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The need for ethics as well as evidence in evidence-based medicine

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1. Introduction

Evidence-based medicine (EBM) stresses the examination of empirical evidence in clinical decision making [1]. Clinical guidelines exemplify the EBM movement, seeking to identify, distil, and disseminate evidence-informed best practice [2]. Such guidelines often include discussion regarding the quality and quantity of evidence for harms and benefits of interventions and methodological discussion regarding how analyses are conducted. Although the processes of distilling evidence have much to applaud—particularly progress to improve the systematic nature of guidance development—they also raise important epistemological questions pertaining to the construction of evidence, and the sociopolitical nature of applying evidence in clinical practice.

In this commentary, we argue that an important yet at present missing element in much EBM is the explicit presentation of the underlying systemic socioethical values or principles that frame and inform guideline development for clinical practice. Decisions regarding the introduction or (often more controversially) the removal of health care can be predicated on questions of evidence of benefits and harm and often present difficult decisions. However, this difficulty is not solely because the evidence is unclear (although often it may be). These decisions are difficult, and often contested because implicit within them are the expression of values; values over which there may be reasonable disagreement. In short, these decisions are value-laden [3,4]. Making these values explicit as part of the guideline-development process will help foster an ethos of transparency and facilitate discussion of best practice, particularly when guidelines present differing recommendations.

2. Differences of opinion regarding best practice may stem from differences in values as much as evidence

The example of recommendations regarding prostate cancer screening is illustrative in terms of how the expression of values may influence decisions in different contexts, despite the evidence being the same. In 2009, Clinical Practice Guidelines (CPG) were issued by the Royal Australasian College of General Practitioners (7th edn. 2009). This stated that men aged 55−69 years should not be offered prostate-specific antigen testing routinely [5]. Conversely, CPGs from the Urological Society of Australia and New Zealand stated that men aged 55−69 years should be offered prostate-specific antigen testing [6,7]. This divergent opinion arose despite both recommendations being produced in 2009 and thus having the same evidence base available to them. In a recent rapid review by the Canadian Agency for Drugs and Technologies in Health on published clinical guidelines for Prostate Cancer Screening [8], it was noted that although ‘‘[a]lmost all the included guidelines reported that their recommendations were based on a balance between the benefits and harms of screening, however, the specific outcomes reviewed in each guideline and the weights given for each outcome varied from one guideline to another.’’

Hence, even when the same evidence is available to researchers or policymakers, there will be judgments made that rely on values held by those making judgments. These values may differ, resulting in different outcomes.

3. Values in the selection and evaluation of evidence

Values are inherent even within a robust evidence-based approach. We use three key questions that illustrate the ethical issues arising at key stages of the EBM process in the following: (1) choices regarding who is involved in the decision-making process; (2) decisions regarding inclusion or exclusion of attributable benefits or harms; and (3) the reflection of values in the selection and evaluation of evidence.

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3.1. Evidence framing: who is involved in the decision-making process?

The selection of membership for development of a clinical guideline, or recommendation, reflects—although only implicitly—the values regarding the legitimacy of individuals to provide assessment of evidence. The framing of questions and evidence, and decisions regarding assessments of evidence, has been shown to be highly dependent on who gets to ''sit at the table.'' For example, in a study of mammography guidelines, Norris et al. found that guideline panels with a higher proportion of primary care physician authors were more likely to recommend nonroutine screening than those with a lower proportion [9].

Discussion of ethical issues regarding panel membership is sometimes limited to discussion of the need for explicit declarations of potential conflicts of interest, with additional calls for panel membership that reflects a broader range of stakeholders and not solely clinicians who may be content experts [2]. Yet such steps provide only a partial solution. They fail to explicitly address larger ethical questions of legitimacy: who are legitimate voices in the development of guidelines, and why? Some authors have, for example, called for greater inclusion of a broad range of stakeholders to be included in guideline development, such as patients and patient representative organizations [2]. Particularly when health care is publicly funded, questions of democratic legitimacy may mean that the recipients of care are legitimate voices in the debate. The National Institute for Health and Care Excellence (NICE) in the UK, for example, has developed a Citizen's Council to provide a public perspective on overarching moral and ethical issues that NICE has to take account of when producing guidance [10]. This, however, raises a further question: how much emphasis should be placed on these views? Indeed, NICE's own Citizen Council does not produce NICE's guidance, nor does it input directly into any individual pieces of guidance that NICE produces.

Consider as a further example the field of pediatrics. In some instances, we may feel that parental voices should hold more weight than in other cases. Parental pressure has been indicated as a barrier to reducing inappropriate antibiotic use in children [11], and one may argue that physicians should resist parental pressure and provide appropriate education to parents regarding antibiotic resistance instead. Given that (some) parents appear to be providing pressure for continued use of antibiotics when this may be contraindicated from a clinician perspective and the evidence regarding increasing antibiotic resistance due to unwarranted overprescription, should parents or parent advocates (with a range of views) be included in discussions to determine recommendations on antibiotic use?

In other instances, such as newborn screening for rare conditions, it might be argued that the rarity of these conditions creates a legitimacy for parental lobbying. We may, for example, feel that parental advocacy for inclusion of a condition on a state or national screening panel is more legitimate because of underlying concerns of equity and justice: these conditions are rare, often require expensive interventions, and without advocacy, afflicted children may experience a long ''diagnostic odyssey'' or fall foul of simple assessments that deem interventions not to be cost-effective. How should parent voices be weighed against existing criteria for screening? If a condition does not meet established criteria, then should lobbying (and the values underlying it) justify screening when to do so would risk negative outcomes? Indeed, the perspectives framing evidence can influence outcomes even when evidence-based processes are followed. Ubel et al. note, for example, that assessments of Health-Related Quality of Life (HRQoL) will vary depending on whether the public or patients are those making assessments [12]. As such, whether we take a societal or patient perspective, assessments of HRQoL may differ and could have important consequences for cost-effectiveness analyses, and ultimately health policy.

At the very least, we also submit that the process(es) by which membership selections are made, and who is selected for such membership, of any policy or clinical guideline panel that will affect the framing or use of evidence need to be made transparent at the outset of the process.

3.2. Decisions regarding inclusion or exclusion of attributable benefits or harms

Recent guidelines on tonsillectomy stipulated that

> tonsillectomy for recurrent throat infection should be limited to circumstances for which clinically important benefits are shown in randomized controlled trials [13].

This statement represents value judgments regarding not only the acceptable benefits and harms—only evidence of ''clinically important benefits'' were to be included in assessments of benefits and harms from watchful waiting in recurrent tonsillitis—but also that this was to be determined from evidence of benefits derived solely from randomized trials (RCTs). The statement therefore excludes other aspects of individual well-being from the evaluation, as well as benefits identified forms of study other than RCTs [13].

Evidence-based recommendations often also require tradeoffs between benefits and harms. This may include assessing evidence with respect to whom the benefits and harms accrue, as well as which outcomes are included in assessments. Such tradeoffs and decisions inherently involve the implicit or explicit expressions of values [14]. For example, should benefit be assessed with respect to the amount of improvement generated for individuals, or the overall level of population health, irrespective of individual health gains? [15] Decisions on such matters not only reflect one's underlying beliefs and values regarding the

goals of health care but also will play a practical role in guideline development by influencing evidence collection and assessment.

3.3. Values and evaluation of evidence

What, therefore, should be included in terms of evidentiary assessments? This is not just an empirical question regarding what information is available. It also raises epistemological issues regarding what should count as evidence [16], as well as any particular "framing" that evidence should have.

As indicated previously, value judgments may influence what is considered (appropriate) "evidence." Is it only evidence accrued through well-conducted RCTs or are observational studies appropriate too? How should judgments on these issues be made, and do they differ by context?

The example of data collection on rare or orphan diseases is also an example of how values may impact such evidentiary assessments. In this context, the rarity of these diseases often makes it difficult to obtain good quality data regarding treatment effectiveness or the natural history of the condition, and evidence collection and appraisal can often lag behind the introduction of the technology or intervention. In the absence of large-scale studies or the gold standard of good quality RCTs, what should be considered as appropriate evidence when making decisions?

4. Being explicit regarding values underpinning decisions may foster debate

It is incumbent on those developing CPGs or recommendations to recognize that the composition of the panel membership will influence many aspects of the evidence review process and, ultimately, the recommendation(s) made. Although some authors have sought to define and provide a taxonomy of evidence types [17], the clinical—and personal—backgrounds of panel members will affect the perspectives taken on legitimate forms of evidence for inclusion. This will also the appropriate scope of content that may be brought forward into an evidence appraisal.

Given these questions, we suggest that there is a need for a richer and more overt consideration of the socioethical issues pertaining to evidence-based practice guidelines. Specifically, there is a need to generate a better understanding of the rationales provided for decisions during the development of clinical practice guidelines.

Although guideline-development tools, such as the Grading of Recommendations Assessment, Development and Evaluation system [18], include steps in which guideline developers should give consideration to the importance of values, preferences, and utilities of stakeholders [19], they do not address specifically the underlying issue of making clear the values held by the guideline-development panel (and how they came to be held) and which inform the selection and evaluation of evidence. Indeed, research that has noted variation between recommendations on the same topic [6] points to a need to better understand the reasons for decisions within clinical practice guideline development.

Explicitly including values within guideline decision making will increase the transparency of decisions, facilitating debate regarding the legitimacy of such decisions and whether they meet the health needs of the population [15]. The explicit presentation of values and their weighting at specific steps in guidelines would allow readers to more easily make judgments as to the recommendations. The recent guidelines on tonsillectomy in children are an example of such transparency of values in the production of clinical guidelines, with each recommendation accompanied by a statement regarding the value judgments made by the panel and that informed the evidence review and decisions for that particular recommendation [13].

5. Analyses that explore values in guideline development may improve our understanding of barriers or facilitators to guideline adoption

Analyses that explicitly identify values and beliefs that underpin rationales informing decisions will also build on recent calls for the empirical assessment of the contingent structural, behavioral, or political factors that facilitate or hinder the adoption or rejection of evidence-based practice. For example, Prasad and Ioannidis have argued that in addition to evidence, there needs to be evaluation of inertia, conflicts of interest, social values, as well as lobbying and financial interests [20]. Developing a program of research to explore these factors, alongside increasing transparency of the values that inform evidence-based guideline decisions at every stage of the process would, we suspect, improve the implementation of new technologies. This may be through the enhancement of the evidence-based assessment process, but may also, in the context of withdrawing health technologies, help in understanding the values underpinning any move away from existing technologies.

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