Prescribing medications with indications: time to flip the script

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► http://dx.doi.org/10.1136/
bmjqs-2022-015452

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Drug indications are the link between a drug and the patient. Indications link the evidence-based benefit of a drug for a specific population to a particular patient's clinical condition. Unfortunately, in prescribing they are more often the 'missing link', with explicit documentation of the indication usually missing from the prescription, despite considerable evidence and recommendations (dare we say exhortations) that documenting the indication would make the entire medication use process safer.[1–4] Patients want to, need to and have a right to know what each of their medications is for.

This issue of *BMJ Quality and Safety* includes a paper urging incorporation of drug indication into the prescription order, which follows several pieces recently published in *BMJ Quality & Safety*.[5–7] In this case, Feather and colleagues conducted a systematic review and narrative synthesis identifying 21 articles germane to advancing indication documentation in electronic prescriptions.[5] Their focus was mainly directed towards examining interventions that could facilitate indication-based prescribing as well as identifying barriers, facilitators and associated outcomes. Their finding of a 'mostly positive' impact of the interventions both in terms of uptake of indication documentation, as well as on various clinical and workflow outcomes, is consistent with prior studies and meta-analyses.[6 8] One of their interesting and important findings is that the biggest benefit observed in several of the studies (mostly antimicrobial prescribing) was in the domain 'appropriateness of medication'. Overall, most of the heterogenous studies they identified were relatively small scale, low on the hierarchy of evidence (with few randomised controlled trials (RCTs)), but nonetheless take us a few steps forward in this long and frankly stalled journey.

For full disclosure, two of the publications cited in Feather's review were from our own group, reporting on an AHRQ (Agency for Healthcare Research and Quality)-funded project aimed at developing multistakeholder consensus for the design of an indication-based prescribing prototype, and then performing a head-to-head comparison of this prototype computer provider order entry (CPOE) module against the two leading US commercial electronic medical record (EMR) CPOE systems (Epic and Cerner).[9 10] While our study was an RCT that had a positive result (ie, more reliable documentation of the indication on the prescription, decreased errors and greater prescriber efficiency and satisfaction), we consider it more a proof-of-concept than definitive evidence of the superiority of our approach. However, we suspect that even the additional evidence that Feather's review provides, the current inertia that prevails despite decades of urging, particularly by pharmacists, consumer groups and safety experts, will not be easily overcome. What is needed is a more radical rethinking of the rationale, design, prescriber workflow, and especially clinician buy-in, of incorporating indications into medication prescriptions and thereby have a beneficial effect in several domains (see table 1).

Former US President Dwight Eisenhower aptly stated: 'Whenever I run into a problem I can't solve, I always make it bigger. I can never solve it by trying to make it smaller, but if I make it big enough, I can begin to see the outlines of a solution.'[11] And as Levins stated: 'Contrary to common sense, big problems are often more soluble than small ones.'[12] In this editorial, we would like to take a step back and look at the broader issues and bigger solutions we think are key to making progress.

Our vision of documenting the indication is *not* based on adding an extra step (entering the indication after the drug has been ordered), which further burdens busy

Table 1 Emerging/evolving rationale and role for indication-based prescribing: going beyond adding indication simply to inform patient and pharmacist[1]

Domain	Emerging function	Example
Decision support for drugs of choice	Help prescribers recall and access best/current Rx for diagnosis.	Enter: *rheumatoid arthritis*—CPOE suggests appropriate next drug to order.
	Facilitating antimicrobial stewardship.	Enter: *cellulitis*—CPOE lists the narrowest spectrum antibiotic choice based on local resistance rates and current recommendation.
Safer prescribing	Second piece of information to cross-check for wrong drug, patient and dose.	Erroneous orders of hydroxyzine 25 mg for hypertension, hydralazine 25 mg for itching would be easily recognised.
	Forcing function to filter CPOE choices to avoid look-alike sound-alike or computer menu 'pull down' errors.	Erroneous ordering of penicillamine instead of penicillin (next to each other on pull-down lists) is not possible since it does not appear as a choice for dental infection.
Patient education and adherence	Permit pharmacists and nurses to more meaningfully counsel patients on their medications.	Explain to patients why (and how) they need to take their prednisone or warfarin (so don't have to guess among scores of indications).
	Help patients understand what each medication is for and avoid confusion leading to erroneously mixing up meds.	Patients stopping their drug for diabetes thinking it was the med for their depression, which had resolved.
Medication reconciliation and deprescribing	Group meds together to visually facilitate spotting duplicates or candidates to stop (or start).	Group/visualise all of patient's blood pressure meds to assess current regimen for that problem, aiding in deciding on any needed changes.
	Reluctance to stop meds started by another clinician if uncertain why it was started.	Why is the patient taking a chronic PPI or digoxin? Depends on the indication whether it can be safely stopped (or tapered).
Prior authorisation (PA)	Prescriptions meeting indication-based criteria could have orders automatically approved without added 'PA' paperwork.	'Headaches refractory (or allergic) to 1st line medications' (this is the indication) automatically approved for second-line more expensive agents.
Artificial intelligence machine learning	Expanding role of mining of big databases for real-world drug discovery and research. Indications needed to evaluate drug's effectiveness (and adverse effects) for that problem.	Exploring subsets of patients who most favourably respond or are more likely to experience an adverse effect. Outcome research of long-term effectiveness for a particular indication.

CPOE, computer provider order entry; PPI, proton pump inhibitor.

prescribers. Instead, our model is based on radically redesigning the CPOE process. Rather than mandating an extra task, even one as beneficial as documenting the indication appears to be, we believe we should turn the prescribing process on its head, by reversing the conventional order of prescribing a drug—and starting with (and thereby capturing) rather than ending with, adding the drug indication. For example, a prescriber would first enter 'gout' into the CPOE system, and because the EMR knows the patient's age, weight, allergies, renal function, current and prior drugs (including those that have been tried and failed) and insurance status (including which drugs are on vs off formulary), the CPOE system could then populate the order with the suggested evidence-based drug(s) of choice (with the correct dosage/regimen) for that specific patient.

This redesign of the prescribing process immediately raises several questions and red flags, especially for prescribing clinicians. Why should 'big brother' tell me what to prescribe and take away my autonomy to prescribe the drug(s) I have always used or that I know would be best for this patient? Who decides on these 'drugs of choice', and how can I trust the CPOE-recommended choice is accurate, up to date and unbiased? How is this list developed and continuously updated and integrated into my CPOE system? What if I (or the patient) disagree with the recommended medication? How is such a transformed CPOE system designed and integrated into my workflow in a way that does not slow me down, or might even make my ordering more efficient? How will we get the commercial EMR vendors motivated to design such streamlined systems? What happens to all the patient's current medications that are not tied to indications or may not be the computer's drugs of choice? And if the indication is (as proposed) transmitted to the pharmacy and put on the patient's medication label, what about potentially stigmatising diagnoses such as sexually transmitted infections (STI) or psychiatric diagnoses? We need to do more than just 'address' these questions but seriously advance more compelling rationales and put in place new mechanisms to ensure these well-motivated concerns are laid to rest, resulting in better safer care.

As a first important step to start addressing some of these questions, we have come to believe that the greatest potential benefit of indication-based prescribing is facilitating optimal prescribing by directing electronic ordering to drugs of choice (also to optimal dosage and regimens).[13] Most readers would agree that it is far from optimal if prescribers are choosing drugs based on a recent sales pitch or a pizza from a pharmaceutical representative, but many of us also realise how difficult it is to keep up with all the new drugs and recommendations in

an ever-expanding pharmacopoeia.[14] Combine this with challenges of keeping track of the latest studies, and all of the patient's clinical variables (renal function, prior and current drugs, disease stage and other diseases, formulary tier coverage and copayments, etc), then it is clear that anything the EMR can do to support prescribers' choice of drugs should be welcomed. Helping prescribers quickly and efficiently compose the best prescription up-front, rather than firing multiple alerts when they go to sign the order, would represent a true and welcome type of 'decision support'.

When treating an acute gonorrhoea infection, many US clinicians will turn to the Centers for Disease Control and Prevention STI online recommended regimens to see an update on current resistance patterns and recommendations. We need to create a similar trusted, transparent, evidence-based and consensus-based authoritative process and structure to delineate and continuously update drugs of choice overall. The outlines and processes for such a structure and mechanism for designating drugs of choice can be seen in various extant models such as local and national pharmacy and therapeutics (P&T) (formulary) committees (eg, the Veterans Affairs National Formulary Committee), American Society of Health-System Pharmacists (ASHP) Guidelines on the Pharmacy and Therapeutics, Pharmacy Benefit Managers (PBMs), Joint National Committee on Hypertension Treatment, the UK National Institute for Health and Care Excellence, Medical Letter Drugs of Choice, as well independent drug bulletins such as Prescrire and Worst Pills, Best Pills. Recommended best choices will likely and appropriately give prescribers more than one alternative when there is no clear evidence of superiority of one versus another option. In addition, the system needs to permit prescribers to enter a different drug of their own choosing for that indication, which may not be listed in the recommended choices—an option that would provide prescriber buy-in and continuous learning from outliers and user-entered choices, including the drugs chosen and outcomes. Any official committee issuing such guidance would have considerable power but also face considerable economic and even political pressures. But with the requisite transparency, proscription on conflicts of interest and evidence-based processes, their expert recommendations can be incorporated into indication-based prescribing. Considering there are already a host of third parties (eg, PBMs, hospital P&T committees) directing physician prescribing, and we acknowledge this system will be far from perfect (eg, the EMR may not know a patient is trying to become pregnant or has an unreported allergy), creating a more expert, unbiased and accountable mechanism for prescribing drugs of choice represents an important step forward.

The second and third compelling domains benefiting from the redesigned prescribing process—safety and patient education—overlap and intersect. Look-alike sound-alike medication errors, overdosing or underdosing, wrong patient errors and pill and route mix-ups should all be rarer in an indication-prescribing environment.[15–17] Protections against these types of errors derive from a layer of cross-checks that indications add. This is akin to current best practice of asking patients for two identifiers—for example, name and birthdate, to guard against wrong patient errors. For example, a pharmacist filling an order for hydroxyzine 25 mg could easily spot 'hypertension' on the indications and question whether the intended drug was, in fact, hydralazine 25 mg, thereby avoiding this frequent look-alike sound-alike error. Moreover, an indication-based order for 'hypertension' would not even display hydroxyzine as a choice, unlike current 'pull down' menus where the look-alike medication is physically adjacent and thus vulnerable to an errant mouse click. Also, a patient erroneously handed a bottle of pills for 'gout' might easily recognise the error and speak up, saying, 'I don't have gout.'

Patients often are confused about 'which pill is for what'. Instead of 20 undifferentiated medications sitting on their bathroom cabinet shelf, they would recognise from the label which pill is for their blood pressure (and thus important to take daily), versus a medication that was for their toothache or dizziness which may have resolved. There will be more minor technical issues related to fitting this information on the small bottle label or translating to lay or non-English language terminology, but these can be overcome. Thornier, but also surmountable, is the avoidance of placing a potentially stigmatising diagnosis on a label when a patient or a clinician feels it is best not to display. In our prototype, we addressed this by: (a) allowing the prescriber to manually click a box to suppress the indication for the prescription, and (b) having all STI and psychiatric indications suppressed by default.

Including the indication would also benefit medication reconciliation and deprescribing, which are increasingly recognised as important components of safe medication management,[18–21] although neither is mentioned in the articles Feather reviewed. Designated indications would permit all the drugs for a given problem (eg, diabetes, hypertension, gout) to be grouped together rather than buried in a long undifferentiated alphabetical list. Thus, allopurinol and Zyloprim (the same drug) come together and can be recognised as duplicates. Having the indication would also empower deprescribers by knowing *why* a drug was *started*, as otherwise they would be appropriately hesitant to stop a drug started by another physician that might potentially be needed for some (otherwise unknown) indication.

Prior authorisation has become a huge administrative burden for physicians, practices, pharmacists and patients. Capturing and transmitting a specific indication with the prescription (eg, dental infection, allergic to penicillin) should in many cases obviate the need for back-and-forth calls and faxes. Naturally, this feature introduces the risk that prescribers will use indications to 'game' the approval process, thereby potentially corrupting the veracity of designated indications.[22 23] While this is not the place to discuss this in detail, we can envision mechanisms which

could make the process both more efficient and truthful, especially by allowing free text to accompany indications that could justify exceptions. Finally, and relevant to accurate data capture, are the rapidly expanding fields of artificial intelligence and machine learning. Given the current general lack of indication documentation associated with individual prescriptions,[24] there have been several efforts to infer indications from medication use databases, with only modest success (in one effort 63% sensitivity, 94% specificity[25]). However, getting the actual indication entered directly by the front-line ordering prescriber avoids the need to (uncertainly) infer the indication and permits machine learning to be more usefully directed towards examining outcomes for that specific indication.

In conclusion, flipping the script so that clinicians first enter the indication (or even click on a problem or diagnosis in their note or patient's problem list) helps the prescriber compose a more optimised prescription as well as capture an accurate indication, and therefore is a win-win-win strategy; less work for the ordering clinician, safer and more appropriate prescribing and documentation of the indication, thereby providing important information that can be used by patients, pharmacists and other members of the clinical team, as well as for reimbursement, research and quality improvement.

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