PERSPECTIVE

A Research Agenda for Enhancing Appropriate Opioid Prescribing in Primary Care

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The challenges facing patients and providers in managing ongoing opioid analgesic therapy for chronic pain are complex. Benefit of long-term opioid therapy, for which there are scant data, must be balanced against myriad potential undesired outcomes, including safety problems, ranging from mild toxicities to overdose and death; inadequate efficacy, which may mean continued patient suffering and unwarranted exposure to toxicities; and misuse of these potent medications. To help patients and providers navigate these challenges and optimize therapy, we present a research agenda in which we first characterize appropriate ongoing opioid prescribing and then describe three areas where quality improvement work is needed: 1) developing brief validated measures of patient-reported safety, efficacy, and misuse that improve outcomes; 2) designing evidence-based algorithms to guide changes in therapy when issues related to safety, efficacy or misuse are identified; and 3) promoting use of patient-centered, multi-modal treatment plans.

KEY WORDS: opioid analgesics; medication safety; provider behavior; quality of care.

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As rates of prescribing rise, large scale pharmacoepidemiologic studies demonstrate increasing rates of adverse outcomes related to opioid analgesic therapy, most notably unintentional overdose deaths.¹ Various policy-level approaches to ameliorating this public health crisis have been proposed,² and innovative metrics for studying quality at the healthcare system level are under development.³ But perhaps the largest area of need for innovation and quality improvement is at the point of care, where inappropriate prescribing may be partly responsible

for poor outcomes. Herein, we focus on ongoing prescribing, as opposed to the initial decision to prescribe opioids, since the former represents the vast majority of opioid prescriptions, yet unfortunately draws little attention in clinical research. One challenge to quality improvement in this area is lack of clarity on what appropriate ongoing opioid prescribing means. To this end, there are two main objectives of this commentary: to characterize appropriate ongoing opioid prescribing concordant with consensus guidelines, and to propose three key areas for research to help provide front-line clinicians with evidence-based strategies to reduce inappropriate prescribing.

CHARACTERIZING APPROPRIATE ONGOING OPIOID PRESCRIBING: SHIFTING FOCUS

Most of the literature on monitoring opioid therapy addresses identifying problematic patient behaviors. While patient assessment is critical, we need to focus on provider behavior, a fundamental component of quality of care evaluations for other medical therapies.^{4,5} Consensus guidelines^{6,7} provide a roadmap for operationalizing appropriate prescribing; herein we highlight concepts that deserve special emphasis and serve as the basis for recommendations described below.

At the core of appropriate ongoing opioid prescribing, and all medical therapies, is timely, effective monitoring for, and response to, evident harms and benefits of therapy, including discontinuation of therapy when harms outweigh benefit or benefit is lacking. Effective monitoring must include assessment of the full breadth of important outcomes that should inform provider decision-making, namely, safety-related, efficacy-related and misuse-related issues. As part of the safety assessment, appropriate opioid prescribing should include consideration of potential interactions with co-prescribed medications, including other controlled substances such as benzodiazepines, alcohol, and illicit substances. With respect to enhancing efficacy, consensus guidelines and a growing body of evidence^{8,9} support multi-modal pain treatment. Opioid therapy is optimal when provided along with education to promote

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patient self-efficacy and self-care, and evidence-based psychological and rehabilitation therapies.

ENHANCING APPROPRIATE ONGOING OPIOID PRESCRIBING: A THREE-PRONGED APPROACH

At least three components are needed to assist clinicians in improving quality of ongoing opioid prescribing: 1) validated ways to measure safety, efficacy, and misuse; 2) evidence-based algorithms to guide changes in therapy when issues related to safety, efficacy or misuse are identified; and 3) the use of patient-centered, multi-modal treatment plans. We describe each in the section that follows in an attempt to outline a blueprint for research in these key areas.

Developing Feasible Ways to Monitor Safety, Efficacy and Misuse

Expert consensus promotes frequent monitoring of benefit and harm in opioid prescribing, but falls short in operationalizing this process.⁶ Currently available tools are too long to be efficiently incorporated into busy primary care settings, do not assess all three of the relevant monitoring domains (i.e. safety, efficacy and misuse), and have not been tested in clinical practice or shown to improve outcomes.^{10–14} We propose that routine monitoring should include a brief, patient-administered screening checklist incorporating items related to safety, including specific adverse effects and toxicities; efficacy, focused on physical and emotional functioning; and misuse performed with regular frequency throughout the course of therapy. An optimal checklist would be highly sensitive; a positive screening test should signal the provider to perform a more thorough assessment before refilling a prescription. This approach would be concordant with the National Institute of Health's¹⁵ and the Agency for Healthcare Research and Quality's¹⁶ recommendations emphasizing the development of assessments that 1) patients can understand, 2) focus on treatment effects important to them, and 3) provide clinicians with meaningful, actionable information. The brief checklist would complement other recommended monitoring tools such as treatment agreements, urine drug testing and the use of prescription monitoring databases.

Refining Treatment Pathways for Use When Safety, Efficacy or Misuse Issues are Identified

Routine, standardized monitoring will have limited value unless providers have clear protocols for next steps in management. Brief instruments might indicate three possi-

ble categories of suboptimal opioid therapy: safety-related issues; low efficacy; or problems related to misuse or any combination therein. Stemming from this determination, evidence-based protocols should be developed that address common clinical scenarios. For example, with regard to safety issues, dose-lowering protocols for patients experiencing adverse effects (e.g. somnolence) should be developed. With regard to low efficacy, much work remains to be done in terms of studying and establishing treatment protocols. When faced with low efficacy, providers have little guidance on the next step: a dose increase, trial of another opioid, intensification of adjunctive pharmacologic and non-pharmacologic treatments or cessation of opioid therapy. Though individual patients' adequate doses will vary depending on pain condition and pharmacokinetic and pharmacodynamic factors, an evidence-based consensus surrounding a morphine equivalent dose, duration and number and type of opioid formulations that constitute an adequate therapeutic trial is needed. Similarly, evidence and guidelines for the appropriate duration of post-surgical opioid therapy, which was continued in 10 % of patients 1 year or longer after same day surgery,¹⁷ are needed so that providers can prospectively discuss and include in their treatment plans the expected date of discontinuation.

When discontinuation of opioid therapy is indicated due to harm outweighing benefit (or due to the absence of benefit), protocols should be developed using evidence-based educational strategies for assisting providers and patients in preventing and managing withdrawal symptoms and transitioning patients to alternative treatments. Symptoms of opioid withdrawal and associated pain flares may complicate or even prevent successful transition off opioids. Provider education in the use of supportive measures to treat withdrawal might reduce this barrier and avoid continuation of opioids, despite patient and provider preference to the contrary. Protocols using partial opioid agonist treatment to bridge patients off of full agonist analgesics may hold promise but require rigorous evaluation. Furthermore, early studies indicate that partial agonist therapy may also be a suitable option for ongoing analgesia in some patients with chronic pain.¹⁸ With effective and safe alternative therapies in their armamentaria, providers may be less likely to continue inappropriate prescribing.

Promoting Patient-Centered, Multi-modal Treatment Plans

Qualitative data consistently show that providers lack comfort and confidence in managing opioid therapy, in large part because they believe the care is unstructured and they lack management options when problems arise with opioids.^{19,20} This underlying discomfort undoubtedly leads

to dissatisfaction in patient–provider interactions and may facilitate inappropriate prescribing if providers opt to refill prescriptions rather than monitor for and address problems. We believe the steps above—developing a monitoring checklist and treatment pathways—could potentially allow providers to better understand the components of appropriate provision of chronic opioid therapy. A critical piece to ensuring that this translates to higher quality care is that research is conducted on how to best help providers implement this framework in a patient-centered manner, as well as how to enhance patients' motivation for engaging in multimodal treatment options like coping skills coaching and physical therapy.

At the outset of therapy, providers should clearly describe the necessary components of multi-modal pain care, what safe and effective opioid use means, how it will be measured and what steps will be taken if safe and effective use is not occurring. Transparent communication around goals and expectations is essential to building a therapeutic alliance²¹ and to increasing patient adherence to future changes in therapy as indicated by the results of ongoing monitoring. Since generalists are trained in this approach for other medications and interventions, application of this model to opioid therapy should be feasible. Written treatment agreements may serve as useful aides in this process, but should only augment two-way, patient-centered discussions, not replace them. Promising training modules²² on shared decision making in chronic opioid therapy need further development and dissemination. Inadequate access to and/or lack of insurance coverage for some modalities of non-pharmacologic pain care are significant barriers to these goals for many patients. We advocate research into cost-effective strategies of service delivery such as group visits, or novel approaches to evaluate costs of non-pharmacologic treatments compared to higher risk treatments.

As harms related to opioid therapy rise, the need for point of care quality improvement efforts has become increasingly apparent. We promote a shift in focus on what appropriate opioid prescribing means and propose a research agenda to enhance it. Future research designing, testing and implementing protocols is much needed to provide front-line clinicians with evidence-based strategies to address these vexing issues.

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