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Evicase: An Evidence-based Case Structuring Approach for Personalized Healthcare

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Abstract. The personalized medicine era stresses a growing need to combine evidence-based medicine with case based reasoning in order to improve the care process. To address this need we suggest a framework to generate multi-tiered statistical structures we call *Evicases*. Evicase integrates established medical evidence together with patient cases from the bedside. It then uses machine learning algorithms to produce statistical results and aggregators, weighted predictions, and appropriate recommendations. Designed as a stand-alone structure, Evicase can be used for a range of decision support applications including guideline adherence monitoring and personalized prognostic predictions.

Keywords. Decision Support, Personalized Medicine, Clinical Guidelines, Clinical Business Intelligence, Machine-Learning Algorithms.

Introduction

With the increased adoption of evidence-based medicine, clinical guidelines have emerged as the most widespread method used for clinical decision support systems (CDSs). Such guidelines apply evidence-based insights for treating groups of patients defined by some fixed clinical criteria, to which we refer as a clinical presentation. These guidelines are typically developed by clinicians, and are mostly based on comparative clinical trials that demonstrate statistical significance between treatment options or placebo [1].

The nature of the guideline development process presents many challenges. First, as clinical trials can have many exclusion criteria, the efficacy and side effects of a particular treatment cannot necessarily be generalized to different settings of the same disease. Second, due to lack of data, many guidelines do not consider the personalized genetic make-up of a patient. Another major challenge of the guideline development process is to keep up with the rapidly increasing pace of new biomedical discoveries. Thus, next generation CDSs must accept the challenge of bringing the latest biomedical discoveries to the bedside of a patient in a rapid and personalized manner.

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Although personalized medicine is still in its infancy, individual genetic profiles have begun to be used to guide patient care [2]. The use of personalized medicine is expected to grow considerably over the next decade, with genetic profiling expected to be used regularly both for diagnostics and to guide treatment. Thus, each time a new medical technology arises, clinicians may need evaluate its efficacy on different genetic compositions and consider its use on a per-patient basis [3].

In light of the emergence of the personalized medicine era, combining evidence-based medicine with personal case-based reasoning in order to improve the care process is increasingly important. To this end, we developed the *Evicase* (Evidence-based case) structure. The purpose of Evicase is to supply clinical decision makers with a holistic view of all aspects associated with the clinical case of a specific patient. Evicase integrates medically-established evidence based on controlled clinical trials along with novel data-driven clinical insights originating from analyzing vast amounts of patient-specific data present at the care delivery organization (CDO). Evicases are meant to be utilized by decision support systems within CDOs. By exploiting the vast amount of patient records accumulated in the clinical systems of the CDO together with the clinical knowledge and experience of the CDO staff, Evicase offers enhancements over traditional guideline-based decision methods.

1. Methods

In this work we suggest a framework and methodology for Evicase construction and utilization. Our framework constructs Evicases as a three-tiered structure that combines available knowledge and guidelines with descriptive and predictive analytics. The tiers are illustrated in Figure 1 and described below.

1) **Knowledge-guided Analysis** (Figure 1, see T1): T1 provides the profiling for a specific patient's presentation, supplying guideline-based presentation-specific treatment options for the patient. It interacts with external resources and encapsulates the guidelines and established evidence within the Evicase for later use by the decision support application.

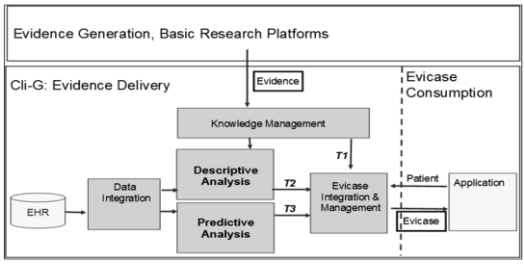

Figure 1. Evicase construction and consumption

2) **Descriptive Analysis** (Figure 1, see T2): T2 incorporates insights generated from statistical retrospective analysis of patient records within the CDO. In particular, it shows the distribution of optional recommended treatments and their associated outcomes among the patient population. Systematic analysis of extensive feature combinations, weighting their relative contribution to the treatment allocation as suggested in [7] may reveal a CDO's implicit rules and physicians' best practices, which may help optimize the treatment for a specific patient. T2 further analyzes the

most informative features regarding guideline deviation decisions, which may assist in guideline personalization and refinement.

3) **Predictive Analysis** (Figure 1, see T3): T3 applies predictive models and machine learning algorithms to patient records available at the CDO in order to provide patient-specific prognostics. Analyzing a patient's clinical data in the context of similar cases may provide prospective outcome insights, which in turn can be used for treatment recommendation and lead to improved patient care.

2. Results

Since 2006, the Fondazione IRCCS Istituto Nazionale dei Tumori di Milano (INT) has been supplying the Region of Lombardy Oncology Network (ROL) with clinical discharge letters containing both coded and free-text data [4]. Based on this clinical data repository, we developed an Evicase-based decision support system for analyzing the treatment of Soft Tissue Sarcoma (STS) patients. Our system analyzed discharge letters of 346 STS inpatients treated at INT between 2006 and 2011. The patients' episodes span 390 distinct presentations, 493 treatment programs and 734 specific treatments. Our framework generated a complete three-tiered Evicase delivered to two different decision support applications, namely i) an application assisting the physician at point of care when examining a specific patient's case and ii) an organizational guidelines adherence application that offers the clinicians an aggregative view into recommended treatments, actual treatments, adherence levels and achieved outcomes. (see Figure 2).

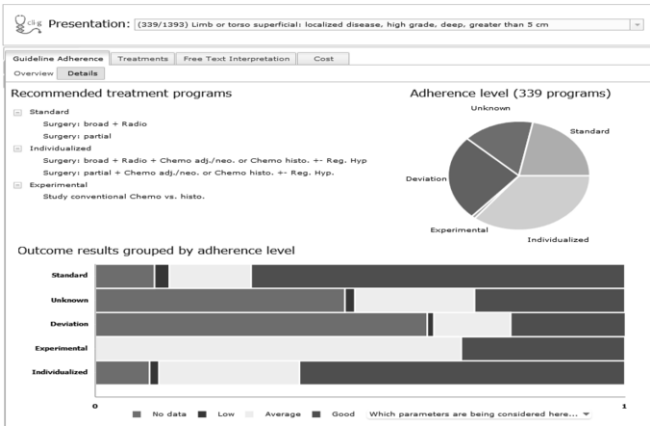

Figure 2: Snapshot of decision support app showing the distribution of patients among treatment options.

Evicase's T1 is based on a classifier dictated by INT's latest guidelines [5]. INT's clinical practice defines the set of guideline-recommended treatments for each presentation, and furthermore allows physicians to deviate from the guidelines as they find appropriate. T1 classifies each case into one of 27 possible STS presentations and indicates the recommended treatment based on INT applicable guidelines. T1 further adds the adherence level — standard, individualized, experimental or deviation, to each provided treatment (see Figure 2).

Evicase's T2 retrospectively analyzes the clinical records of the patients that are classified as similar according to INT guidelines. It then indicates the distribution of

the provided treatments (Figure 2, pie chart), as well as their associated outcomes. It further uses machine learning techniques to suggest refined patient-similarity metrics, yielding more fine-grained similar patient groups. T3 further predicts the probability of each outcome for different possible treatments based on the outcomes observed among the group of the most similar patients and indicates the most effective treatment for an examined case. To alleviate possible bias in outcome prediction due to bias in treatment allocation, we limit the prediction to cases for which it is less harmful [6]

To demonstrate the use of Evicase, consider a patient classified as belonging to the following presentation: 'Limb or Torso Superficial: Localized, High Degree, Deep, Greater than 5cm'. INT guidelines recommend four possible treatment options for this clinical presentation: two standard treatments that fully adhere to the guidelines, namely broad or partial tumor excision with complementary radiotherapy, and two individualized treatments allowing the physician to add a complementary chemotherapy based on the patient's individual characteristics. In addition, the physician may recommend a clinical trial if possible, or elect to deviate from the guidelines for any particular reason.

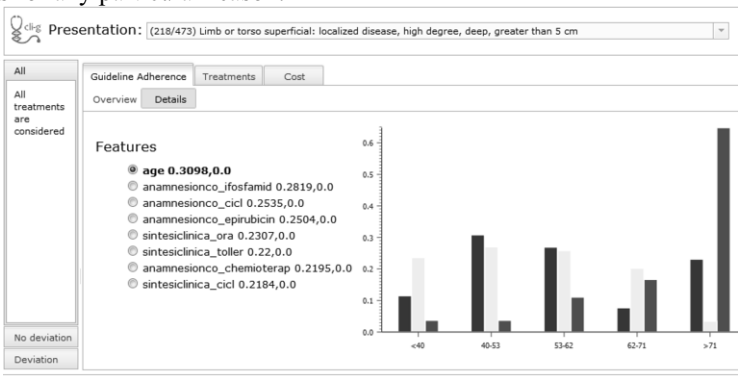

Figure 3: Treatment distribution along patient age: standard treatment in green, individualized treatment in yellow and deviation in red

Using retrospective analysis of the actual treatments given to patients having the same presentation, Evicase's T2 identifies i) the percentage of patients treated with each treatment (25% standard treatments; 40% individualized treatments) together with the percentage of patients who received therapy other than one of the recommended treatments (12% deviation; 23% unknown) as depicted in Figure 1, and ii) the distribution of outcomes within each of these treatment groups.

T2 further highlights the clinical characteristics that best differentiate these groups. T2's descriptive analysis identified patient age as one of the most significant differentiating features (see Figure 3). T2's analysis clearly shows that physicians tend to prescribe individualized treatment or deviate from the guideline while treating younger patients.

Finally, T3's statistical-analysis aims to predict the prognosis of a patient by considering the outcome of different treatments given to similar patients as identified in T2, e.g., to younger patients having the same presentation.

The above example shows how combining all of Evicase's analyses and insights into a holistic structure can lead to improved patient outcome by refining guideline recommendations for patients with specific clinical characteristics, by identifying

customary treatment for identified patient groups, and by revealing reasons for cases of deviation successes.

3. Discussion

Our work aims at providing enhanced patient care through the development of methods, models, and software components that enable computer-based clinical decision support. To this end we introduced the concept of Evicase and suggested an implementation framework. Designed as a standards-based, three-tiered framework, Evicase provides physicians with various means to retrospectively analyze care processes and results and to prospectively answer questions regarding an individual patient. The core value of the Evicase approach lies in providing a single coherent framework for integrating classical evidence-based insights stemming from existing clinical knowledge with additional clinical insights revealed by data-driven statistical mining algorithms.

We intend to further develop Evicase in various clinical domains aside from Soft Tissue Sarcoma, specifically in domains heavily influenced by genomics. We also intend to find new routes for Evicases to enable organization-wide optimizations to the current care process through activities such as cost/benefit analysis.

Evicase is designed to help physicians make more informed decisions when uncertainty arises regarding the various possibilities for diagnosis and treatment. Generated by mining clinical patient records within the CDO, Evicases can be used to generate decision support aids, providing clinical benefits for patients as well as cost reduction. In addition, Evicases generated at a specific CDO can bring value beyond the CDO boundaries; the stand-alone nature of the Evicase allows it to be exchanged with other CDOs, bringing new business potential while minimizing the problems associated with privacy regulations, as it is not the actual patient data being shared. This business model has the potential to drive a more productive healthcare economy by encouraging comparative effectiveness and pay-per-performance as a crucial step towards more effective care.

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