Clinical Guidelines: A Crossroad of Many Research Areas. Challenges and Opportunities in Process Mining for Healthcare

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Abstract. Clinical Guidelines, medical protocols, and other healthcare indications, cover a significant slice of physicians daily routine, as they are used to support clinical choices also with relevant legal implications. On the one hand, informatics have proved to be a valuable mean for providing formalisms, methods, and approaches to extend clinical guidelines for better supporting the work performed in the healthcare domain. On the other hand, due to the different perspectives that can be considered for addressing similar problems, it lead to an undeniable fragmentation of the field. It may be argued that such fragmentation did not help to propose a practical, accepted, and extensively adopted solutions to assist physicians. As in Process Mining as a general field, Process Mining for Healthcare inherits the requirement of Conformance Checking. Conformance Checking aims to measure the adherence of a particular (discovered or known) process with a given set of data, or vice-versa. Due to the intuitive similarities in terms of challenges and problems to be faced between conformance checking and clinical guidelines, one may be tempted to expect that the fragmentation issue will naturally arise also

in the conformance checking field. This position paper is a first step on the direction to embrace experience, lessons learnt, paradigms, and formalisms globally derived from the clinical guidelines challenge. We argue that such new focus, joint with the even growing notoriety and interest in PM4HC, might allow more physicians to make the big jump from user to protagonist becoming more motivated and proactive in building a strong multidisciplinary community.

Keywords: Conformance Checking · Clinical Guidelines · Computer Interpretable Clinical Guidelines.

1 Introduction

Process Mining (PM) is the discipline focusing on techniques, tools and methods to discover, monitor and improve real processes by extracting knowledge from event logs commonly available in today's information systems [1]. This sort of analysis of operational data can extract knowledge from the underlying sequences of activities and model the actual organizational workflow; for this reason, PM is sometimes described as a bridge between data mining and Business Process Management (BPM). There are three main areas subsumed by Process Mining: Process Discovery, Conformance Checking (CC), and enhancement. Buijs et al. [8] explain how automatic Process Discovery allows process models to be extracted from an event log; how CC allows monitoring deviations by comparing a given model with the event log; and how enhancement allows extending or improving an existing process model using information about the actual process recorded in the event log.

One of the most prominent domains of application of PM is healthcare, as suggested by a recent review of the area [48], based on 1,278 articles. Additionally, it is to be acknowledged that Process Mining in healthcare poses unique, non-trivial challenges because *hospital is not a factory and patients cannot be cured using a conveyor belt system*, as correctly reported by [28, 15]. Indeed, the care pathway of a patient is often a long and demanding journey, whose complexity is tightly linked to the high number of professional figures, diagnostic opportunities and therapeutic strategies that are available for each particular clinical need. Multidisciplinary teams are often involved in the care process, and choices have to be made among several treatment options and based on a variety of evidence such as laboratory tests, imaging data, medical visits. The patients can usually play a role according to their values, beliefs or expectations. In coping with this complexity, even if the domain has well-established strategies, each single task –treatment or diagnostic procedure– can be seen as a chess move, where the physician and the patient wait to see the results, before deciding the next move. In a nutshell, to appropriately apply Process Mining for Healthcare (PM4HC), there is the need to reckon *medical treatment processes are, in fact, highly dynamic, highly complex, increasingly multidisciplinary, and often ad hoc* [44]. Therefore, the dedicated field of PM4HC has been identified to mediate general PM with the needs of the clinical application domain.

According to our experience, what physicians are mainly and foremost keen on, when exposed to this kind of analysis techniques, is monitoring how patients flow through Clinical Guidelines (CG), in order to check not only the conformance agreement, but also to spot a light on those groups of patients that did not follow it, in the quest of understanding why that was the case and what are the implications [30]. This kind of needs has been also identified, in the last decades, by other research areas of Computer Science applications, such as BPM, Computer Interpretable Clinical Guidelines, Clinical Decision Support System (CDSS), Case Based Reasoning (CBR), among other disciplines. On the one hand, this fragmentation of perspectives and disciplines created a rich set of initiatives. On the other hand, the fragmentation may have reduced the concrete real-wold impact that a unified and compelling vision could have allowed to deliver. From this point of view, physicians need to be assisted in coping with CG, and their growing interest in PM4HC can really be a fertile ground to capture physicians engagement and make them take the leap to be proactive in leading effective application in the daily clinical practice.

In this paper, 12 research centers (out of which 6 are hospitals) propose their ideas on Conformance Checking in PM4HC, meant to provide a unified view on the future of the discipline in coping with the challenges of CG. The paper is organised as follows. We describe the notion of CG. Then, we introduce one of the most active areas of research in the field of CG, namely Computer Interpretable Clinical Guidelines (CICG). We then show the overlap between CICG and BPM, and how CG and PM have co-evolved in the last decade. Finally, discussions on opportunities and challenges posed by CG to the PM4HC discipline are given.

2 (not only) Clinical Guidelines

CG are defined as *statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options* [23]. CG are growing in importance due to their potentially positive effect on the quality of care, efficiency in the use of resources, and in their ability to precisely define the legal duties and responsibility of providers and institutions. In the last years numerous evidence-based guidelines have been developed by a wide range of organizations and bodies. Such heterogeneity, often caused an enrichment of the general definition, according to specific needs. For example, the World Health Organization (WHO) defined three different types of guidelines: Rapid advice guideline, Standard guideline, Full guidelines. Other International organizations, individual state health policy departments, medical specialty organizations, and profit and no-profit entities can adopt personalized enrichment of the definition.

In addition, due to the need to put emphasis on specific aspects of the definition, a quite rich set of different satellite concepts has been defined over time (e.g., Indications, Recommendations, Standards, Consensus Statements, Expert Advice, etc.). Even if such items can be significantly different in terms of aims,

they are often quite similar in terms of tools and methods for their representation (e.g. workflows, rules, decision trees, etc.).

Some of the commonly accepted issues concerning clinical guidelines are:

- they must be relevant to the care setting, clear, easy to access and apply, and auditable for feedback and reporting. [58];
- they should be based upon the best available research evidence and practice experience, developed using clear, explicit processes to minimize bias and optimize transparency. Possibly, the quality of guidelines should be measures with one of the existing system (e.g. GRADE, AGREE II, etc.);
- they tend to address the common or average patient, and do not evaluate the impact of multiple chronic conditions, socio-personal context, etc.;
- they need to be updated and re-evaluated over time to be re-validated when new clinical evidence is available;
- they need to be adapted from international to local context. Adaptation is *the systematic approach to the modification of a guideline produced in one cultural and organisational setting for application in a different context* [59];
- their purpose is to support and inform, not to dictate. There may be the temptation to use them as legally-binding documents, but clinicians are the only Decision Makers, and have the responsibility of decisions;
- as guidelines have been used for decisions about insurance coverage and standards for measuring quality of care, they have become increasingly influential, and conflict of interest (COI) in developing guidelines has become an important potential source of bias in the development of CGs[53].

In dealing with other workflow-based similar concepts, the heterogeneity of definition can also be more dramatic: Care Pathway, for example, is defined by the European Pathway Association as *a complex intervention for the mutual decision making and organisation of care processes for a well-defined group of patients during a well-defined period.* In 264 articles, the concept was referred to with 84 different definitions [11], with differences mainly based on three features: nouns, characteristics and aims and outcomes.

Summarizing, even if CG (and related concepts) have relatively well established definitions, practical needs and goals can induce in some *ad hoc* redefinition or interpretation: this should generally be discouraged by a stronger consensus, aiming at a reduction of the fragmentation of terms and ambiguity.

3 Computer Interpretable Clinical Guidelines

Given the rising attention to evidence-based medicine, and the wide-spread adoption of electronic health records, the development of clinical decision support systems (CDSSs), in general, and Computer Interpretable Guidelines (CIGs), in particular, have emerged as relevant fields of research [38]. Starting from the late '90s, several research groups have devoted their attention to the development of languages for the representation and of tools for the execution of CIGs. Well-known examples of such languages include Asbru [51], GLIF [7], GLARE [55],

PROforma[54], EON [37], and GUIDE[10]. These languages, which can be considered as task-network models, allow formally representing CGs, and executing them through an execution engine, which delivers recommendations by coupling the represented guideline knowledge to patient's data. The systematic comparison of CIG models carried out by Peleg et al [40] highlighted that, although using different computational models, all these methodologies allow formalizing guidelines through a set of actions (the so-called plan) that are executed over time. The control-flow is defined by organizing plan components according to different routing schemes (e.g. sequence, parallel, etc), and all the models support nesting of processes and the explicit management of temporal constraints. A common challenge for those formalisms are the complexities derived from their local adaption [38]. Although formalisms such as GLIF were designed for reusing procedural knowledge across organizations, the complexity related to their adaption to local contexts and their connection with the Electronic Health Record (EHR) has limited their broad adoption [38, 27]. This is actually a challenge shared by all computerized CDSS[57, 27]. With the raise of interest into the use of standards for EHR, some researchers focused on the need for a proper connection between the CDSS/CIG and the EHR. Various standards have been proposed for defining summarized EHR data views that the CIG accesses (a.k.a. virtual medical record). Clinical information standards allow the procedural component (i.e. the decision algorithm) of the CDSS to reference standard data schemas (defined with HL7 CDA, openEHR, etc.) rather than proprietary data schemas. One of the original works to overcome the challenges for connecting the CIG and the EHR data schemas in a flexible manner was the GELLO language [52]. GELLO allowed for defining restrictions over object oriented models to allow the Arden syntax rules accessing data that could be represented in HL7 v3 [52]. In the United States, the adoption of HL7 CDA as a part of the meaningful use initiative has significantly contributed to boost the adoption of standard-based CDSS [12, 16].

Many CDSS use clinical information standards for defining their virtual medical records, however CDSS often use a summary of the information contained in the EHR, for this reason CDSS-specific standards have been defined. Kawamoto et al. led an international collaboration that elicited a standard specifically designed for the definition of virtual medical records (HL7 vMR) [26]. In European nations such as Sweden, Denmark, or the UK, openEHR -based CIGs have also defined mechanisms for better scaling and decoupling procedural knowledge from EHR data schemas.

The Guideline Definition Language (GDL), introduced by Chen et al. is a rule-based language that allows to directly reference openEHR archetypes [9]. This allows the seamless integration of CDSS modules with openEHR-based EHRs. GDL has been used at large scale for classifying population according to their risk of suffering a particular disease [2]. Recently, the openEHR community published the specification for Task Planning that complements the GDL language by enabling the definition of workflows and actions as archetypes [4]. Both GDL and the openEHR Task Planning models are designed to run over

openEHR compliant repositories, thus posing a requirement on the data format to be supplied to the CIG decision algorithm. When the clinical information is in a format (proprietary or standard) different from openEHR, a pre-processing stage can be performed for making it openEHR compliant [33, 32].

Latest developments not only take care of the information format, but also define a common service interface for exposing CIGs functionality. Examples of this are OPEN CDS, SMART ON FHIR, CDS HOOKS, openEHR REST specification, among others.

Another important challenge that is currently being addressed by the research community is related to the management of patients with multiple health conditions [5]. From a technical perspective, using guideline-based CDSSs to handle comorbidities requires the integration of multiple disease-specific CIGs, by preserving patient safety and maximizing efficiency during execution. The approaches proposed in this area include on the one hand the manual definition of a comprehensive guideline starting from separate CGs, and on the other the automatic integration of multiple CIGs [45, 60, 13], considering the temporal and runtime aspects as well [3, 24].

4 CIGs and BPM

Languages from the CIG field provide a wide range of constructs to accommodate the rich variety of CG knowledge. Peleg et al. distinguish two main dimensions, namely knowledge about structuring of CG procedures in plans of decisions and actions, and about linking to patient data and medical concepts [40]. The parallels with the BPM and workflow fields as regards the former dimension have been recognized and exploited for some time in several works. A seminal work is the analysis of CIG languages based on the implementability of workflow control-flow patterns, by Mulyar et al. [35]. In the same line, another work provides a formal method to determine the implementability of patterns in a CIG language, with illustrations in the PROforma language [19]. To take another example, BPM notations have been advocated as a tool to facilitate the acquisition of CG procedural knowledge [34], motivated by the fact that CIG languages are not always comprehensible for clinicians.

In addition, the growing interest into the application of business process modeling and workflow management systems (WfMs) to the representation of clinical workflows [18], brought to the integration of CIGS into WfMS for the definition of the so-called careflows [43, 50] or care pathways [49, 17], which constitute the implementation of CGs or protocols in specific healthcare environments, consider the resource and the organizational settings.

To sum up, although there has been some exchange of ideas between the fields of CIGs and BPM, the benefits from an actual cross-fertilisation have not yet been achieved. Several authors argue that both CIG and workflow systems fail to address important aspects of healthcare processes when used individually (see e.g. [39]). The fact that CIG languages stand out for their expressive power in some regards, e.g. to represent the logic of decisions, may explain why this

field has not embraced to a greater extent the methods and tools of the BPM one. In doing so, however, the GCs do not allow their conjoint application with BPM tools and, thus, do not provide an effective support to the hospitals from a managerial point of view (e.g. resource allocation, performance analysis, etc.).

In a recent review about clinical decision-support models and frameworks, Greenes et al. question whether it is possible at all (and even desirable) to develop an over-arching framework integrating all related aspects (design, modeling, formalization, integration into workflow, deployment, etc.) [20]. Then, a possible path is the co-existence and coordination of different frameworks for each one of these CIG aspects.

5 Conformance Checking and (not only) Clinical Guidelines

The Process Mining field was established to bridge the gap between the process-oriented nature of BPM and the need of a more data-driven approach to build processes. Originally, the prominent role was played by Process Discovery, while Conformance Checking was relegated to represent an ancillary activity on automatically mined processes [36].

PM4HC inherited from PM the culture of being Process Discovery oriented: the most recent and extended meta-review [21] shows that only the 20-30% of the papers on PM4HC deals with conformance checking. However, while PM is data-driven and domain-agnostic, PM4HC is data and domain-driven and it has to face domain specific needs, issues and culture. It is quite common, for physicians, to see in PM4HC an opportunity to deal with the problem of CG, protocols, workflows, pathways, all concepts quite invasive in their daily routine and seems to have a solution in the languages we use to deal with processes. This is increasingly evident, but was also clear at the dawn of PM in healthcare, when Mans and van der Aalst [31], in defining four typical questions to be answered by medical process specialists, asked *Do we comply with internal and external guidelines?*. Due to this kind of need, in 2015 the same authors [47] represented a Clinical Guideline with DECLARE [41] and performed Conformance Checking with ProM [56]. A 2016 review [46] reveals that Conformance Checking to a predetermined model (not automatically mined), has been applied in 14 of the 71 reviewed studies. Another review [29], more specific for oncology, counts 7/37 papers where PM4HC was adopted in measuring the distance between expectation and data evidences on CG compliance. More recently, [25] used Conformance Checking on CG for alcoholism, [30] and [6] for the treatment of rectal and skin (melanoma) cancer respectively.

Generally speaking, CG contributes in coping with the measure of conformance on a known clinical process and, as mentioned, can be found in PM4HC, BPM, CICGs, DSS, WfMs but also in other research areas, such as Case Based Reasoning (e.g. [42])

Summarising, the overall picture reveals that (i) the clinical activity can benefit by PM4HC when dealing with known clinical processes; (ii) previous

attempts to propose models and tools can be found in many areas of Computer Science and this fragmentation led to a plethora of solutions and point of views. A significant part of the PM4HC community intercepted (ii) and saw a possible solution in what they name Conformance Checking, even if this means that PM4HC needs to be enriched of formalisms, models, etc., to tackle with this specific issue.

This represents a new challenge for PM4HC specialists because requires to collect the previous experiences from many research areas and re-shape such knowledge in the perspective of their discipline. However, this awareness represent an opportunity to avoid to *re-invent the wheel*, wherever this is possible and reasonable.

6 Conclusion and Future Trends

Clinical decision making is complex and of high responsibility, and a professional (or a team) must balance the benefit chances against the chances of harm. Diagnostic, especially therapeutic prescriptions, entails risks for patient's health: therefore, decisions must be supported by strong evidence, sufficient information and professional expertise.

CIGs can support the clinical decision making when some of the mentioned factors is missing or lacks reliability. However, even though they are built on the basis of consensus, evidence, and wide agreements, CIGs application can be compromised when the clinical context outstrips their constraints and assumptions. BPM provides tools to overcome these limitations by inferring and describing longitudinal data at different levels of granularity and multiple perspectives.

CIG was the ICT solution to traditional Evidence Based Medicine thesis in order to support medical care. Process Mining provides a great opportunity to fill the traditional gap between engineers and Health Professionals in this field. However, we should leverage on this opportunity not only to close this gap, but also to evolve CIGs to a new concept that provides a solution to new trends and paradigms in health care beyond Evidence Based Medicine. Combining CIGs and CC, we can push to create Value-Based Health Care solutions that provides not only better guidelines, but also being more personalized, providing Better Care, Better Health and Lower Cost [22]. This is far to be a trivial question. To engage health professionals in the ICT world it is mandatory to provide real solutions for real scenarios. Taking into account that there not exists one-fit-all solutions working in healthcare. For that, the models should be adapted to the final scenario in an iterative and interactive way [14]. That means the we need to provide models formal but understandable; complete, but usable; standard, but adaptable; specific, but flexible; general, but personalized... Otherwise, we will fail in the application of ICT to the healthcare domain.

The community of PM4HC is young and dynamic, close to the real world problem. It has the potential to give an important contribution in dealing with CG, also thanks to the attitude to be real-data oriented and the extensive use of Machine Learning. The exploitation of Machine Learning, for example, can lead

to a vision of a CIG describing tools and methods to analyze clinical data and suggesting possible decision scenarios based on confidence indicators, instead of depicting decision work flows with concrete thresholds.

Future work will focus on fostering *consensus* about the role of PM4HC in dealing with CG (and related fields), by developing initiatives aimed at sharing experience and results, and the inclusion of other centers.

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