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Will 'Computable' Clinical Guidelines Be Compatible with Personalised Care?

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Abstract. Introduction. The potential benefits from digitalisation processes will only be fully realised if the conceptual challenges they uncover are accepted and addressed, alongside the technical ones such as interoperability. Will 'computable' clinical guidelines be compatible with personalised care if the definition of the relevant disease embeds preferences that pre-empt those of the individual patient? Method. As a case study we investigated the definition of diabetes in glycaemic management guidelines. Result. The dominant component of its definition – HbA1c ≥6.5% – embeds the consensus preference judgement of a 2009 International Expert Committee. Discussion. This preference-sensitive threshold for the diagnosis of diabetes has subsequently been endorsed in many guidelines relating to glycaemic management, though there are signs of awareness and concern with its implications. Conclusion. Those seeking to digitalise guidelines by making them 'computable' need to acknowledge and address their inbuilt preference-sensitivity - if they wish to further care that respects patient's preferences.

Keywords. clinical guideline, computable, diabetes, patient's preferences

1. Introduction

The possibility of Clinical Decision Support (CDS) being delivered in *computable* and, ultimately, computer-*executable* clinical guidelines, has led to some of the major ongoing projects in the digitalisation of healthcare. The Mobilizing Computable Biomedical Knowledge (MCBK) and OpenClinical projects are particularly noteworthy [1-4]. MCBK's stated mission is to disseminate biomedical knowledge in formats that can be shared and integrated into health information systems and applications. Making biomedical knowledge 'easily findable, universally accessible, highly interoperable and readily reusable' is seen as the way to further the joint goals of enhancing the care of the patient and the learning capacity of the healthcare system.

The multiple technical and organisational challenges in guideline digitalisation are well-appreciated, including by the UK chapter of the MCBK movement [5-7]. Most of the challenges are being tackled by the communities and stakeholders involved. The pervasive issues surrounding interoperability implementations and standards are the focus of HL7 FHIR (Health Level Seven - Fast Healthcare Interoperability Resources). Their clinical guideline implementation guidance [8] draws on the Multilayer

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Knowledge Representation Framework (MKRF) [9] with its four levels of guideline formatting, moving upwards from the currently dominant narrative level, initially to the semi-structured, then to the fully structured/computable, and finally to the fully computer-executable version.

While the fundamental aim of all these efforts is to improve the care of patients, the focus of most of this work is actually on providing support for the clinician. That CDS has been effectively *Clinician* Decision Support [10] led Sittig and colleagues to offer a 'lifecycle framework' to help guide digital initiatives towards patient-centered clinical decision support (PC CDS) [11]. The fundamental aim of a PC CDS would be to "ensure the right information is delivered to the right person, in the right format, via the right channel, at the right point in the workflow" - the so-called CDS Five-Rights. In keeping with this aim, the Sittig paper differs from all those previously cited in that it actually contains the word 'preferences' (whereas the others do not). Among its several appearances we find "In some circumstances, the patient's preferences for specific outcomes may be different from those of their clinicians. For example, a patient might prioritize the ability to drive over pain management for some musculoskeletal disorders, or even quality over quantity of life."

However, what does not appear to be appreciated, even by Sittig and colleagues, is that the 'knowledge' represented (at any level of structuring and computability) may be incompatible with the aim of a PC CDS. The patient's right to have *their* preferences make their decision on the basis of the information/knowledge delivered in a PC CDS is jeopardised if that information is not 'right'. And it will not be 'right' for that patient if it contains previously embedded preferences.

Pre-emptive preferences which make the knowledge within the guideline sensitive to preferences other than those of the patient have two possible origins. The simple and obvious level is in the compilation of the guideline, where movement from evidence and information (the 'is') to the recommendation (the 'ought') necessarily involves the introduction of preference (value) judgements. So long as the embedded preferences, and their basis, are transparent, the guideline remains useful in person-centred care, if used conditionally. If the embedded preferences come concealed (in the form of covert 'oughtism') this is ethically suspect – and legally questionable under a 'reasonable patient' standard for informed consent. The second possible source of pre-emptive preferences is the one investigated here: the preferences that may be embedded in the definition of the relevant disease (disorder, condition, syndrome).

2. Method

We took type 2 diabetes as our case study and traced the source and nature of the widely-accepted diagnostic criterion for diabetes and uncovered the reasoning behind it. We paid particular attention to whether the reasoning focused on the group level consequences of alternative possible cutoffs on a continuum, since the selection of one of these on this basis would potentially jeopardise person-centred care [12]. (To ensure the reasoning is reported accurately we quote extensively.)

3. Result

The currently dominant definition of diabetes can be sourced to an International Expert Committee (IEC), convened jointly by the American Diabetes Association, European Association for the Study of Diabetes, and International Diabetes Federation. Its 2009 report is clear and simple: "Diabetes should be diagnosed when A1C [i.e. HbA1c] is ≥6.5%" [13]. While there were other supporting considerations, the key reason provided for adopting this defining threshold was based on an analysis that included " ~28,000 subjects from nine countries and showed that the glycemic level at which the prevalence of "any" retinopathy begins to rise above background levels (any retinopathy includes minor changes that can be due to other conditions, such as hypertension), and for the more diabetes-specific "moderate" retinopathy, was 6.5% when the data were examined in 0.5% increments. Among the ~20,000 subjects who had A1C values <6.5%, "moderate" retinopathy was virtually nonexistent... the substantial increase in the prevalence of moderate retinopathy at A1C levels ≥6.5% supports a threshold level of glycemia that results in retinopathy most characteristic of diabetes... Any suggestion that the relationship between chronic glycaemic levels and the long-term complications of diabetes may be better expressed as a continuum, rather than as a strictly dichotomous relationship, is belied by the retinopathy findings presented herein."

So, the IEC placed the diagnostic threshold at the point where the prevalence of moderate or severe nonproliferative diabetic retinopathy (NPDR) was 2.6%, rejecting alternative thresholds, such as that associated with a prevalence of 0.7% (at 6.0% A1c) and of 4.3% (at 7.0% A1c) (data from [14]). That there were major possible health consequences from 'elevated' A1C, other than those of NDPR (kidney failure, peripheral neuropathy, heart disease) was emphasised, but the Committee seems happy to have used that one microvascular complication as a proxy for these.

The cutoff selection was not uncontroversial. "There is likely to be some initial debate concerning the cut point—A1C of 6.5%—chosen to define diabetes. This is, of course, a problem whenever one coerces a diagnosis, which by definition must be dichotomous, from a continuous variable... Concern will be compounded by the fact that the upper limit of normal for A1C is 6.0%, leaving something of a gray zone between this value and the 6.5% cut point for diabetes... The lack of an A1C value for a formal definition of "pre-diabetes" is likely to raise further and related concerns... The International Expert Committee is indeed careful to point out that the threshold does not identify an A1C level below which risk is nil but, instead, one below which risk is lower: an inflection point in a continuous positive relationship rather than a true step function*"* [15].

Surveying both the 2009 report and subsequent commentaries we conclude that reasoning has largely focused on the shape and position of functions for the consequences arising from alternative cutoffs, such as 2.6% NPDR at 6.5% A1c versus 4.3% at 7.0% A1c. Notably, the chosen disease-defining cutoff is presented as grounded in 'objective' medical/clinical data. The IEC does say that its decision "balanced the stigma and costs of mistakenly identifying individuals as diabetic against the minimal clinical consequences of delaying the diagnosis in someone with an A1C level <6.5%." But there is no other acknowledgement that the assignment of a cutoff installs, in the disease definition, a human preference for the consequences (harms and benefits) below the threshold as compared with those above it – in other words, it installs preferences in

relation to the possible false positive versus false negative errors that the IEC accept exist. This means the disease definition is preference-sensitive, specifically sensitive to the particular preferences installed in the Committee's cut-off selection. Despite a widespread contrary assumption, this conclusion holds up even if the function is of a strict 'hockey stick' shape, since patient's preferences may lead to a cut-off with medical consequences, even if ones without any are on offer.

4. Discussion

The UK chapter of MCBK has formed, in collaboration with the National Institute for Health and Social Care Excellence (NICE), a NICE Computable Implementation Guidance (NCIG) group with the ultimate objective of achieving HL7 FHIR standard-compliant digital guidelines. Its first major effort related to NICE Guideline (NG28) *Type 2 diabetes in adults: management* [16]**.** Of particular relevance here, this recommends that practitioners "Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences..." Quite quickly, NCIG found the diabetes management guideline contained significant challenges to its project in the form of "unstructured knowledge unlikely to be coded and some subjective judgement, for example, NG28 1.6.5 says 'Discuss and agree an individual HbA1c target with adults with type 2 diabetes. Encourage them to reach their target and maintain it unless any resulting adverse effects'" [17].

The NICE representative was acutely aware of the challenges of digitalisation [18]. "NICE is primarily still at level 1 of the [MKRF] knowledge hierarchy, producing much of its content as narrative text that, in computing terms, is unstructured... NICE has identified that adding structure and standard clinical codes to its guidelines, even to a semi-structured level, has significant methodological implications and an impact on the steps required to develop guidance... NICE understands that structured data and structured knowledge are crucial to enable the concepts of a continually learning healthcare system... Technically there are challenges of agreeing which existing formalisms, coding and information standards for representing clinical knowledge could be used to share knowledge effectively between systems, and where there are gaps, filling these by extending these standards or, if necessary, working to develop entirely new standards."

However, nowhere in the MCBK discussion or their later publication is the preference-sensitivity of the disease definition mentioned, or its major implications for digital structuring and computability explored. The definition of diabetes will, through the diagnostic threshold/s used in defining patients with it, embed the preferences of others over the probabilistic consequences of intervention and non-intervention. The preferences of a patient over those consequences are pre-empted in whole or substantial part by those of a group of medical experts. The guideline recommendation that the patient's preferences be 'taken into account' in the clinical consultation is therefore devoid of operational meaning.

Paradoxically, NICE can be interpreted as recognising the ontological problem, albeit in oblique fashion. In NG28 at 1.6.5 we find "Discuss and agree an individual HbA1c target with adults with type 2 diabetes. Encourage them to reach their target and maintain it, unless any resulting adverse effects (including hypoglycaemia), or their efforts to achieve their target impair their quality of life. Think about using the NICE

patient decision aid on weighing up HbA1c targets to support these discussions." The aid *Type 2 diabetes: agreeing my blood glucose (HbA1c) target* informs the patient that "For reducing the risk of long-term health problems, the evidence is unclear about how much extra benefit comes from aiming for a lower target HbA1c compared with aiming for a slightly more relaxed target. Discuss with your diabetes team how much benefit you might expect, thinking about your age, how long you have had diabetes and whether you already have some of the health problems that can come with it." There is no mention of what the 'slightly more relaxed target' might be, or of what the major long-term consequences of it would be. Instead, the remainder of the aid shifts attention solely to two possible downsides of 'aiming for a lower blood glucose target': having to take more medicines and being more likely to get side effects and being more likely to experience 'hypos'. The logic of NICE's acceptance of a 'relaxed target' (higher than 6.5%) for informed patients who decide to maintain glycemic control at (say) 7.2% HbA1c, is that the construction and diagnosis of a disease called diabetes is unnecessary.

5. Conclusion

The project to digitalise clinical guidelines for diabetes provides the opportunity to confront the currently undetected and undiagnosed challenge that follows from the preference-sensitivity of the disease definition. In making their decision on glycemic-related interventions, the preferences of the patient diagnosed with diabetes are currently pre-empted by those embedded in their diagnosis. Incidentally, the individualisation of care, as well as its personalisation, is jeopardised, because the knowledge about interventions being input into clinical decisions will often be compromised by the preference-sensitivity of the disease definition having affected the underlying research - such as trials being confined to persons with diabetes diagnosed at HbA1c $\geq$6.5%.

The informed consent process is jeopardised when the harms and benefits of interventions are not those associated with the observations for the individual patient, but ones mediated by their diagnosis. Specifically, we ask how can biomedical 'knowledge' in relation to a 'disease' support the personalised decision of a patient, if that 'knowledge' is sensitive to (more strongly, contaminated by) the preferences of the group of medical experts who created the disease, through the implicit installation of their consensual preferences in setting the threshold for its diagnosis? Patient's preferences should trump those of medical experts, whose expertise is confined to the medical consequences of options and does not extend to preferences over those - or any other - consequences.

Identifying a problem is not providing a solution, but it is a necessary condition for making progress towards one. What should digitalised Clinical Decision Support in the form of a Patient Decision Aid be doing? Pre-eminently it should be facilitating the elicitation of the patient's preferences in regard to the probabilistic consequences (benefits and harms) of available interventions at alternative cutoffs (e.g. 5.5, 6.0, 6.5, 7.0, 7.5), knowledge about which it is the aids function to provide, in conjunction with the clinician.

Most readers will have inferred that the argument has implications for all guidelines where the definition of the target condition involves a preference-based cut-off on a biophysical continuum (or instrument-based index). Osteoporosis and hypertension are just two of innumerable examples.

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