Using Knowledge Modelling to Measure How Clinical Practice Could Actually Be Evidence-Based: A Preliminary Analysis with Arterial Hypertension Management

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Abstract. ASTI is a guideline-based decision support system to be used in primary care. We analyzed the knowledge modelling carried out in the development of ASTI knowledge base (KB) from French clinical practice guidelines (CPGs) on arterial hypertension management to evaluate the evidence status of therapeutic propositions issued by the system. We defined three status: “evidence-based” (EB) when propositions are graded A, B, or C, “consensus-based” (CB) when propositions are explicitly mentioned in CPGs but supported by professional agreement (grade D), and “non-supported” (NS) when propositions are expert-based and provided by a domain specialist. We compared the distributions of evidence status on the 44,571 theoretical patient profiles extracted from ASTI KB, and on a data set of 435 actual hypertensive patients. Only 8.3% of actual patients, managed by 0.5% of the KB, have an EB profile and 46.9% of patients, managed by 12.6% of the KB, have a CB profile. Thus, there is no CPG recommendation for nearly half of the patients (44.8% have a NS profile).

Keywords. clinical practice guidelines, clinical decision support systems, evidence-based medicine, hypertension management

1. Introduction

In order to provide optimal care, physicians are expected to follow evidence-based medicine (EBM) principles making an “explicit, judicious, and conscientious use of current best evidence from health care research in decisions about the care of individuals and populations” [1]. Clinical practice guidelines (CPGs) are information resources in which evidence from health care research has been pre-graded for validity by people with expertise in research methods and assessed by experienced practitioners for clinical relevance. Usually developed by health professional societies or national

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health agencies, CPGs are thus textual documents organized as a catalog of clinical situations for which therapeutic recommendations are provided along with grades of evidence. Unfortunately, only a proportion of the evidence supporting CPGs comes from randomized clinical trials (grade A), cohorts (grade B) or case-series studies (grade C) with the majority of the “evidence” coming from experts clinical panels in charge of CPGs development (grade D).

Many studies have shown that the sole dissemination of textual CPGs has no impact on physicians behaviour and that clinical decision support systems (CDSSs) can be effective in increasing physician compliance with CPGs [2]. We have developed ASTI² [3], a prototype guideline-based CDSS, applied to therapeutic prescribing in primary care. The “critiquing mode” of ASTI operates classically as a reminder-based system to control physician’s orders. On the contrary, the “guiding mode” of ASTI, ASTI-GM, operates on demand when the general practitioner (GP) needs support to determine the drug prescription of a patient case. As opposed to the critiquing mode that only relies on CPG content, the knowledge base (KB) of the guiding mode has been structured to provide a therapeutic proposition in all theoretical clinical situations. We used the decision tree framework to represent patient profiles as a set of variables. In order to achieve completeness and consistency of variables modalities at each depth level, the formalization process often required interpretation assumptions [4] and the combination of different knowledge sources [5]. As a consequence, the status of system propositions in terms of grade of evidence is not obvious to evaluate.

The objective of this exploratory work is to characterize the evidence status of the therapeutic propositions issued by the system. Based on this characterization, we analyzed the theoretical distribution of therapeutic proposition status, and how this theoretical distribution is practically implemented in primary care. This work has been conducted on the French CPGs for the management of essential arterial hypertension (AHT) [6].

2. Material and Method

2.1. Knowledge Modelling of the AHT CPGs in ASTI-GM

French AHT CPGs have been modelled as a two-level decision tree made of a clinical level to represent clinical situations descriptions and a therapeutic level to explore clinical-situation-specific therapeutic sequences based on a given patient history and identify the best recommended treatment [7]. Knowledge formalization was performed following the approach to guideline implementation proposed by Shiffman et al. [5]. At the clinical level, extracted concepts were mostly related to AHT comorbidities, either cardiovascular risk factors or specific patient conditions, that lead to a specific management strategy and for which graded recommendations exist. We proceeded to the systematic combination of corresponding clinical variables, dropped non-medically relevant associations, and organized the resulting patient profiles that represent, by construction, a nosological repository of all possible clinical descriptions of a patient based on AHT criteria, as the clinical level of the KB. These theoretical clinical

² ASTI (Aide à la Stratégie Thérapeutique Informatisée) has been partially supported by a grant from the French CNAMTS.
situations are far more numerous than those described in CPGs which schematically consider comorbidities one by one in combination with AHT.

Sub-trees were developed for each theoretical clinical situation to account for a patient therapeutic history, thus building the therapeutic level of the decision tree. Decision variables including the identification of the current drug combination level, past treatments and response to past treatments in terms of tolerance and therapeutic efficiency, as well as contraindicated drugs have been introduced. AHT CPGs provide EBM recommendations in clinical situations involving only one comorbidity and only for treatment initialization. When the first intention treatment is given, second and third intention treatments, in case of inefficiency or intolerance, can be assumed on a consensus basis from CPG contents. For many other situations, there is no hint in CPGs to elaborate the appropriate treatment. These numerous cases correspond to CPG knowledge gaps that should be filled in to provide users with consistent decision support. This process has been carried on by an expert that participated to the development of AHT CPGs. Thus, we provided additional therapeutic sequences for the non-explicitly mentioned clinical situations generated by the systematic modelling of the decision tree clinical level, additional steps of incomplete sequences of explicitly mentioned clinical situations, as well as alternative therapeutic options taking into account drug substitutes to manage patients with contraindications to recommended drugs. In AHT CPGs, drugs explicitly mentioned as possibly contraindicated are ACE inhibitors (ACEi) substituted by angiotensin receptor blockers (ARBs). The expert also added calcium channel blocker (CCB) as substitutes of beta-blockers (BB) when BB were contraindicated. As a result, the number of handled therapeutic sequences was significantly increased.

Finally, a path of the decision tree that forms the KB of ASTI-GM corresponds to a formal patient profile P characterized as a set of instantiated decision variables. Each path is attached to the recommended actions plan A. System propositions are thus defined as a set of $R = (P, A)$.

2.2. Evidence Status Definition

We assume that the evidence status of a therapeutic proposition $R$ can be characterized only by the patient profile $P$ to which it is attached. By extension, we consider that $P$ has the status of the proposition $R$ it supports. We only considered the decision variables explicitly described in CPGs, i.e., 9 comorbidities (elderly, antecedent of stroke, myocardial infarction, stable angina, ischemic cardiac failure, diabetes, microalbuminury, renal disease, left ventricle hypertrophy), the drug combination level of the current treatment (mono, bi, tritherapy), and contraindications (CI) to BB and ACEi. We define three evidence status:

**Evidence-based (EB) profile:** $P$ is “clinically EB” ($EB_{cl}$) if there exists at most one comorbidity among elderly, antecedent of stroke, MI, stable angina, ischemic cardiac failure, diabetes or microalbuminury) for which explicit EBM statements are provided in CPGs. $P$ is “therapeutically EB” ($EB_{th}$) when treatment is initialized and evidence exists. $P$ is “EB with respect to contraindications” ($EB_{ci}$) if there is no CI to BB and no CI to ACEi except in the case of ischemic cardiac failure where a graded recommendation exists. As a result:

$$EB(P) \iff EB_{cl}(P) \land EB_{th}(P) \land EB_{ci}(P)$$
Consensus-based (CB) profile: P is “clinically CB” (CB_cl) in some contexts explicitly described in CPGs and for which consensus-based advices are provided: renal disease alone, left ventricle hypertrophy alone, (renal disease and diabetes), (myocardial infarction and ischemic cardiac failure). P is “therapeutically CB” (CB_th) when the current treatment level is at most a bitherapy since CPGs recommend up to tritherapies. P is “CB with respect to contraindications” (CB_ci) when contraindications to ACEi are not handled by CPGs. As a result:

\[ CB(P) \Leftrightarrow \neg EB(P) \land (EB_{cl}(P) \lor CB_{cl}(P)) \land (EB_{th}(P) \lor CB_{th}(P)) \land (EB_{ci}(P) \lor CB_{ci}(P)) \]

Non-supported (NS) profile: By construction, P is NS, when it is neither EB nor CB. For these profiles, there is no explicit recommended action in CPGs:

\[ NS(P) \Leftrightarrow \neg EB(P) \land \neg CB(P) \]

2.3. Implementation and Experiments

Based on the specifications of the previous section, we implemented an algorithm which automatically yields, for a given patient profile, its status category: EB, CB, or NS. It has been first applied on each patient profile of ASTI-GM KB to provide the theoretical distribution of status. In a second step, a sample of 435 actual patient profiles were extracted from manually codified electronic patient records from a GP medical practice. Then, the same program was run to deliver the distribution of status within this patient set.

3. Results

The 44,571 theoretical patient profiles handled by ASTI-GM when its KB is fully expanded have been classified with respect to their status (Table 1, left part). It is noticeable that CPG-covered profiles (EB or CB) represent less than 13% of all theoretical profiles, the remaining being non explicitly covered by CPGs.

The analysis of actual patient profiles provides data about the frequency with which the previous theoretical profiles are instantiated (at least in this sample). Table 1 (right part) shows that only 8.3% of antihypertensive orders are prescribed in a situation supported with EBM recommendations. This means that 91.7% of the prescriptions cannot be strictly evidence-based. In these situations, CB recommendations exist for only one half of the prescriptions. For the other half, representing 44.8% of the total, there is no explicit CPG support.

Table 1. Distributions of patient profile evidence status in the KB and in the data set

<table>
<thead>
<tr>
<th>Profile types</th>
<th>ASTI-GM KB</th>
<th>Patient data set</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Percentage</td>
</tr>
<tr>
<td>EB profiles</td>
<td>206</td>
<td>0.5%</td>
</tr>
<tr>
<td>CB profiles</td>
<td>5,424</td>
<td>12.2%</td>
</tr>
<tr>
<td>NS profiles</td>
<td>38,941</td>
<td>87.4%</td>
</tr>
<tr>
<td>Total</td>
<td>44,571</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
4. Discussion and Conclusion

Beyond many intrinsic limits, this work suggests that, on the basis of French AHT CPGs, EBM provides little help for GPs: indeed, CPGs handle only 12.7% of theoretical patient profiles and half of actual situations (55.2% of patients), leaving GPs unsupported for the remaining half in accordance with conclusions reported in the literature [8, 9]. This is not surprising since actual patients are complex patients with multiple comorbidities and chronic diseases, evolving on the long term, distinct from the one-comorbidity oversimple patients starting a new treatment usually described in CPGs. Because AHT is a chronic disease, all anti-hypertensive drug orders but the first are prescribed to a patient already treated, a situation rarely EBM-supported.

Even if weaker than EB recommendations, CB recommendations support the management of progressive drug combinations so that 46.9% of actual patient profiles are finally classified as CB profiles. This suggests that the complexity of AHT management would not proceed from clinical profiles but, as a chronic disease, rather from the complexity on the long term of drug management for which EB data is missing whereas CB advices are available.

As far as compliance with CPGs is concerned, one would expect GPs to be more compliant with ASTI-GM for patients with EB and CB profiles, since the system provides “expert-based” recommendations for NS profiles. Thus, we compared actual orders in the dataset with ASTI-GM propositions and computed the compliance rate. GPs’ compliance rate with ASTI is 69.4% in EB profiles and 38.7% in CB profiles. In NS profiles, the compliance rate falls to 21.5% illustrating the variability of GPs’ prescriptions off the beaten paths. Due to the patient profile distribution in the data set, the overall compliance rate of GPs is 33.5% as compared with ASTI’s propositions and 43.3% as compared with CPG recommendations, computed only for EB and CB profiles. These preliminary results should be assessed more formally.

References