MEDINFO 2017: Precision Healthcare through Informatics
A.V. Gundlapalli et al. (Eds.)

doi:10.3233/978-1-61499-830-3-1148

Using Therapeutic Circles to Visualize Guideline-Based Therapeutic Recommendations for Patients with Multiple Chronic Conditions: A Case Study with GO-DSS on Hypertension, Type 2 Diabetes, and Dyslipidemia

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Abstract

Clinical decision support systems (CDSSs) have proven to potentially improve the compliance of physician decisions with clinical practice guidelines (CPGs). However, actual patients suffer from multiple conditions and CPGs that are usually single-disease-focused provide disease-specific recommendations with no support on how to manage adverse interactions between the recommended treatments. We have developed GO-DSS, a CDSS that implements an ontological reasoning process to perform CPG reconciliation. GO-DSS is applied to the concurrent management of hypertension, type 2 diabetes, and dyslipidemia. We proposed an innovative graphical interface to display medication recommendations as "therapeutic circles". A qualitative evaluation of the system and of this graphical layout has been performed on simulated patient cases by a sample of 12 users with various backgrounds (think aloud method). The resulting usability of the system is highly appreciated with a mean rating of 90.7% according to the standardized System Usability Scale.

Keywords:

Computer Graphics; Decision Support Systems, Clinical; Decision Making, Computer-Assisted.

Introduction

Clinical practice guidelines (CPGs) are evidence-based recommendations to manage patients with specific conditions (e.g., 2014 Evidence-Based Guidelines for the Management of High Blood Pressure in Adults[1], Standards of Medical Care in Diabetes – 2016[2], or 2016 ESC/EAS Guidelines for the Management of Dyslipidemia[3]). Based on the best available research evidence, CPGs are currently developed by health professional societies and national health agencies to improve the quality of clinical care and decrease health care costs. CPGs are usually elaborated as textual narrative documents. They may also include tables and graphs. More recently, the National Institute for Health and Care Excellence (NICE) has started to provide guidelines as structured dynamically interactive pathways[4].

Despite the wide development and dissemination of CPGs, there are still unwarranted variations in clinical practice [1,2]. Indeed, simply providing CPGs in their original narrative format has proven to have a limited effect in changing physician behavior. Several reviews [3,4] suggest that clinical decision support systems (CDSSs) that provide patient-specific guideline-based recommendations may be efficient tools to promote the adoption of CPGs by physicians. However, although many studies have indeed showed positive effects, others have found only a limited impact of these systems upon physician practices [5]. Delivering patient-specific recommendations at the point of care appears to be “neither necessary nor sufficient” to ensure compliance [6]. Research is thus currently carried out to assess which factors are responsible of the success or the failure of CDSSs [7]. Beyond variations in clinical setting, culture, training, and organization, the aim is to analyze when CDSSs are used and how, in order to elicit the technical features, e.g. design, implementation, level of description, as well as usability and display that would predict their correct use and effectiveness to increase clinician compliance with CPGs. Some authors of this article already studied the patient effect on non-compliance with the ASTI system [8] concluding that for “complex” patient cases, general practitioners (GPs) accept help and on-demand guidance-based systems are more appropriate, whereas for “simple” patient cases, GPs do not think they need to be helped, and automatic alert-based CDSSs are both efficient and mandatory since GPs would not spontaneously seek for information.

However, although the implementation of CPGs in CDSSs may be useful to provide clinicians best patient-centered recommendations to manage a given pathology (e.g. hypertension, type 2 diabetes, or dyslipidemia), this does not solve the problem of improving care quality and overall public health which is the ultimate target of CPG development and dissemination. CPGs are focused on the management of a single disease, whereas multimorbidity is a common phenomenon [9]. This is known for elderly patients but also true for younger patients [10]. Thus providing CDSSs to improve adherence with monomorbidity-focused, mono-disciplinary CPGs for patients with multiple conditions may result in undesirable effects: each guideline provides a recommendation but there is a lack of support as to how to manage adverse interactions between recommended treatments and conflicting management strategies. For people with multimorbidity, current guidelines and recommendations rapidly cumulate to drive polypharmacy without providing guidance on how to compare relative beneficence of risks of treatments according to the severity of the different conditions to best prioritize recom-

[1] http://jamanetwork.com/journals/jama/fullarticle/1791497

[2] http://care.diabetesjournals.org/content/39/Supplement_1/S4

[3] https://academic.oup.com/eurheartj/article/37/39/2999/2414995/2016-ESC-EAS-Guidelines-for-the-Management-of

[4] https://pathways.nice.org.uk

mendations or to select the recommendations that might be dropped.

To improve the management of patients with multiple conditions, some research is conducted on the *a priori* development of guidelines that account for multimorbidity. Epidemiological strategies based on the provision of a checklist of disease combinations that should be systematically considered during guideline development have been proposed to help guideline developers [11]. Other research teams have proposed to work on the *a posteriori* reconciliation of multiple single-disease CPGs. Wilk et al. [12] have proposed a framework employing first order logic to represent CPGs and to mitigate possible adverse interactions (drug-drug or drug-disease) when concurrently applying multiple CPGs to a multimorbid patient. This mitigation algorithm is used as an alerting tool to support the physician in the concurrent application of CPGs. More recently, this work has been refined to extend the mitigation algorithm and include patient's preferences [13]. Other authors have proposed semantic web ontology-based approaches [14] for the integration of multiple single disease clinical pathways in a unified disease-specific clinical pathway. The execution of the ontological clinical pathway model is achieved through abstraction processes to assign functional behaviors to existing semantic properties and facilitate their execution [15].

Information visualization may be defined as the use of visual representations of data, information, and knowledge to help users gain a deeper understanding of the contents of a domain. Numerous research works are currently being carried out to develop health information visualization techniques expected to increase the benefits of health informatics databases and networks. The underlying principle is that the right display of health information should match the mental constructs and cognitive tasks of the user and thus should reduce the cognitive load of data interpretation. As a consequence, the capacity of patients, clinicians, and public health policy makers to make better decisions should be improved [16]. Indeed, literature shows that different types of graphical information can help or arm the accuracy on decision-making [17]. This has been shown at the population level [18], but also at the patient level with Computerized Physician Order Entry (CPOE). Poorly designed CPOE can lead to usability problems, users' dissatisfaction, and may disrupt the normal flow of clinical activities. Wipfli et al. [19] proposed an alternative strategy to alert display and layout that reduces interruptions to physicians' workflow. Payne et al. [20] recommended using visual cues, minimal text, formatting, content and reporting standards to improve drug-drug interaction alerts. The same conclusions apply to information retrieval of CPGs with an interactive graphical interface using an iconic language [21]. Understanding how to best visualize data, information, and knowledge, especially in CDSSs is a central challenge to improving healthcare.

We have developed GO-DSS, a guideline-based decision support system applied to the management of the cardiovascular risk [22]. GO-DSS uses an ontology-based approach to allow for the flexibility needed to deal with patients with multiple chronic disorders. A first implementation concurrently applying hypertension (HT) and type 2 diabetes (T2D) CPGs was previously developed [23]. The system was then successfully extended to integrate the management of patients with dyslipidemia (D). GO-DSS guideline-based recommendations have been extended to be displayed as "therapeutic circles". This graphical layout of recommended drugs and drug combinations was evaluated by a sample of users with various backgrounds (clinicians, GPs, pharmacists, informaticians, engineers).

Materials and Methods

In this section, we describe the three CPGs we worked with, summarize the main functionalities of the guideline-based GO-DSS CDSS, introduce the therapeutic circles we used in GO-DSS to display recommendations, and present the protocol implemented to evaluate the global system.

Hypertension, type 2 diabetes, and dyslipidemia CPGs

We used CPGs synthesized by Vidal[5], a French company that markets a drug database and medical situations which have been evaluated for quality by medical professionals for decades. CPGs were manually translated into IF-THEN decision rules. THEN-parts contained "possible" actions, "recommended" actions, and "contra-indicated" actions according to CPGs. The 2016 dyslipiedimea CPG was translated following the same method and format as the HT and T2D CPGs [22]. We therefore had generated three rule bases, for HT, T2D, and D CPGs.

GO-DSS ontological reasoning

The first step was to build an ontology of the cardiovascular domain. We reused an emergency care ontology (OntolUrgences[6]) where concepts relevant to cardiovascular risk management were extracted. This first ontology was then enriched to integrate the CPG-specific concepts used by the decision rules (IF- and THEN-parts) of the three rule bases. Concepts were structured by subsumption, equivalence, and disjunction relationships.

IF-parts of rules are logical expressions (mainly conjunctions) built with concepts from the ontology. The set of IF-parts of rules represent the set of theoretical patient profiles covered by CPGs. Each theoretical patient profile is equivalent to a new concept in the ontology, and as such can be classified by the ontological reasoner. Therefore, these profiles, and their corresponding rules, are organized in a subsumption graph, with the least specific profiles at the top and the most specific ones at the bottom.

At execution time, when an actual patient's case is considered, patient data is encoded as a conjunction of concepts of the ontology to build the closest formalized patient profile. Processing the ontological reasoning consists of identifying all the CPG-based, rule-issued, patient profiles that subsume the formalized patient profile to collect the decision rules that apply to the patient. All the linkages between co-illnesses covered by CPGs are returned by the ontology. However, knowledge gaps in CPGs still produce missingness errors in the reasoning process. The subsumption graph of patient profiles/rules is also used to solve potential conflicts between inferred actions (within or across CPGs) by selecting the actions recommended by the most specific rules in the subsumption graph of profiles and by eliminating the actions of the more general rules, thus implementing a kind of non-monotonic reasoning [22].

As a result, we get all the actions (either "possible", "recommended", or "contra-indicated") filtered by the conflict resolution process that apply, for the best management of the patient.

Display of recommendations

Therapeutic recommendations that are issued from CPGs for a given patient correspond to possible, recommended, or contra-indicated drug classes and drug combinations. In order to summarize all these drug-related recommendations for a given

[5] https://www.vidal.fr/recommandations/

[6] https://bioportal.bioontology.org/ontologies/ONTOLURGENCES

pathology/CPGs, we have introduced a graphical representation we called "therapeutic circles". A therapeutic circle corresponds to the circular disposal of discs where each disc represents one of the drug classes that can be prescribed for a given pathology (HT, T2D, and D) according to CPGs. When the drug class is just mentioned in CPGs, with no other inferred information, the disc is colored in grey. The disc is colored in yellow when the drug class has been mentioned as "possible" for the patient, in green when it is "recommended", and in red when it is "contra-indicated". When the disc has a bold outline, this indicates that the corresponding drug class is currently administered to the patient. Lines between therapeutic discs describe the combination of drug classes with the same color rules. Yellow lines indicate the combination is "possible", green lines indicate the combination is "recommended", and red lines indicate the combination is "contra-indicated". Figure 1 displays the therapeutic circle to represent guideline-based therapeutic propositions for a patient currently treated by ACE inhibitors (bold circle) for whom it is recommended to go for a bitherapy by adding a thiazide diuretic (green link). Adding calcium a channel blockers (CCB) or a beta-blocker is possible (yellow links), but adding an angiotensin II receptor antagonist (ARB) is contra-indicated (red link).

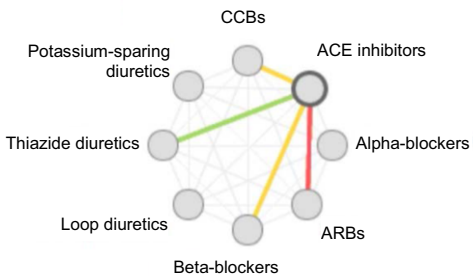

Figure 1 – Antihypertensive drug recommendations represented as a therapeutic circle

For a given patient, multiple pathologies/CPGs must be considered simultaneously. Following the principle of having patient problem lists in medical records as a way to "encourages doctors to think holistically about their patients" [24], we have structured the display of guideline-based decision support propositions per problem, with one column for HT, one for T2D and one for D. Within each column, we deliver six levels of information:

1. The description of the current treatment with the combination level and the list of drugs and their class,
2. The assessment of the current treatment in terms of compliance with guidelines and therapeutic efficacy,
3. The recommended level of drug combination (no drug, mono-, bi-, tri- and quadritherapy),
4. The therapeutic circle to represent guideline-based drug recommendations,
5. Indications about alerts, risks, and surveillance,
6. Non-pharmacological recommendations.

Figure 2 displays the six levels of information for a man of 84 years with asthma and uncontrolled HT despite a bitherapy of antihypertensive drugs, ACEi and a thiazide diuretic, a non-efficient metformin monotherapy for T2D, and a dyslipidemia non-currently treated. The current treatment globally complies with CPGs but is not efficient:

- For hypertension, a tritherapy is recommended, but a quadritherapy is contra-indicated. The recommended tritherapy is made of the combination of ACEi, thiazides diuretic, and calcium channel blocker (CCB). ARBs are recommended as a therapeutic drug class (green disc) but not in association with ACEi (red line). Beta-blockers are contra-indicated because of asthma (red disc) as well as any combination including them (red lines).
- For type 2 diabetes, a bitherapy made of a combination of metformin and a sulphonylurea is recommended.
- For dyslipidemia, a monotherapy is recommended, by either statins or ezetimibe.

Evaluation protocol

A pilot evaluation of the system has been made off-line for test cases. The evaluation protocol comprised four steps: (i) a tutorial to introduce GO-DSS, (ii) a training step, (iii) the unsupervised use of the system on simulated patient cases, and (iv) a qualitative user assessment through questionnaires. A whole evaluation session was expected to last about 45 minutes.

The first step presented the aim of the system, the context of its development, its main functionalities, and how to recognize and interpret the different types of information displayed in the user's interface (UI). During the second step, the user utilized the system under the supervision of the evaluator on commented simulated patient cases. The aim was to make the user explore and discover GO-DSS functionalities. During this step, the user could ask any question about the system. The third step consisted in the autonomous use of the system by the user alone, without supervision. Two simulated patient cases were proposed. These cases corresponded to the longitudinal management of patients and included multiple consultations, the follow up of evolving chronic conditions, and multiple decision points with drug prescription and adaptation. Such cases were built to illustrate the different operating functionalities of the system. User prescriptions were collected, as well as any enunciated remarks (think aloud method). The user could exit the scenario planned for the simulated cases and he/she was permitted to try any arbitrary patient conditions to test the system response. At the fourth and last step, the user filled a questionnaire to indicate his/her professional profile, as well as his/her familiarity with CPGs and decision support tools. Questions about the medical relevance of recommendations, the consistency with the original CPGs, and the perceived utility were encoded using a 4-valued Likert scale. It was also possible to enter further comments about the system. Finally, a standardized SUS (System Usability Scale) [25] questionnaire was filled in by each participant.

Results

The assessment of GO-DSS was conducted according to the evaluation protocol by 12 testers with different professional backgrounds, and from different organizations. Five were general practitioners (GPs), two were medical specialists, all of whom were actual experimented practitioners (more than 20 years of practice). One was a pharmacist, two were non-clinician e-health informaticians, and two were engineers. Among them, 66% (n=8) already used a CDSS, and 75%

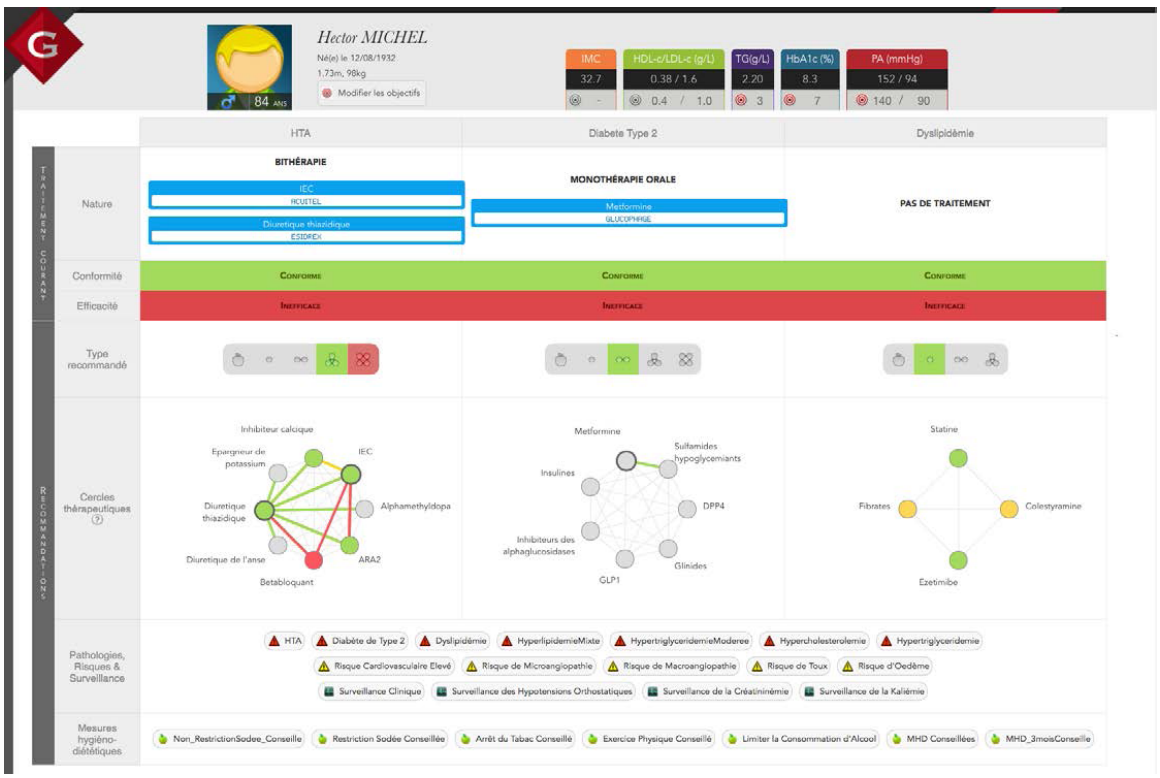

Figure 2 – GO-DSS display of guideline-based recommendations for hypertension, type 2 diabetes, and dyslipidemia

(n=9) were familiar with CPGs. Figure 3 reports the distribution of the participants' answers to the qualitative questionnaire. Most of the responses, beyond 9/12, are positive ("yes" or "rather yes"). Free comments have been manually classified as positive or negative. Positive remarks were: clarity of the user interface, intuitive use, synthetic presentation of the patient case, possibility to get back to the original text of CPGs, the innovative presentation of recommendations as therapeutic circles (sometimes with some reservations). Negative remarks were: lack of connection with any EHR or CPOE, risk of an overloaded interface in case of many comorbidities, need for more classical textual expression of recommendations. The SUS score obtained from the 12 participants was measured as 90.7%. This result, according to the ratings of the standard with respect to usability, classifies the GO-DSS as an "excellent system" of "grade A".

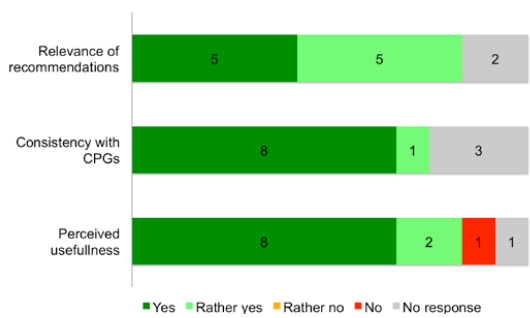

Figure 3 – Distribution of responses to the qualitative questionnaire

Discussion and Conclusion

GO-DSS is a CDSS to manage patients with multiple pathologies from single-disease guidelines. An ontological reasoning process allows for the management of intra and inter CPGs conflicts. Conflict resolution is completed before the display of therapeutic propositions, categorized as possible, recommended, or contra-indicated options. Therapeutic propositions are displayed per pathology in a new graphical representation called "therapeutic circles". GO-DSS processing and interface have been evaluated by a sample of testers on simulated cases. The therapeutic options proposed by GO-DSS have been considered as medically sound by the clinicians, and in good coherence with CPG contents. The innovative presentation of recommendations as therapeutic circles was diversely appreciated: some testers were not comfortable with such a display considering it was not easy to understand, whereas others were enthusiastic asking for some refinements such as the possibility to link GO-DSS to a drug data base which allows to access the list of drugs when clicking on the disc of a given drug class, and select the appropriate drug. This could incrementally build the prescription in a way similar to the "Add to Cart" button used to build a shopping list. All testers considered that with some training, the display of CPGs as therapeutic circles was astoundingly modern and convenient. Another issue discussed concerned the increase in the number of pathologies and the possibility to have comorbidity-based columns used as tabs that could be dynamically opened/closed. The question of having a unique therapeutic patient-centered circle was set but considered as rapidly unreadable.

The design of GO-DSS's interface and the display of medication recommendations as therapeutic circles were finally well accepted by the testers. However, due to the small size of the sample (although the analysis was qualitative), and the fact

that testers worked on simulated cases outside the actual clinical workflow, we cannot conclude that our results may be generalizable, and further work is needed to assess under real conditions the true value of such a display of guideline-based therapeutic recommendations. The first step will be to increase the size of the sample and organize an online evaluation of GO-DSS based on the same evaluation protocol and using GP social/professional networks for recruiting participants.

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