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Review article

A three-step health services research approach to improve prescribing

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ABSTRACT

Medications are often prescribed suboptimally; some effective medications are underused, some ineffective medications are overused, and some medications that should be received by a few are instead given to many. The underlying causes of suboptimal prescribing likely differ for each medication, and therefore must be understood anew, although previous studies can help generate hypotheses. This perspective sets forth a 3-step research agenda, which has worked well for us in several recently completed and ongoing projects. The three steps are to 1) demonstrate variation in suboptimal prescribing for the targeted medication; 2a) use mixed methods to understand the patient-, provider-, and system-level causes of suboptimal prescribing for this medication; 2b) develop a justification for improving the use of this medication, often involving a business case analysis; and 3) develop and implement interventions to improve prescribing of the targeted medication, informed by what has been learned in Steps 1 and 2 and relying on the principles of implementation science. Previous efforts have focused disproportionately on Step 1, or documenting gaps in practice, and Step 3, or deploying and evaluating efforts to improve practice. Our contention is that addressing all three steps sequentially, while effort-intensive, will maximize the chances of deploying a more effective intervention that will impact population health. We commend this three-step approach to health services researchers who wish to maximize impact by basing their research on a natural progression from documenting problems, to understanding their causes, to formulating and deploying a solution.

1. Improving medication use: producing more and better evidence is not enough

The field of medications research is dominated by clinical trials and observational comparative effectiveness studies. There are thousands of researchers employed in expanding the evidence base for which medications work and under which conditions. The output of this large research community is indeed helpful at expanding our evidence base about medication efficacy, effectiveness, and safety over time. However, only a fraction of research on medications approaches them from a health services research (HSR) point of view. This leaves important problems with medication use unaddressed, because producing more and better clinical evidence is not sufficient in and of itself to improve care delivery.[4] The present article is therefore an attempt to interest more practitioners of HSR in focusing their efforts on improving medication use, as well as to define one logical way to proceed with such research efforts.

The present manuscript will propose a 3-step approach to building a research agenda to improve the use of medications, often one medication or medication class at a time. Examples will be drawn predominantly from our own group's recent work, in part because our efforts have been organized using this 3-step model and therefore can serve to explain how it works. The 3-step research agenda proposed here is not entirely new. Indeed, there have been important efforts to improve medication use going back decades. While there are too many to fully cover in this brief narrative review, we would mention the rational drug use movement, accepted at the World Health Organization in 1985.[28] This idea led to numerous interventions to promote more judicious use of medications, which have been summarized elsewhere.[13] For example, academic detailing is one particularly well-known approach to improve prescribing.[25]

However, despite this extensive history, the context within which prescribing occurs has changed considerably over the past several decades, as the practice of medicine has evolved. While gaps in practice remain, most clinicians today are at least familiar with the idea of evidence-based medicine. We also have new tools at our disposal to facilitate improved practice, including real-time data on prescribing from electronic medical records, resources that efforts of the past did

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not have. Just as the reality within which clinical practice has changed, our approach to improving medication use also must evolve to fit the changing reality. The present manuscript recommends systematically investigating the causes of suboptimal prescribing prior to formulating an intervention – an idea that has not previously been emphasized, to our knowledge, and which holds the promise of possibly accelerating system improvements through more precisely targeted efforts. It is thus hoped that readers will use this article as a helpful guide to organize their medication-related research agendas to maximize the impact on population health.

2. A related conceptual framework: reducing health disparities

Our conceptual framework owes much to the influential 3-step framework first advanced by Amy Kilbourne and colleagues for health disparities research.[12] In that article, Kilbourne and colleagues proposed 3 steps for HSR to address health disparities: 1) Detection: document the existence and extent of the disparity in process and/or outcomes of care between vulnerable patients and non-vulnerable patients; 2) Understanding: identify the determinants of these gaps, including patient-, provider-, and system-level determinants; and 3) Reducing Disparities: develop and implement an intervention to reduce or eliminate disparities, informed by what was learned in Step 2. Before Kilbourne's article, there were many articles and projects documenting disparities (i.e. Step 1), but relatively few about understanding them (Step 2) and even fewer about reducing them (Step 3). While it remains easier to document a disparity than to understand or address one, journal editors and especially grant review panels have increasingly demanded that health disparities research address all three steps. Thus, while the ideas in the article by Kilbourne et al. were not entirely new, their ability to clearly articulate these ideas has done much to advance the field of health disparities research over the past decade. Here, we advance a similar 3-step model for addressing the problem of suboptimal prescribing. It is our hope that a lucid articulation of this model will similarly advance efforts to address suboptimal prescribing within HSR. We explicitly acknowledge our debt to the paper by Kilbourne et al.

3. The problem: suboptimal prescribing

Medications often are not prescribed in ways that optimize patient outcomes, despite the existence of evidence to the contrary. There are at least five ways that prescribing can be suboptimal:

1. *Superior medications may be underused*. An example would be persistent underuse of clozapine, the only medication proven effective for treatment-resistant schizophrenia.[11] While guidelines recommend that all patients with treatment-resistant schizophrenia should be offered a trial of clozapine, only a few ever receive it, and most continue to receive inferior treatments.[14] There are reasons to explain this underuse, but it has important consequences for these patients.
2. *Inferior medications may be overused*. A current example of this phenomenon is the use of digoxin as a first-line agent for rate control in atrial fibrillation. Digoxin can be used for atrial fibrillation (for rate control) or heart failure (for symptom reduction). While its use for heart failure appears to be relatively safe, numerous well-performed observational studies have pointed to an increased risk of mortality, as summarized in a recent meta-analysis.[15] It would seem, therefore, that unless contrary evidence emerges, beta-blockers or calcium channel blockers should be the first-line agents used for rate control in atrial fibrillation, and digoxin should be reserved for unusual patients that do not respond adequately to the first-line agents or do not tolerate them. It is not yet known to what extent practice patterns have changed in response to these findings, but the area is ripe for research.
3. *Medications that should be used by a select few, but are given to a great many instead ("wrong person")*. There are many medications that fall into this category, and it is especially challenging to combat this form of overuse or misuse; because some patients genuinely qualify for the medication, it must remain available. A good example would be testosterone therapy, which is indicated for patients with hypogonadism due to diseases of the testes, pituitary, or hypothalamus. Testosterone is prescribed to some men with valid indications – and also to approximately twenty times as many men without valid indications, for less clear reasons.[8]
4. *Dosing errors ("wrong dose")*. The classic example of a situation in which the dose of a medication should be altered or customized is renal failure. A substantial literature has documented widespread failures to adjust doses for renal function[3] and programs have been developed to help ensure that such adjustment happens more consistently.[10] There are other situations, however, in which doses should be tailored to each patient, but are not. Adequate management and titration of warfarin doses, for example, can make a major contribution to improving the safety and efficacy of this medication.[17]
5. *Inadequate evaluation before initiation, or inadequate monitoring after initiation ("wrong process")*. For example, we have documented inadequate evaluation before initiation of testosterone for as many as 97% of recipients, compared with what is recommended by clinical practice guidelines.[9] Fischer et al. have described widespread failures to complete recommended laboratory monitoring for a variety of medications.[5]

The existence of these five kinds of suboptimal prescribing also help to guide what sort of improvement will be the goal of the research program. For example, if a superior medication is being underused, the goal should be to increase the appropriate use of that medication. If an inferior medication were being overused, then the goal should be to limit its use to appropriate situations (which may be never). The other categories also lend themselves to logical improvement goals.

Given these five kinds of suboptimal prescribing, we need a framework within which we can systematically understand what drives suboptimal prescribing, and then, based upon that understanding, act to address it. Below, we will lay out a 3-step research agenda that moves from understanding the causes of suboptimal prescribing for each medication to designing an effective remedy.

4. A word about scope

There are many mechanisms which have been recommended as a pathway to improved use of medications, including 1) improved mechanisms for initial drug approval; 2) better ongoing safety oversight by the US Federal Drug Administration (FDA); 3) changes in regulation, such as banning direct-to-consumer advertising; or 4) changes in payment models. While all of these ideas have merit, they would all require changes in law or policy, and are therefore outside the scope of this article. The intention of this piece is to outline a pathway to improved prescribing, explained through the prism of a three-step research agenda. This pathway has the advantage of not requiring any changes in law or policy, and can be enacted within the limits of presently existing conditions.

5. General approach to understanding suboptimal prescribing

Before considering how to address suboptimal prescribing, it makes sense to consider its underlying causes. In the examples discussed above (such as clozapine and testosterone), we purposely avoided a discussion of why those medications are suboptimally prescribed. In fact, there are many reasons why medications may be suboptimally prescribed: there is a vast literature that relates to this topic, and a full exposition would be beyond the scope of this article. The relative importance of different