BMJ Rapid Recommendations: Creating Tools to Support a Revolution in Clinical Practice Guideline Adoption

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Abstract

BMJ rapid recommendations hold the potential to revolutionize clinical practice guidelines, achieving both timeliness, trustworthiness, and usefulness to clinicians and patients to allow well informed decisions in clinical practice.

Resume

Les recommandations rapides de BMJ ont le potentiel de révolutionner les directives de pratique clinique, en apportant à la fois la rapidité, la fiabilité et l'utilité aux cliniciens et aux patients pour leur permettre de prendre des décisions éclairées en pratique clinique.

In this article we describe the limitations of currently existing clinical practice guidelines; how the BMJ Rapid Recommendations were developed to address these limitations; the process underlying BMJ Rapid Recommendations; and make a case that BMJ Rapid Recommendations represent a model for the future of clinical practice guidelines.

Three Kinds of Problematic Guidelines

Clinicians increasingly rely on clinical practice guidelines produced either by prestigious medical organizations, or by very widely used electronic textbooks such as Dynamed or UpToDate. There are, however, three kinds of problematic guidelines that may tempt, and mislead, clinicians: (1) guidelines that seriously violate standards of trustworthiness; (2) those that were once trustworthy but are now out of date; (3) guidelines that are current and meet many standards of trustworthiness, but nevertheless fail in some other important criteria.

The first, and worst, are produced by prestigious organizations, but seriously violate current, widely accepted standards of trustworthy guidelines. Indeed, many are best characterized as following the GOBSAT model: good old boys sitting around a table. Over the years, investigations have documented the limitations in such guidelines.[1–3]

In March, 2011, in response to the problem, the Institute of Medicine promulgated standards for trustworthy guidelines.[4] The standards include effective management of conflict of interest; appropriate panel selection; conduct or identification of systematic reviews addressing all important questions related to the guidelines; rating quality of evidence and strength of recommendations; and undergoing peer review. In 2013 the Guideline International Network published similar standards, based on wide agreement between their 100 organizational members.[5]

A study reported in 2012 documented the necessity for the Institute of Medicine suggestions.[6] The authors selected at

random, 130 guidelines from the National Guideline Clearinghouse (which, by the way, is no longer be available as of July 16, 2018 because the US government has discontinued its funding). Of 18 Institute of Medicine standards, 50% of guidelines met 8 or fewer. Fewer than half provided information regarding conflicts of interest, and of the guidelines that did provide the information, committee chairs had important conflicts in 71.4% and co-chairs in 90.5%. Committees developing guidelines rarely included an information scientist or patients and caregivers with experience of the condition. Guidelines published from 2006 through 2011 varied little with regard to average number of standards satisfied.

Fortunately, although documentation is unavailable, it is our impression that since 2012 an increasing number of guidelines produced by prestigious organizations do meet trustworthiness standards based on use of the GRADE framework: identify clear questions; use systematic reviews of the best available evidence; enlist panels that included experts, front-line clinicians, methodologists, and patients, all of whom are free of problematic address conflict of interest; rate the quality of evidence and strength of their recommendations; provide evidence summaries in a clinician-friendly manner; and make their underlying values and preferences explicit.

Over 100 organizations worldwide have adopted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, likely increasing the availability of trustworthy recommendations. The GRADE working group has developed a methodologically sophisticated, transparent approach to rating the quality of a body of evidence to inform a guideline.[7] In this approach a body of randomized trials start as high-quality evidence (on a scale of high, moderate, low, or very low) but may be rated down because of risk of bias, imprecision, inconsistency, indirectness, or publication bias. Observational studies start as low quality evidence, but may be rated up, usually because of large or very large effects. Figure 1 summarizes the GRADE approach to rating quality of evidence.

GRADE has identified issues that guideline panels should consider in moving from evidence to recommendations, and deciding on the strength of the recommendations. The primary criteria are the magnitude of the benefits, harms and burdens of the interventions and the comparators; the quality of evidence associated with the evidence of benefits, harms and burdens; and the underlying values and preferences of the population to whom the recommendation applies.[8] Additional criteria include cost, equity, feasibility, and acceptability.[9]

GRADE specifies two categories of strength of recommendations, strong and weak. Strong recommendations represent "just do it" situations in which benefits clearly outweigh harms and burdens – or the reverse.[10] Weak recommendations represent "think about it" situations in which the right course of action will differ depending on patients' circumstances, and their values and preferences, and should involve shared decision-making.[11] In some cases, patients may also appreciate such discussions even when recommendations are strong.

<table>
<tr><th>Study Design</th><th>Confidence in estimates</th><th>Lower if</th><th>Higher if</th></tr>
<tr><td>Randomized trials</td><td>High</td><td rowspan="4">Risk of bias
-1 Serious
-2 Very serious

Inconsistency
-1 Serious
-2 Very serious

Indirectness
-1 Serious
-2 Very serious

Imprecision
-1 Serious
-2 Very serious

Publication bias
-1 Likely
-2 Very likely</td><td rowspan="4">Large Effect
+ 1 Large
+ 1 Very large

Dose response
+1 Evidence of a gradient

All plausible confounding
+1 Would reduce a demonstrated effect or

+1 would suggest a spurious effect when results show no effect</td></tr>
<tr><td></td><td>Moderate</td></tr>
<tr><td>Observational studies</td><td>Low</td></tr>
<tr><td></td><td>Very Low</td></tr>
</table>

Figure 1. GRADE's approach to rating quality of evidence

Over 100 organizations worldwide have adopted the GRADE approach, markedly increasing the availability of trustworthy recommendations. These include international organizations such as the World Health Organization and the Cochrane Collaboration; major American professional groups including the American College of Physicians and the American Thoracic Society; and health technology assessment organizations such as the Swedish Agency for Health Technology Assessment. Canadian organizations that have adopted GRADE include the Canadian Cardiovascular Society, the Canadian Agency for Drugs and Technology in Health (CADTH), and the Ontario Health Technology Advisory Committee.

The second type of problematic guidelines are produced by medical organizations, are well done and thus trustworthy, but end up being rapidly outdated due to the publication of important new evidence long before their next iteration. This unfortunate circumstance results because professional organizations typically take years to produce trustworthy guidelines[12] in part, perhaps, because of the bureaucratic structures they have in place.

The third type of problematic guideline, perhaps best characterized by the recommendations appearing in UpToDate, are current. Despite considerable methodologic sophistication (UpToDate includes over 10,000 that adhere to GRADE criteria[13] and are presented as GRADEd recommendations[14]) they do not meet all important criteria for trustworthiness. In particular, they rely on previously published evidence summaries that may be limited or unavailable; they seldom present structured evidence summaries; they do not adhere to rigorous conflict of interest policies; and their process for deciding on the direction and strength of recommendations is not transparent.

Is it possible to produce guidelines that overcome the limitations of all three types of existing guidelines: that is, they meet trustworthiness standards and take into account the latest evidence?

A Fourth Type of Guideline that Addresses Problems of the First Three

A group of physicians and methodologists who ultimately became the Rapid Recommendations team, believed it was. We set out to create, in response to the publication of practice-changing evidence, new trustworthy guidelines over a very short period – 90 days was our initial target. Following a set of innovations to improve the authoring, publication and updating of trustworthy guidelines, we created the Rapid Recommendations project. We thought that the research and innovation program with which we are involved and which we call "MAGIC" (Making GRADE the Irresistible Choice, www.magicproject.org),[15] a non-profit research and innovation could provide the base from which to launch the project. In particular, the MAGIC electronic platform for systematic reviews and guidelines (MAGICapp), would be well suited to the dissemination of the guidelines produced. The MAGIC executive, potentially with other key players, would form a Rapid Recommendations steering committee (the current steering committee includes four of the authors of this article, TA, GG, RS and PV).

The MAGIC group developed a number of innovations to improve the authoring, publication and updating of trustworthy guidelines in the context of practice-changing evidence.[15] These included establishing a network of people to collaborate on the creating systematic reviews and guidelines, thus circumventing barriers of organizations currently undertaking guideline development. In pilot work, a group directed from McMaster University produced a series of systematic reviews, each in a matter of a few weeks. Knowing that this key step was possible, the steering group led two pilot recommendations that included gathering an appropriate panel, reviewing systematic review evidence, and producing recommendations.

Convinced from this pilot work that the endeavour was feasible, the Rapid Recommendations team now faced the challenges of ensuring the product was credible to medical audiences, and developing a dissemination strategy that would ensure medical practitioners would notice the new recommendations. To deal with this challenge, the Rapid Recommendations team succeeded in establishing a partnership between MAGIC and the BMJ.

The terms of the arrangement are as follows. The MAGIC group scans the literature, picking practice-changing new studies, updating the relevant systematic reviews, and producing guidelines that meet trustworthiness standards – all within a target of 90 days from the publication of the new evidence. All reviews and guidelines are consistent with GRADE guidance.

The BMJ is responsible for vetting the potential Rapid Recommendations topics and the guideline panel members' conflicts of interest, and conducting the peer review of the systematic reviews and the guidelines that emerged from the process. The outline of the endeavour and its process,[16] and the first of the Rapid Recommendations,[16] including the associated systematic reviews,[17] were published in the BMJ in September 2016. Since then, ten such Rapid Recommendations have appeared (Table 1).

Producing Rapid Recommendations requires the development and implementation of a rigorous process that would meet all the trustworthy recommendation standards and still allow guideline production in an extremely tight time frame. The first step in the development of a Rapid Recommendation is to identify potentially practice-changing new evidence. To do this, MAGIC has partnered with the McMaster Health Information Research Unit (HIRU), which produces a stream of pre-appraised evidence, widely disseminated, such as in the American College of Physicians Journal

Table 1. Published and ongoing Rapid Recommendations

RapidRec	Guidance
Antibiotics after incision and drainage for uncomplicated skin abscesses: a clinical practice guideline.[18]	We suggest TMP-SMX or clindamycin plus incision and drainage rather than incision and drainage alone (weak recommendation). We recommend trimethoprim and sulfamethoxazole or clindamycin over cephalosporins (strong recommendation). We suggest trimethoprim and sulfamethoxazole over clindamycin (weak recommendation).
Antiretroviral therapy in pregnant women living with HIV: a clinical practice guideline.[19] a	We suggest a zidovudine and lamivudine-based antiretroviral regimen over one that includes tenofovir and emtricitabine (weak recommendation). We recommend a zidovudine and lamivudine-based antiretroviral regimen over tenofovir and emtricitabine with ritonavir-boosted lopinavir (strong recommendation).
Arthroscopic surgery for degenerative knee arthritis and meniscal tears: a clinical practice guideline.[20]	We recommend against arthroscopic knee surgery in patients with degenerative knee disease (strong recommendation).
Atraumatic (pencil-point) versus conventional needles for lumbar puncture: a clinical practice guideline.[21]	We recommend the use of atraumatic over conventional needles (strong recommendation).
Corticosteroids for sore throat: a clinical practice guideline.[22]	We suggest short course steroids (weak recommendation).
Corticosteroid therapy for sepsis: a clinical practice guideline.[23]	We suggest corticosteroid therapy rather than no corticosteroid therapy (weak recommendation).
Low intensity pulsed ultrasound (LIPUS) for bone healing: a clinical practice guideline.[24]	We recommend against the use of LIPUS (strong recommendation).
Patent foramen ovale closure, antiplatelet therapy or anticoagulation therapy alone for management of cryptogenic stroke? A clinical practice guideline.[25]	For patients to whom all options are acceptable, we suggest PFO closure followed by antiplatelet therapy over anticoagulation therapy (weak recommendation). For patients to whom anticoagulants contraindicated, unacceptable, or unavailable, we recommend PFO closure followed by antiplatelet therapy over antiplatelet therapy alone (strong recommendation). For patients to whom PFO closure is contraindicated, unacceptable, or unavailable, we suggest anticoagulation over antiplatelet therapy (weak recommendation).
Transcatheter or surgical aortic valve replacement for patients with severe, symptomatic, aortic stenosis at low to intermediate surgical risk.[26]	For patients aged <65 years, we recommend SAVR over transfemoral TAVI (strong recommendation). For patients aged 65-74 years, we suggest SAVR over transfemoral TAVI (weak recommendation). For patients aged 75-84 years, we suggest transfemoral TAVI over SAVR (weak recommendation). For patients aged 85+, we recommend transfemoral TAVI over SAVR (strong recommendation). For people with severe aortic stenosis who are unsuitable for transfemoral TAVI, we recommend SAVR over transapical TAVI (strong recommendation).
Prostate cancer screening with prostate-specific antigen (PSA) test: a clinical practice guideline.	In press
Oxygen therapy for acutely ill medical patients: a clinical practice guideline.	In development
Colorectal cancer screening: a clinical practice guideline.	In development
Arthroscopy for patients with shoulder impingement syndrome: a clinical practice guideline.	In development
Clopidogrel and aspirin versus aspirin alone in patients with mild stroke or high risk transient ischemic attack: a clinical practice guideline.	In development

Club (ACPJC).[27] As part of HIRU's screening for new articles, they provide the Rapid Recommendations team, every day, with the latest articles that have the highest relevance and quality rating.

One member of the Rapid Recommendation steering group reviews the articles from HIRU. If a particular article looks promising (i.e., possibly practice changing) the team member identifies any recent systematic reviews addressing the topic, and reviews existing guidelines. If, at this point, the reviewer still considers the article has potential (in particular, they have a strong sense that one or more recommendations would change on the basis of the new evidence) the article is referred to the Rapid Recommendations steering group.

The steering group considers a number of issues in deciding whether to pursue the article further. These include the current Rapid Recommendations team workload (if overwhelmed, less likely to move forward); the complexity of the issue (more complex, less likely, though the team has repeatedly violated this criterion); the availability of a recent systematic review (if available more likely); and the probability that the Rapid Recommendation would indeed differ from existing recommendations (higher probability, more likely). After considering all the issues, the steering group either decides against moving forward, or presents the issue to our BMJ colleagues who then accept or decline the suggestion.

An acceptance at the BMJ level triggers the production of an updated systematic review. The exceptions are situations in which the article is itself a high-quality review – providing all needed information as defined by the guideline panel - that triggers the process in first place. There have been two such situations thus far: systematic reviews that demonstrated that atraumatic needles decrease post lumbar puncture headaches compared to conventional needles, and that high levels of inspired supplemental oxygen can increase mortality.

The reviews, when undertaken by the Rapid Recommendations team meet, as one might anticipate, criteria for rigor. These include explicit eligibility criteria; a comprehensive search; assessment of risk of bias; duplicate assessment of both eligibility and risk of bias; a quantitative summary; and rating of quality of evidence using GRADE criteria. Typically, an international team of methodologically trained individuals undertakes the review.

While the review is taking place, the Rapid Recommendations team recruits panelists, attending to issues of international representation and gender balance. Panels include content experts, front-line clinicians, patients and/or carers, and methodologists.[16] (LL) is responsible for all aspects of patient/carer partnership, including their recruitment and training. One notable feature of the process is zero tolerance for financial conflict of interest, and attention to and management of non-financial conflict.[28]

The latter, non-financial conflict, occurs most frequently when authors become attached to a particular piece of work they have produced, and the inferences one might make from that work – a frequent phenomenon in academic medicine. Other examples include previous statements of strong opinions regarding an issue, and professional conflict (e.g., radiologists sitting on guideline panels, in comparison to family physicians, tend to favour breast cancer mammograms as a screening strategy).[29]

Patient partners are typically those who have experienced the condition under consideration (individuals within the patient population of the Rapid Recommendation), whereas carer partners are informal caregivers of such patients. We recruit patients from multiple sources including organzations such as Citizens United for Evidence-Based Healthcare or the Society for Participatory Medicine, from the Cochrane Consumers/ Task Exchange databases, and organizations relevant to the guideline topic (e.g., in a guideline addressing prevention of vertical transmission of HIV, the International Community of Women Living with HIV), Twitter, and referrals from guideline panel members.

To ensure optimal involvement, patient/carer partners receive training in the technical aspects of the condition of interest, the methodology of evidence summaries, and the interpretation of magnitudes of effect. At the panel meeting, the chairs ensure that for many issues, and for all issues that pertain to values and preferences, the patient/carer partners have the first input into the discussion.

Despite the very strict conflict of interest rules, finding content area experts, typically academic clinicians, has generally proved relatively easy. There have been two exceptions: for one recommendation related to orthopedics, almost all candidates had received funds from device manufacturers that precluded their participation. The same was true for a recommendation regarding the vertical transmission of HIV. Nevertheless, even in those instances, we succeeded in obtaining the necessary expertise.

The Rapid Recommendation steering group seeks a diverse group of both experts (surgeons, medical specialists, academics from the allied professions) and front-line clinicians. Recruiting front-line clinicians often involves both primary care and specialist physicians, but also allied health professionals including nurses, nurse practitioners, physio- and occupational therapists. For both specialist and front-line clinician roles, Rapid Recommendations seek both geographical (typically four or more continents are represented) and gender diversity.

The least difficult recruitment for the panel is clinician methodologists. Both the chair and methods co-chair typically fall in this category, and thus far several of the Steering Group have been involved, ensuring that all of the leadership becomes acquainted with the not insubstantial challenges that repeatedly have arisen.

The primary leadership for each Rapid Recommendations rests with the chair and the methods co-chair. The latter is a particularly onerous role because it involves ensuring that the systematic review is conducted in a timely and optimally rigorous manner; the panel is recruited ensuring all relevant parties; all runs according to a very tight time line; and the recommendation, along with supporting documentation including an interactive decision aids, appear online in the MAGICapp for widespread dissemination.

The final Rapid Recommendations product includes innovative presentation formats (for example, see Figure 2). To facilitate shared decision-making, the team produces electronic decision aids in MAGICapp designed for the patient-clinician encounter that are available for every BMJ Rapid Recommendation.

One limitation of the Rapid Recommendations is that the funding constraints, time frame, and geographical diversity of the panel preclude any face-to-face panel meetings. Even for the electronic meetings required, with typically in the order of 20 panel members, scheduling meetings represent a challenge. Scheduling exigencies not infrequently require more than one parallel panel meeting. Other challenges have included ensuring open access to the recommendations, limitations in evidence available regarding user testing and dissemination of recommendations, co-ordinating with the journal editorial process, and achieving publication timelines.

The first of these Rapid Recommendations appeared in September 2016 and addressed transcatheter versus surgical aortic valve replacement (TAVI for the older, SAVR for the younger).[16] The review required not only a systematic review of the relevant randomized trials,[17] but also a review of the prognosis of SAVR.[17] Table 1 presents all the BMJ Rapid Recommendations to date, both those published and those in process. Clinicians can access all published RapidRecs guidelines and affiliated systematic reviews through the following link: https://www.bmj.com/rapid-recommendations.

BMJ Rapid Recommendations hold the potential to revolutionize clinical practice guidelines, achieving both timeliness,

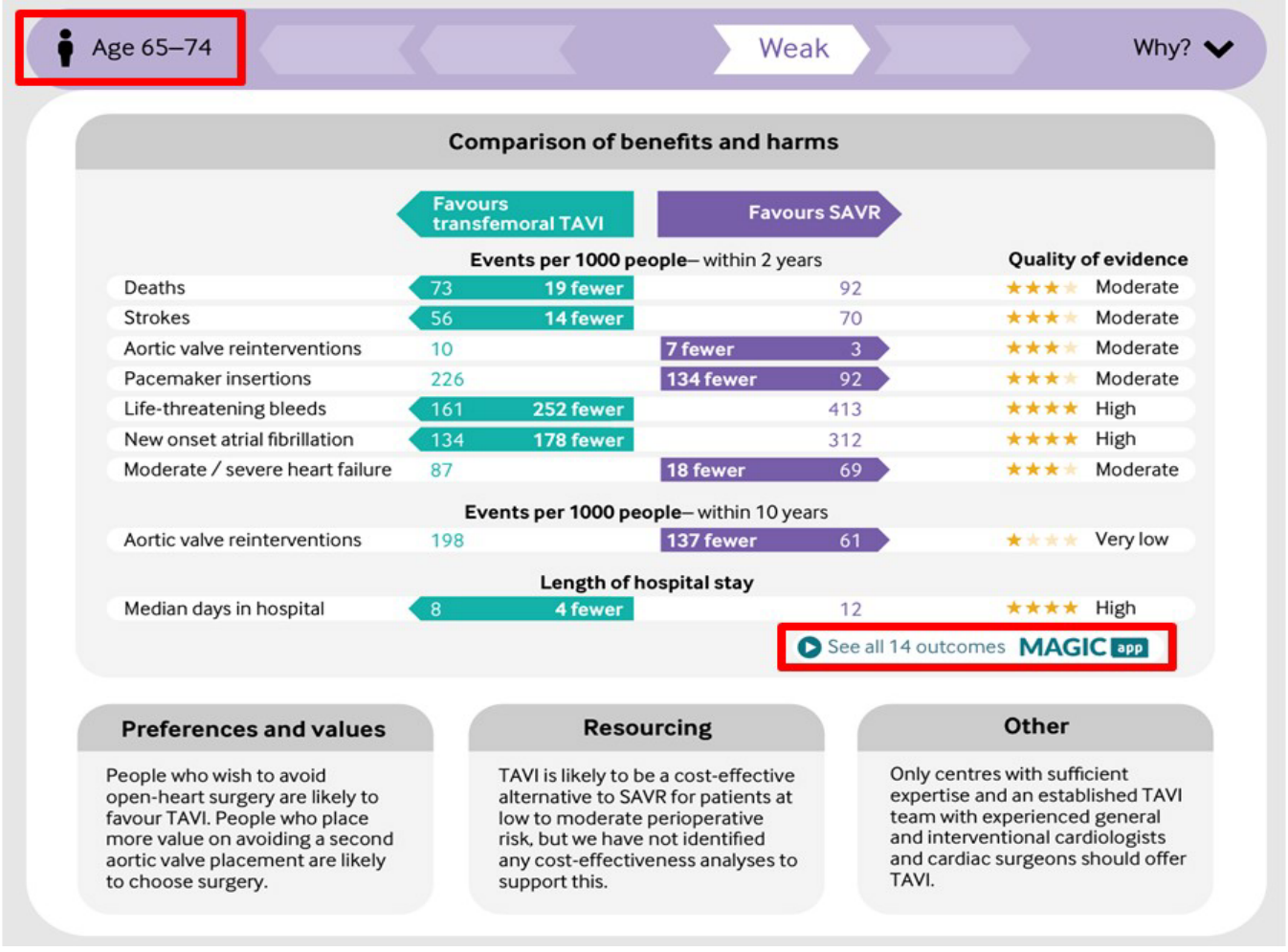

Figure 2. Infographic from Rapid Recommendation TAVI versus SAVR.

trustworthiness and usefulness to clinicians and patients to allow well informed decisions in clinical practice.

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