EDITORIAL AND COMMENT

Mounting a Scientifically Informed Response to the Opioid Crisis in the Veterans Health Administration

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Since at least 2012, the opioid crisis has been widely recognized as a leading public health crisis in the USA. Overdose deaths involving opioids, including prescription opioids, heroin, and synthetic opioids (i.e., fentanyl), claimed the lives of nearly 47,000 Americans in 2018, with 32% of those deaths involving prescription opioids.[1] Opioid use disorder (OUD) has had an even greater impact among Veterans,[2] where the rate of overdose deaths is double that of the general population. The risk for opioid use disorder—defined as the compulsive taking of opioids despite harm—also is higher among Veterans than the general public. This is partly because patients who receive care in the Veterans Health Administration (VHA) have a high rate of comorbidities that contribute to the incidence and severity of OUD—including major depression, post-traumatic stress disorder (PTSD), and chronic pain.

The association between chronic pain, prescription opioids, and OUD is complex and unpredictable, and at the public health level a clear trajectory has emerged over the last 25 years. Over that period, opioid prescribing quadrupled in the USA, most of it for chronic, non-cancer pain conditions. What followed seems tragically inevitable through today's lens: a marked rise in OUD incidence and prevalence and an increase in non-fatal and fatal overdose as OUD led to the over-consumption of prescription medications and a transition to higher potency formulations and routes of administration. Most recently, this includes the use of illicitly manufactured fentanyl analogs—the highest potency opioids in history.

VHA responded early to the opioid crisis. In 2013, VHA established a system-wide effort called the Opioid Safety Initiative[3] including programs to expand non-opioid alternatives for pain, such as complementary and integrative treatments and behavioral therapies. Most of the decline in prescribing was due to sharp drops in the numbers of patients started on opioids, thereby reducing addiction and overdose long-term. However, overall reductions in opioid prescribing within VA did not reduce fatal overdoses or suicides among those who already had OUD, which continued to climb among Veterans,[2] especially those using heroin or fentanyl.

In order to highlight the accomplishments and remaining challenges related to delivering high-quality pain management and OUD care in the VHA—the nation's largest integrated health system, VA's Health Services Research and Development (HSR&D) service convened the 15th State-of-the-Art (SOTA) conference, titled "Effective Management of Pain and Addiction: Strategies to Improve Opioid Safety."

SOTA conferences bring together a multidisciplinary group of VHA and non-VHA experts on a priority clinical topic to (1) outline critical clinical questions; (2) summarize where evidence is sufficient to make specific policy and practice recommendations; and (3) where evidence is lacking, to define a research agenda to close those knowledge gaps. HSR&D was assisted in this process by the VA Evidence Synthesis Program, which produced evidence reviews of the most vital questions identified by each of three workgroups.

This editorial highlights the key clinical and research recommendations of the SOTA on Opioid Safety in the context of major completed studies, including those featured in this special issue, as well as ongoing and future VHA work in the three SOTA workgroup topic areas. These areas include medications for OUD (MOUD); long-term opioid therapy for pain, especially issues related to tapering; and co-occurring chronic pain and substance use disorders (SUDs).

Decades of efficacy and effectiveness research establish that MOUD saves lives. Despite this, less than half of eligible Veterans are prescribed MOUD. Thus, this workgroup focused on what was known about strategies that will help healthcare providers more effectively engage patients in long-term MOUD. Two major implementation initiatives—Stepped Care for Opioid Use Disorder Train the Trainer (SCOUTT) and the Consortium for Disseminating and Understanding Implementation of OUD Treatment (CONDUIT)—were highlighted as important VHA initiatives likely to improve MOUD access and advance implementation science (scientific study of

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methods to promote the uptake of evidence-based practices into routine health care) in the field.

In this special issue, Chang et al. report on the use of Evidence-Based Quality Improvement (EBQI) as a promising implementation strategy for expanding access to MOUD in primary care settings,[4] where the capacity to expand needed treatment is greatest. Important new information is expected from an ongoing VHA Cooperative Study, led by Petrakis and Springer, to examine the benefits of sublingual vs. injectable buprenorphine among a projected 900 Veterans at 20 sites. This trial also should provide important insights into how to implement use of the injectable formulation, an ultra-long acting preparation that is an increasingly attractive option in the pandemic era.

Highlighted by Frank et al.,[5] the clinical and policy recommendations related to MOUD propose to reduce barriers to MOUD access through measures such as reducing classroom hours required by the Drug Enforcement Administration (DEA) to prescribe buprenorphine, as well as allowing expanded telehealth options for engaging and retaining patients in MOUD. With its nation-wide VA Video Connect system—a two-way real-time audio/visual clinical application—VHA was well-positioned to respond to access challenges deepened by the COVID-19 pandemic. Innovations developed during this time should continue.

Participants in the SOTA workgroup focused on long-term opioid therapy for chronic pain agreed that research should focus on strategies to avoid the initiation of long-term opioid therapy and to improve the reduction of opioid therapy when benefits no longer outweigh harms. This decision was informed by seminal VHA-funded work by Krebs et al., which showed no benefit in function and increased harms of opioids compared to non-opioid medications in patients with moderate to severe chronic musculoskeletal pain.[6]

Reviewed by Frank et al. and updated by Mackey et al., the evidence on opioid tapering strategies included studies from 2017 through 2020.[7] However, since both reviews found limited evidence to guide safe and effective tapering, this workgroup called for more research on pragmatic approaches to tapering in primary care settings, as well as more research into potential harms and unintended consequences of tapering. The workgroup further noted VA research reporting an increased risk of suicide among patients who abruptly tapered opioids.[8] In this issue, Morasco et al explore factors associated with dose *increase* in long-term opioid therapy, a key to designing prevention efforts that may lead to fewer patients requiring tapers.[9] This workgroup also recommended research on whether low-dose and/or intermittent opioid therapy might be safe and effective for certain populations, particularly the elderly or those with contraindications to other common pain medications.

An important clinical and policy issue identified by the workgroup was the challenge of applying the Diagnostic and Statistical Manual-5's OUD criteria to patients on long-term opioid therapy for pain who have symptoms of physical dependence but do nor exhibit compulsive use. Highlighted in this special issue by Manhapra et al.,[10] these concerns are the subject of an ongoing Delphi study of subject matter experts called for by the SOTA to explore whether a new diagnostic entity is needed for this population and, if so, what its criteria should be.

The third workgroup on co-occurring chronic pain and SUDs—noting the remarkably high co-prevalence of these conditions among Veterans—emphasized the need to scale-up promising pilot studies of pain treatment in SUD settings into broader pragmatic and hybrid implementation/effectiveness research. This workgroup called for observational research into the harms and potential benefits among patients with SUD of long-standing (e.g., gabapentinoids) and emerging (e.g., cannabinoids and ketamine) chronic pain treatments that may have elevated risk among patients with SUDs. Clinical and policy issues discussed by this group led to the formation of a task force to define best practices in the peri-operative management of patients on MOUD, an effort that will be funded by HSR&D's Pain/Opioid Consortium for Research.

In summary, the public health crisis posed by opioids has not diminished in the COVID era—indeed, it may have increased. Yet we hope that recommendations from the SOTA on Opioid Safety, along with ongoing large-scale initiatives for increasing access to MOUD, will allow VHA to continue a leading role in defining integrated, patient-centered management of pain, opioid tapering, and treatment for OUD.

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Compliance with Ethical Standards:

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