The Importance of Learning Health Systems in Addressing the Opioid Crisis

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Interventions and research to address the US opioid crisis have, for the most part, targeted opioid use, misuse, and addiction specifically. While such a focus can lead to useful innovations in the care of opioid use disorder, the fact that many persons with opioid use disorder use multiple substances (both over their life course and simultaneously in drug-using episodes) makes it imperative to address broader issues of addiction in persons who have opioid use disorder as their presenting concern. Because of integrated care and the ability to target multiple clinical concerns in parallel, the Veterans Administration (VA) may be uniquely situated to address the key issue of multi-morbidity that persons with opioid use disorder so frequently exhibit. Research at the VA can build on new interventions developed by the National Institutes of Health (and others) and can help to determine the best ways to implement these interventions. Research at the VA does not need to duplicate efforts supported by other funders but can complement such work by providing an integrated platform for determining the best approaches to implementing innovations. The real-world learning health system that has been developed in the VA is poised to contribute in just such important ways.

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INTRODUCTION

The US opioid crisis continues to exert a major impact on health and social outcomes. Over the last 15 years, deaths due to opioid overdoses exceed 400,000¹ and declines in overall US life expectancy are at least partly explained by this increase in overdose mortality.^{2, 3} Morbidity caused by opioids includes increasing infectious disease (particularly HIV, hepatitis, and endocarditis), sleep disorders, affective disorders, and increasing neonatal opioid withdrawal, among other outcomes.^{4–8} Overall economic impact from opioid misuse was estimated at \$500 billion per year in 2017.⁹ In response, prevention and treatment practices and policies have been expanded, although gaps remain.⁵ These include increasing access to medications for opioid use disorder,^{10–12} reducing

opioid prescribing,^{13–15} increasing access to naloxone,^{16, 17} improving public health surveillance,¹³ increasing access to harm reduction programs such as syringe services,^{13, 18, 19} and major investments in research.^{20, 21}

The Veterans Administration (VA) with its health care system, the Veterans Health Administration, has an exceptional ability to address these opioid issues by bringing to bear integrated health and social services. But how can these programs maximize their impact? Are there outside research and health services developments that can complement the innovative programs implemented by the VA? We suggest that several areas of work and developments outside the VA might be considered resources to help. Furthermore, linkages of VA- and non-VA-supported research may lead to greater impact than either group alone.

In this commentary, we highlight the following: (1) developments in the opioid crisis including the prominence of synthetic opioids in recent years and a shift to stimulants, especially methamphetamine, as major contributors to overdose mortality; (2) an evolving focus on learning health systems as a goal both for short- and long-term solutions; and (3) a focus on major research efforts inside and outside of the VA that could be relevant to the care of veterans and non-veterans.

DEVELOPMENTS IN THE OPIOID CRISIS

Although involving compounds very similar in their pharmacologic properties, the opioid crisis in the USA is better conceptualized as two sets of intertwined issues noted since about the year 2000: misuse of and addiction to prescription opioid analgesics, which predominated in the first decade of the crisis, and, during the second decade, use of and addiction to illicit opioids.⁵ Thus, the first wave of the opioid crisis refers to overdose deaths related primarily to prescription-type opioids, and the second wave refers to heroin as the predominant illicit opioid. However, within the rubric of illicit opioid use, a further distinction can be drawn between the resurgent use of heroin and the problem of both deliberate and unintentional use of even more potent synthetic opioid drugs (namely, illicitly made fentanyl and its analogs).⁵ A rapid rise in deaths involving these synthetic opioids, beginning in 2013, marked the third wave of the opioid crisis.⁵ From 2010 to 2018, deaths from fentanyl and other synthetic opioids increased nearly tenfold, from around 3007 (14.3% of opioid-related deaths) to 28,466 (59.8%).^{1, 5}

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Figure 1 Overdose deaths from 1999 to 2018 for prescription-type opioid analgesics, heroin, synthetic opioids other than methadone (i.e., fentanyl-related compounds), and stimulants (methamphetamine and/or cocaine).

Use of stimulants, especially methamphetamine, has also recently expanded in many locations and is a major cause of morbidity and mortality as seen in the rising rates of stimulant-related overdose deaths over the past 5 years (Fig. 1). While opioids remain a major contributor to morbidity and mortality, the clinical issues presented by persons with opioid use disorder are not limited to this one class of substances. Persons with opioid use disorder very frequently use other substances,^{22, 23} and these combinations may be particularly lethal, as seen in the synergy of opioids and sedating substances such as alcohol and benzodiazepines.^{24, 25} Even the combination of opioids and methamphetamine may cause synergistic lethality, as suggested by preclinical research,²⁶ in addition to the expected toxicity of each substance itself. Research on the impact of co-administration of opioids and methamphetamine (and other combinations of substances) needs both basic and applied approaches in order to maximize the ability to treat patients who use such complicated combinations of substances.

Overall, persons with opioid use disorder experience a broad range of clinical needs with major impacts on their health outcomes, including polydrug use as well as issues related to legal, housing, mental illness, employment, and family domains.^{22, 23} Because of this, the opioid specificity of current interventions may limit their ability to address the broader problems of persons with opioid use-related problems. One advantage for the VA in responding to these broad issues is the ability to implement effective treatments into the system of care. For instance, the VA has been able to implement contingency management therapies into routine clinical care.²⁷ By contrast, non-VA Medicaid supported treatment has not been able to implement contingency management due to concerns about payments to patients.²⁸ Yet, such care is one of the few treatments to show an impact on methamphetamine²⁹ and the lack of uptake outside of the VA remains a major concern.²⁸ This is an area where VA-led research may pave the way for care improvements for veterans and non-veterans alike.

LEARNING HEALTH SYSTEMS

An evolving theme in health care delivery research has been the focus on learning health systems as a goal both for short- and long-term solutions, and the VA has been highlighted as an exemplar of a learning health system.³⁰ Learning health systems are designed to address organizational and process of care-related weaknesses in treatment systems. Rather than targeting discrete practices for individual improvements, a learning health system is inherently designed for continuous quality assessment and improvement. Key elements that can facilitate such a progressive system are as follows: integrated health records, seamless links of different levels of care, reduction of financial barriers to care access, and integrated clinical practices. All of these exist in the VA at the present time because of years of innovation and visionary leadership. Such systems can facilitate testing of novel practice improvements that may have implications for both veteran and non-veteran populations. Even so, research within the VA setting has helped to demonstrate that a learning healthcare system must always attend to data in order to ensure that performance gains are sustained over time. The VA provides a unique platform for understanding how to sustain and build on improvements overtime across an entire system of care.^{30, 31}

MAJOR OPIOID RESEARCH EFFORTS

A focus on major research efforts outside of the VA also could be useful to the care of veterans. Relevant research that is outside of VA includes especially the National Institutes of Health's Helping to End Addiction Long-term (HEAL) program.²¹ Within HEAL, of particular relevance to opioid crisis efforts at the VA are the expanded medication development programs that could lead to new treatments for all with opioid use disorder, including veterans.³² HEAL also includes services research to expand access to effective treatments for opioid use disorder which also may provide useful approaches

to improve the care of veterans. These include efforts targeting general medical settings and large-scale systematic efforts focused on criminal justice settings, the Justice Community Opioid Innovation Network.³²

Of potential relevance to the NIH-supported program of research in criminal justice settings is the veteran-specific use of Veterans Justice Outreach Specialists. Veterans with justice involvement are particularly vulnerable to negative health outcomes,³³ and are less likely to receive medications for opioid use disorder than their non-justice-involved counterparts.³⁴ Veterans Justice Outreach Specialists proactively seek to identify veterans who are justice-involved and advocate on their behalf, for example helping them to connect to veteran drug courts or services such as housing, healthcare, or addiction and mental health treatment. While Veterans Justice Outreach Specialists do not single out veterans with opioid use disorder for intervention, the approach may be broadly applicable. Furthermore, outside of the VA, we are aware of no other example of such a role embedded within the medical or treatment system. This kind of system-spanner role focused specifically on the needs of the most vulnerable veteran populations is innovative and should be tested more robustly, including adaptations to work with those outside of the veteran context.

Much research supported by the National Institutes of Health is particularly focused on advancing basic science. In addition, National Institutes of Health studies reach more heterogeneous populations than VA research programs as well as populations unlikely to be the focus of the VA research, including children/adolescents and non-veteran justice-involved persons. While the VA supports basic research, where the VA has particular and often unique strengths is in the area of health care system research.³⁰ The VA's large, integrated system of care provides clear opportunities for studying implementation of innovations. The VA may be particularly suited to study variation while at the same constraining it. Of course, there are many areas of shared strength and for many basic and clinical studies, VA- and non-VA-supported work can both be important. In these areas, careful coordination to avoid inefficient duplication and enhance synergies is essential.

CONCLUSIONS

Interventions and research to address the US opioid crisis have, for the most part, targeted opioid use, misuse, and addiction specifically. While such a focus can lead to useful innovations in the care of opioid use disorder, the fact that many (and perhaps most) persons with opioid use disorder use multiple substances (both over their life course and simultaneously in specific drug-using episodes) makes it imperative to address broader issues of addiction in persons who have opioid use disorder as their presenting concern. Because of

integrated care and the ability to target multiple clinical concerns in parallel, the VA may be uniquely situated to address the key issue of multi-morbidity that persons with opioid use disorder so frequently exhibit. Research at the VA can build on new interventions developed by other groups and can help to determine the best ways to implement these interventions. Research at the VA does not need to duplicate efforts supported by the National Institutes of Health (and other funders) but can complement such work by providing an integrated platform for determining the best approaches to implementing innovations. The real-world learning health system that has been developed in the VA is poised to contribute in just such important ways.

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Compliance with Ethical Standards:

Conflict of Interest: W.M.C. reports ownership of stock in General Electric, 3 M, and Pfizer Inc. unrelated to the submitted work. Other authors have no interests to declare.

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