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Methodological Review

Computer-interpretable clinical guidelines: A methodological review

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ABSTRACT

Clinical practice guidelines (CPGs) aim to improve the quality of care, reduce unjustified practice variations and reduce healthcare costs. In order for them to be effective, clinical guidelines need to be integrated with the care flow and provide patient-specific advice when and where needed. Hence, their formalization as computer-interpretable guidelines (CIGs) makes it possible to develop CIG-based decision-support systems (DSSs), which have a better chance of impacting clinician behavior than narrative guidelines. This paper reviews the literature on CIG-related methodologies since the inception of CIGs, while focusing and drawing themes for classifying CIG research from CIG-related publications in the Journal of Biomedical Informatics (JBI). The themes span the entire life-cycle of CIG development and include: knowledge acquisition and specification for improved CIG design, including (1) CIG modeling languages and (2) CIG acquisition and specification methodologies, (3) integration of CIGs with electronic health records (EHRs) and organizational workflow, (4) CIG validation and verification, (5) CIG execution engines and supportive tools, (6) exception handling in CIGs, (7) CIG maintenance, including analyzing clinician's compliance to CIG recommendations and CIG versioning and evolution, and finally (8) CIG sharing. I examine the temporal trends in CIG-related research and discuss additional themes that were not identified in JBI papers, including existing themes such as overcoming implementation barriers, modeling clinical goals, and temporal expressions, as well as futuristic themes, such as patient-centric CIGs and distributed CIGs.

1. Introduction

Trustworthy clinical practice guidelines (CPGs) are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefit and harms of alternative care options [1]. Clinical guidelines aim to improve the quality of care, limit unjustified practice variations and reduce healthcare costs. In order for them to be effective, clinical guidelines need to be integrated with the care flow, and provide appropriate recommendations when and where needed. Hence, their formalization as computer-interpretable guidelines (CIGs) [2] makes it possible to develop CIG-based decision-support systems (DSSs) through computer-based reasoning and execution of these formalized models. Such CIG-based DSSs match formalized guideline knowledge with updated patient clinical data to provide patient-specific advice at the point of care, increasing the chance of impacting clinician behavior compared to using only the narrative guidelines [3].

Research on CIGs started about 20 years ago and became more wide-spread in the late-1990s and early 2000s. Different approaches have been developed to represent and execute clinical guidelines over patient-specific clinical data. They include document-centric models, decision trees and probabilistic models, and "Task-Network Models" (TNMs) [2], which represent guideline knowledge in hierarchical structures containing networks of clinical actions and decisions that unfold over time. This review does not concern modeling of CPGs using case-based reasoning, chaining of individual decision rules (e.g., Arden syntax [4] or rule-based systems), or using CIG formalisms to represent individual decision rules (e.g., rules for adverse drug event prevention [5]). Both formal and semi-formal CIG representations are included in this review; formal models represent decision criteria in a formal interpretable language that enables binding of individual patient data item values to determine the value of the decision criteria, whereas semi-formal representation structures the clinical guideline as linked CIG elements where decision criteria can be represented informally, either as text or structured, but without an interpreter that can bind decision variables to values of patient data and evaluate complex criteria. Semi-formal CIGs could still be interpreted with user assistance (e.g., by making selections between decision options) and they have been used as intermediate step to simplify development of formal models (e.g., the Many-headed Bridge ap-

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proach [6] which allows bridging the gap between knowledge contained in one or several narrative guidelines and one or several CIG formalisms).

In this paper, I review CIG-related methodologies since the inception of CIGs, while focusing and drawing themes for classifying CIG research from past JBI issues. Being a methodology-focused journal, this paper's hypothesis is that the papers related to this area published in JBI since 2001 would be representative of the different themes found in other medical informatics journals. Creating a manual classification of JBI papers was more tractable than categorizing the full set of papers from the five journals. While adding the remaining papers, I reviewed the themes that had been identified to see whether changes were needed.

The rest of this paper is organized as follows. Section 2 presents the methods used to construct this review. Section 3 presents the emerging themes identified through the methodology papers already published in JBI, ordering them in a life-cycle approach. Section 4 reviews the CIG-related literature in the five selected medical informatics journals, as well as older papers that presented important methods developed in the CIG field. The paper ends with a discussion of additional themes that were not identified in JBI papers, including existing and futuristic themes, trends identified in CIG research, and limitations of this review.

2. Methods

The starting point of this review was to collect JBI papers related to CIGs. The term "CIG" was not used in the search string as not all publications use this exact term; other terms include, among others, electronic clinical guidelines, computerized clinical guidelines. Therefore, I conducted broad Pubmed searches of JBI papers relating to clinical/medical guidelines ("Journal of Biomedical Informatics"[journal] clinical guidelines; "Journal of Biomedical Informatics"[journal] medical guidelines) and a second similar search for JBI papers related to clinical/care pathways (i.e., similar search strings containing the terms clinical pathway, clinical pathways, care pathway, or care pathways). The last search was conducted on February 7, 2013. Forty-three papers were retrieved from the search with the guideline terms and 16 from the pathway terms. The titles and abstracts of these papers were manually checked to prune out those papers that did not address CIGs (e.g., papers that addressed clinical DSSs that do not rely on a reusable guideline formalism) or papers that were not fundamentally about methodology, such as applications and their evaluation without stressing novel methodology, organizational approaches, comparative analyses (including reviews and lessons learned), and the like. After this manual pruning step, 21 of the 59 collected papers remained, spanning the 12 years in which JBI has been published (2001–February 2013).

After reading the set of 21 papers, eight themes were identified. These were organized in a life-cycle approach, starting from knowledge acquisition and conceptualization and ending with CIG sharing.

Next, I followed the same Pubmed search and manual pruning procedure for papers published since 2001 in four additional prominent journals in the field of medical informatics: Journal of the American Medical Informatics Association (JAMIA), International Journal of Medical Informatics (IJMI), Artificial Intelligence in Medicine (AIIM), and Methods of Information in Medicine (MIIM). The numbers of papers found in each journal using the two search criteria are provided in Table 1. Because I decided to use a very wide search term (clinical guidelines, care pathways) so as not to miss CIG-related works in a specific journal searched, I had to limit the number of results and especially irrelevant results by focusing on the most prominent medical informatics journals.

When there have been papers since 2001 about a certain topic, earlier seminal papers on the same topic (either from journals or conference proceedings) were included if the later papers had a strong dependency on them. They are represented by the numbers in parentheses in Table 1.

3. Emerging themes in CIG research

After reviewing the 21 CIG papers from JBI, I identified eight themes. The themes span the entire life-cycle of CIG development, as shown in Fig. 1. The cycle begins with CPG analysis and CIG design. The usual practice is to base CIGs on previously published narrative CPGs. Hence the starting point of the life-cycle is knowledge acquisition and specification for improved CIG design. CIGs are defined using (1) CIG modeling languages while following (2) CIG acquisition and specification methodologies. To acquire CIGs, teams of knowledge engineers and clinical experts start with the CPGs, supplementing the knowledge contained in them with clarification of implicit medical knowledge and specifying this guideline knowledge in a CIG modeling languages using CIG authoring (or knowledge acquisition) tools. In order to provide patient-specific advice based on existing patient data from EHRs, the CIG can be (3) integrated with EHRs and organizational workflow. Such integration may necessitate restating of CIG logic according to availability of EHR data. Once the CIG is represented in a CIG language (i.e., at some point after step 2 is carried out), (4) validation and verification of the CIG can begin, to ensure that the CIG can be

Table 1
Number of CIG-related methodological papers found in prominent medical-informatics journals.

Journal	# Papers retrieved by PubMed search (added during review)		#of papers left after manual pruning		Total papers left since 2001
	Clinical guidelines, Medical guidelines	Clinical pathways, Care pathways	Guidelines	Pathways	
JBI	43	16	20	1{+1}[a]	21
JAMIA	74 (3)[b]	16	7 (3)	0	7
IJMI	95	11	12	1	13
AIIM	27 (1)	7	21 (1)	1{+1}	22
MIIM	46	3	5	0	5
Additional seminal papers[c]	Not applicable		5	0	0
Total	285 (4)	53	65 (9)	3	68

[a] Numbers in curly braces indicate number of papers in the pathways category that were also retrieved by searching for clinical guidelines and therefore were counted in the guidelines category.
[b] Numbers in parentheses show early seminal papers from the four other journals that later papers referred to.
[c] The numbers of additional seminal papers from other sources, not including the four journals, are provided in this row.