(Kwag, 2016) evaluated 26 web-based point-of-care information sources in a study. Some of the most valued systems in terms of scope, evidence and quality were, among others, *DynamedPlus*, *UpToDate* and *BMJ Best Practice*. The sources were characterized by the fact, that they offer extensive evidence-based information to assist clinicians in decision-making. They all work in a similar way: in order to retrieve information, consultants can use full-text search (Ebsco Health, 2017; BMJ Best Practise, 2017; Wolters Kluwer, 2017). A condition-based search is not offered. In particular, semantic matching of EHR data with EBM guidelines as described in this paper is not possible.

IBM Watson is a system capable of answering questions posed in natural language. It has been adapted for various application domains, including health care and in particular oncology (IBM Watson Health, 2017). To keep up-to-date, Watson is constantly updated and trained with new information. Consultants can use the corpus of knowledge by asking relevant questions, using

a detailed search mask. However, automatic matching of relevant EBM guidelines based on the EHR is also not provided.

6. Conclusions and Future Work

EBM is a good method to assist physicians in decision-making, which results in an improved treatment of patients (Borgerson et al., 2005). So far, there are a number of systems and approaches to support consultants with EBM, and development is fast-paced. However, it is a great challenge to integrate these systems sensibly into the workflow of a clinician whose daily workload is high (Fowler et al., 2014). So far, adoption of EBM in clinical practice is low.

In this paper, we have presented a concept and prototypical implementation of a personalized EBM service to alleviate those issues. The focus was therefore on the usability of the service, in order to allow consultants to retrieve information they need without having to actively search in the system. For this purpose, the data extracted from the EHR was used to semantically match EBM guidelines and present the relevant sections to the consultant.

The EBM recommendation service has been integrated into an EHR application for melanoma treatment as part of a CDSS. Towards this end, future work is required. A comprehensive analysis with consultants in the field needs to take place. It is planned to put the EHR application including CDSS into productive use at hospitals as a commercial pilot system. This work may eventually help consultants improve patient care.

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