The Practice of Patient Centered Care: Empowering and Engaging Patients in the Digital Era
R. Engelbrecht et al. (Eds.)

doi:10.3233/978-1-61499-824-2-33

Weighting Experience-Based Decision Support on the Basis of Clinical Outcomes' Assessment

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Abstract. Technologies such as decision support systems are expected to help clinicians implement clinical practice guidelines (CPGs) with the aim of decreasing practice variations and improving clinical outcomes. However, if CPGs provide recommendations to improve patient care, they may fail to take into account actual clinical outcomes associated to the recommended treatment, such as adverse events or secondary effects. In this paper, we present a novel experience-based decision support approach applied to the management of breast cancer, the most commonly diagnosed cancer among women worldwide. Capitalizing on the clinical know-how of physicians and the modeling of patient's outcomes and toxicities in a computer interpretable way, we are able to discover new knowledge that helps improving patient-centered clinical care. This work is conducted within the EU Horizon 2020 project DESIREE.

Keywords. Experience-Based Clinical Decision Support, Patient-Reported Outcomes, Clinical Practice Guidelines, DESIREE

1. Introduction

Clinical practice guidelines (CPGs) have been proven to be reliable knowledge resources that reduce practice variations, improve the quality of care, and decrease costs [1]. Nevertheless, CPGs have some limitations and are often described as incomplete and ambiguous. These defaults may lead clinicians to not comply with guideline-provided propositions in certain clinical situations.

Guideline-based clinical decision support systems (CDSSs) have been proposed to help multidisciplinary tumor boards (MTBs) decide according to CPGs for cancer patients [2]. CDSSs are designed to improve clinical care and decrease medical errors by providing the best patient-specific propositions (based on patient's clinical parameters) in a short execution time. However, CDSSs efficiency rely on the

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knowledge formalized in guidelines. Consequently, they are not able to adapt to special clinical cases and to discover new knowledge related to toxicities (e.g. adverse events) or patient outcomes (e.g. ICHOM questionnaires [4]).

This paper presents an extension of usual guideline-based CDSSs by processing the experience acquired from previous cases. The approach allows the production of new knowledge and the assessment of its reliability by the evaluation of a set of clinical outcomes. This method has been applied within the EU project DESIREE, developed in the context of breast cancer management.

2. Clinical outcomes usage

When measuring the response of a patient to a given treatment, different kinds of outcomes could be considered. In the next subsections, we will analyze the main patient- and treatment-related outcomes.

2.1. Patient Reported Outcomes (PROs)

Patient reported outcomes (PROs) are subjective reports provided by patients that define how they feel about a health condition or the treatment they are following [5]. PROs reflect the information related to clinical signs and functional status. Moreover, they involve patients to directly retrieve the information related to symptoms, perceptions, and treatment tolerance in a subjective way. These outcomes are usually collected in the form of questionnaires, which include not only clinical measurements but also the satisfaction that patients may have with a given treatment and the quality of life resulting from it.

2.2. Adverse Events (AEs)

An adverse event (AE) is defined as "any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may not be considered related to the medical treatment or procedure" [6]. Identifying and estimating a treatment-related AE is not a straightforward task. In the one side, the information about adverse events comes usually from previously studied clinical cases, so not being totally applicable to new incoming cases. On the other side, the more reliably adverse events measurements come from around a decade old clinical trials [7]. Several efforts have been made to report and grade these adverse events. One of the most relevant systems is the one developed by the US National Cancer Institute (NCI) and known as the NCI Common Terminology Criteria for Adverse Events or CTCAE[2].

2.3. Treatment response outcomes

Treatment response outcomes are valuable in order to adapt the planned treatment regarding the patient response. Analyzing this response could guide clinicians when deciding to continue the therapy or to stop it based on a subjective medical judgement guided by the study of clinical parameters evolution [8]. Some of the guidelines that

[2] https://evs.nci.nih.gov/ftp1/CTCAE/About.html

define improvement, stagnation, or deterioration of the patient condition during treatments are RECIST[3] (Response Evaluation Criteria In Solid Tumors) and the World Health Organization (WHO) criteria.

3. Including outcomes into the reasoning process: Experience-based CDS

Using clinical outcomes as an evaluation tool of CPGs at a time *t* is vastly known [9]. Nevertheless, CPGs do not evolve continuously on the basis of upcoming cases and taking into account clinical outcomes as a source of knowledge. Thus, this information is lost for the decision-making process and CPGs need to be checked and updated offline. In this work, we propose to use various kinds of clinical outcomes to assess the confidence value (CV) of the new knowledge coming from non-guideline-compliant decisions, which is the basis for developing experience-based CDS.

Experience-based CDS relies on a Decisional Event (DE) structure that allows the exploitation of all the information related to a decision, including the clinical know-how and other parameters such as the toxicities and outcomes of a treatment. The DE structure is made of the following components:

1. The set of patient clinical parameters
2. The set of clinical statements expressed in a computer-interpretable format (i.e. IF-THEN rules)
3. The final decision made by clinicians which could be compliant or not with the recommendation coming from the clinical statements output
4. The treatment administrated after the decision has been made
5. The set of criteria considered by clinicians to justify a non-compliant decision
6. The set of clinical outcomes of the given treatment to be able to assess the success or failure of the final decision made [11]

New knowledge is acquired through the building of new rules, which the IF-part is the conjunction of the set of patient clinical parameters, enriched by the set of criteria taken into account by clinicians to decide, and the THEN-part is the decision made by clinicians. The CV of the newly generated rule is zero at the time it is built. Then, clinical outcomes are integrated to increase the CV of the rule when positive outcomes are collected after the application of the rule, and to decrease the CV of the rule when negative outcomes are observed. The principle of the CV computation of an expert-based rule *R* is as follows: CV_R = (# of positive outcomes of *R* – # of negative outcomes of *R*) / (number of observed outcomes as the result of applying the rule *R).*

When talking about patient's outcomes we make the following classification:

- Outcomes coming from AEs (e.g. the ones measured in the CTCAE)
- Outcomes coming from the treatment response (i.e. generic outcomes such as survival, local relapse, loco-regional relapse, metastasis, exitus related to the disease and exitus not related to the disease along with the neoadjuvant therapies clinical response if any)
- Outcomes reported from the patient (i.e. PROs)

[3] http://www.irrecist.com/recist/

4. Experience-based decision support and clinical outcomes assessment in the DESIREE project

The DESIREE project aims at providing the best available treatment options in the domain of breast cancer management using guideline-based knowledge, experience from previous cases, and patients' outcomes. Therefore, DESIREE overcomes the limitations of pure guideline-based CDSSs with new experience-based and clinical-outcome-adjusted rules that model the clinical know-how expressed in non-compliant decisions. The principle is to analyze the patient profiles for which physician decisions do not comply with guidelines along with the criteria defined in the decision-making process to justify the non-compliance. In each case, extracting what is specific in the patient profile that justifies the non-compliance will allow the generation of a new experience-based rule. This rule integrates the new knowledge coming from that patient in the IF-part (e.g. the inclusion of the specific clinical parameters identified in the decision-making process) and the actual final physician decision as the THEN-part. To assess the CV of the new rule, clinical outcomes are studied. The CV of the new rule is initialized at zero and is continuously updated according to the assessment of the performance of the rule quantified by the quality of its clinical outcomes. The goal is to apply the presented methodology based on the study of different known outcomes to represent the CV of new experience-based rules. The next points define AE outcomes and PROs used in DESIREE along with the treatment response outcomes, defined in this context as "survival", "relapse" or "exitus".

4.1. Common Terminology Criteria for Adverse Events (CTCAE)

The NCI CTCAE is a report that gathers and grades the different AEs for several illnesses using an agreed grading scale and a descriptive terminology. The defined grade scales go from 1 to 5 and refer to the severity of the evaluated AE where 1 represents mild, asymptomatic symptoms, with no intervention indicated and 5 represents death related to the AE [5]. The CTCAE has proved to be valid and reliable in a large heterogeneous US sample of patients suffering from cancer with at least one symptom reported by 99.8% of the patients from the first visit questionnaires [11].

4.2. ICHOM questionnaires

The International Consortium for Health Outcomes Measures (ICHOM) is a non-profit organization that provides standard measurement sets of patient-centered outcomes for a variety of illnesses and medical conditions [4]. The aim of these questionnaires is to improve the doctor-patient relationship while reducing health care costs, supporting informed decision-making processes, and improving the overall health care quality.

5. Conclusions

In this paper we have proposed to improve the clinical knowledge used by clinicians in the decision-making process by including the study of clinical outcomes in experience-based decision support. This approach is applied to the management of breast cancer patients within the DESIREE project. The clinical know-how of MTB clinicians has been modeled in a computer interpretable format that allows for the discovery of new

knowledge. This new knowledge needs to be evaluated on patient clinical outcomes before being widely used. Different kinds of outcomes have been studied (i.e. PROs, AEs, and treatment responses) that should be integrated to weight the validity of this new knowledge.

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 690238.

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