



The Shadow at the Intersection of the COVID-19 Pandemic and the Opioid Crisis

Be aware of these two simultaneous
health issues.

BY ROBERT G. SMITH, DPM, MSC, RPH

Learning Objectives

Participants completing
this course will be able to:

1) Explain how the
negative economic impact
response to COVID-19 can
exacerbate the opioid crisis
in America.

2) Identify and acknowl-
edge certain factors of
patients with substance
abuse disorders who are
compromised by excessive
and prolonged isolation and
social distancing.

3) Describe strategies for
managing chronic pain and
access to medical care.

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Following this article, an answer sheet and full set of instructions are provided (pg. 144).—Editor

Introduction

Boslet, et al. used a secondary data analysis of the universe of drug overdoses in 1999–2016 obtained from the National Center for Health Statistics. They detailed multiple cause of death records to demonstrate that the number of deaths attributed to opioid-related overdoses could be 28 percent higher than first reported due to incomplete death records.¹ This discrepancy was more pronounced in several states, including Alabama, Mississippi, Pennsyl-

vania, Louisiana, and Indiana, where the estimated number of deaths more than doubles, obscuring the scope of the opioid crisis and potentially affecting programs and funding intended to confront the epidemic.¹

Logistic regression and random forecast models were performed to determine contributing causes that substantially improved predictive accuracy, while including county characteristics. Using a superior prediction model, they found that

71.8% of unclassified drug overdoses in 1999–2016 involved opioids, thus translating into 99–160 additional opioid-related deaths, or approximately 28% more than previously reported.¹

It is hoped that the podiatric physician relies on census data as essential tools for understanding the importance of place-level characteristics on opioid mortality. Opioid overdose and mortality rates overall are higher in counties characterized by

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more economic disadvantage, more blue-collar and service employment, and higher opioid-prescribing rates.²

Further, Monnat, et al. suggest national policies to combat the opioid and larger drug crises with emphasis on developing locally and regionally tailored interventions, and with attention to place-based structural economic and social characteristics.²

As of April 2020, the United States now has 22 million unemployed, wiping out a decade of job gains. Moreover, state tax revenues are plunging due to shelter-in-place orders and initiatives in place to have only essential workers attending their place of business. Additionally, the share of persons who have lost or left a job who lacked coverage was 22.1% versus 8.3% for employed persons—a difference of 13.8 percentage points.³ These authors acknowledge that although the COVID-19 crisis demands urgent action, it also exposes the carelessness of tying health insurance to employment and the need for more thoroughgoing reform.³ Woolhandler and Himmelstein assert that, with jobs and health insurance coverage disappearing as the COVID-19 pandemic rages, states that have declined to expand Medicaid should urgently reconsider.³

It is hoped that the issue of families who face the dual disaster of job loss and health insurance loss and who may suffer from opioid use disorder will be among the foremost issues on the legislative branch of the United States' agenda. Haffajee, et al., report opioid overdose deaths in the United States continue to increase, reflecting a growing need to treat those with opioid use disorder.⁴

Acknowledging that, fading economic opportunity has been hypothesized to be an important factor associated with the United States opioid overdose crisis. Automotive assembly plant closures are culturally significant events that substantially erode local economic opportunities.⁵

Moreover, Venkataramani, et al. explore and investigate the effect a community's economy has on opioid overdose mortality. Their primary outcome was the county-level age-adjusted opioid overdose mortality rate.⁵ Their

secondary outcomes included the overall drug overdose mortality rate and prescription vs. illicit drug overdose mortality rates.⁵ They discovered that from 1999 to 2016, automotive assembly plant closures were associated with increases in opioid overdose mortality.⁵

These findings highlight the potential significance of eroding economic opportunity as a factor in the United States opioid overdose crisis.⁵ Finally, Langbeer, et al., concluded that opioid-related mortality was positively correlated with tobacco use, being a non-Hispanic or Caucasian individual, living in a rural area, obesity, being 65-years of age or older, and having a higher rate of unemployment.⁶

As people across the United States and the rest of the world contend with coronavirus disease 2019 (COVID-19), the medical community, including podiatric physicians, should realize the possibility that COVID-19 infection

COVID-19 pandemic, frequently turn to substances to alleviate their negative feelings.⁸ Those in substance recovery will face stresses and heightened urges to use substances and will be at greatly increased risk for relapse.⁸

Further, vulnerable populations... those who smoke or vape, use opioids, or have a substance use disorder (SUD) may have direct challenges to respiratory health; those with SUD may be especially susceptible to infection by the virus that causes COVID-19 and associated complications.⁸ Impediments to delivering care to this population, persons with SUD who develop COVID-19 may find it harder to get healthcare.⁸

Those in recovery will also be uniquely challenged by social distancing measures.⁸ Lastly, a risk for severe COVID-19 and death escalates with older age but is also concentrated among those who are immunocompromised or have underlying health

People with opioid use disorder (OUD) and methamphetamine use disorder may also be vulnerable due to those drugs' effects on respiratory and pulmonary health.

could hit some populations with substance use disorders (SUDs) particularly hard.⁷ The coronavirus that causes COVID-19 attacks the lungs and could be an especially serious threat to those patients who smoke tobacco, marijuana, or who vape.

People with opioid use disorder (OUD) and methamphetamine use disorder may also be vulnerable due to those drugs' effects on respiratory and pulmonary health.⁷ Additionally, patients with a substance use disorder are more likely to experience homelessness or incarceration than those in the general population, and these circumstances pose unique challenges regarding transmission of the virus that causes COVID-19. All these possibilities should be a focus of active surveillance as we work to understand this emerging health threat.⁷

According to Volkow, those persons who are isolated and stressed, as much of the population is during the

conditions, including diabetes, cancer, and heart and respiratory diseases.⁸

Mukherjee and El-Bassel report that people with opioid and other substance use disorders are disproportionately incarcerated, and recently released prisoners are ten times more likely to become homeless.⁹ The COVID-19 pandemic, coupled without adequate planning for release from prison, may move people with opioid use disorder from one at-risk environment to another one.⁹

Upon release, the risks associated with COVID-19, as well as HIV, viral hepatitis, TB, overdose and homelessness that often accompany incarceration must be considered.⁹

It is an accepted fact that not only does COVID-19 make addiction services harder to access but people who use drugs may be at higher risk of infection given the dangerous overlap between addiction, incarcer-

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THE PANDEMIC UPDATE

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ation, and the rapid spread of infections within confined spaces.

Community campaigns to get non-violent drug offenders released during this pandemic may not be sufficient to avoid incarcerated persons from

Opioids and Increase of Infections

Schwetz, et al. rely on clinical evidence to assert in their commentary that the rise in Opioid Use Disorder (OUD), bolstered by injection opioid use, conveys numerous downstream consequences and is fueling a surge in infectious diseases, such as human

trends observed with the opioid epidemic.^{10,12} They cite that the example of the rate of methicillin-resistant Staphylococcus aureus infections among people who inject drugs more than doubled between the years of 2011 and 2016.¹³

Additionally, they assert that the growing evidence has shown that certain opioids, including both morphine and fentanyl, have putative effects on both the innate and adaptive immune systems, dependent on drug dosage and duration of delivery.¹⁰ Finally, using published data, these authors concluded that the growing trend of infectious diseases emerging across the United States in areas with high rates of opioid use has created a significant combined impact on morbidity and mortality.¹⁰

Wiese, et al. conducted a retrospective cohort study to investigate long-acting opioid use and the risk of serious infections.¹⁴ They used multivariable Poisson regression models to calculate adjusted incidence rate ratios and 95% confidence intervals

to compare the infection risk among patients using long-acting opioids with known immunosuppressive properties (morphine, fentanyl, methadone) to the infection risk among patients using long-acting opioids without known immunosuppressive properties (oxycodone, oxymorphone, tramadol) accounting for demographics, opioid dose, comorbidities and pain conditions, medication use, frailty indicators, and healthcare encounter history using exposure propensity scores.¹⁴

Moreover, they compared users of individual long-acting opioids to long-acting morphine users, which is considered

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Schwetz, et al. note that the increasing infection rates and demographic trends of bacterial and fungal infections appear to mirror trends observed with the opioid epidemic.

becoming infected with COVID-19. A prisoner re-entry into regular society is difficult and dangerous from a health perspective, even during normal times. As the economy collapses, shelters and food banks have been overwhelmed, with already limited resources stretched thin on all levels in many communities.

immunodeficiency virus (HIV) infection with or without AIDS, the viral hepatitises, infective endocarditis, pneumonia, and skin and soft-tissue infections.^{10,11}

Further, Schwetz, et al. note that the increasing infection rates and demographic trends of bacterial and fungal infections appear to mirror

TABLE I:

Comparison List of the Typical Symptoms of COVID-19 Infection and Opioid Withdrawal Symptoms

| COVID-19 Infection Symptoms | Opioid Withdrawal Symptoms Symptoms Appear 72 Hours After Last Dose | |
|-----------------------------|--|----------------|
| Fever | 87.9% | Fever |
| Dry Cough | 67.7% | Chills |
| Fatigue | 38.1% | Body Aches |
| Sputum Production | 33.4% | Diarrhea |
| Shortness of Breath | 18.6% | Insomnia |
| Myalgia-Arthralgia | 14.8% | Muscle Pain |
| Sore Throat | 13.9% | Nausea |
| Headache | 13.6% | Dilated Pupils |
| Chills | 11.4% | |
| Nausea-Vomiting | 5.0% | |
| Nasal Congestion | 4.8% | |
| Diarrhea | 3.7% | |

Source: Report of the WHO China Joint Mission on Coronavirus Disease 2019 20-Feb-20

Source: National Institute of Drug Abuse



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the prototypical immunosuppressive opioid.¹⁴ They determined that the risk of serious infections among long-acting opioid users varies by opioid type.¹⁴ They suggest that providers should carefully consider the risk of serious infections when making pain management decisions.¹⁴

Karagiannis, et al. acknowledge that chronic opioid usage not only causes addiction behavior through the central nervous system, but also modulates the peripheral immune system.¹⁵ Further, they ask the question of how opioids impact the immune system and recognize it is still barely characterized systematically.¹⁵ In order to understand the immune modulatory effect of opioids in an unbiased way, they perform single-cell RNA sequencing (scRNA-seq) of peripheral blood mononuclear cells from opioid-dependent individuals and controls to show that chronic opioid usage evokes widespread suppression of the antiviral gene program in naive monocytes, as well as in multiple immune cell types upon stimulation with the pathogen component lipopolysaccharide.¹⁵

Furthermore, scRNA-seq reveals the same phenomenon after a short in-vitro morphine treatment was started.¹⁵ Their findings indicate that both acute and chronic opioid exposure may be harmful to our immune system by suppressing the antiviral gene program.¹⁵ Lastly, their results suggest that further characterization of the immune modulatory effects of opioids is critical to ensure the safety of clinical opioids.¹⁵ These results are of utmost importance in understanding the use of opioids during the current COVID-19 pandemic.

Strategies for Managing Chronic Pain

The COVID-19 public health crisis has strained healthcare systems, creating an enigma for patients, pain medicine practitioners, hospital leaders, and regulatory officials.¹⁶ Pain management providers rely on infection control precautions from a backbone of interventional-based and some alternative medicine to include acupuncture and hands-on therapies such as massage and manual thera-

py practices.¹⁶ These precautions are even more important during a pandemic where the potential exists for viral shedding from asymptomatic patients, and disease transmission.¹⁶

Podiatric physicians need to acknowledge that many patients who would be seen for chronic pain issues during the COVID-19 pandemic are in higher risk groups. Full consideration should be given to minimizing patients congregating in a waiting room. Podiatric physicians should familiarize themselves with the new Health and Human Services and Centers for Medicare and Medicaid Services waivers on telemedicine, providing a method for new patient and established patient visits.¹⁶

In patients on opioids who may have run out of medications because of logistical obstacles or overuse, assessment of withdrawal signs can be challenging during remote visits. Symptoms such as diarrhea, rhinorrhea, abdominal pain and chills can be garnered from patient interviews, but may be difficult to corroborate.¹⁶ On the other hand, some physical signs indicative of opioid withdrawal, particularly if prominent, can be observed remotely, including agitation, diaphoresis, piloerection, and possibly even pupillary size.¹⁶

Monitoring patients for an elevated heart or pulse rate, which is a classic sign of opioid withdrawal, can sometimes be done by reliable patients or their caregivers.¹⁶ The salient point that typical symptoms of COVID-19 overlap the typical symptoms of opioid withdrawal has to be realized by the podiatric physician so that a correct diagnosis can be determined and a negative outcome can be avoided. A list of the typical symptoms of COVID-19 infection along with the presenting typical symptoms of opioid withdrawal are presented in Table 1 so a comparison can be appreciated.^{17,18}

Conclusion

First, the negative economic impact of the COVID-19 pandemic and how it exacerbates the opioid crisis in America was presented. Then certain factors of patients with substance abuse disorders and how they are disadvantaged by excessive and pro-

longed isolation and social distancing are presented. Lastly, strategies for managing chronic pain and access to medical care were presented. It is hoped that the podiatric physician can appreciate the over shadowed area at the intersection of the COVID-19 pandemic and the opioid crisis. **PM**

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CME EXAMINATION

SEE ANSWER SHEET ON PAGE 145.

1) Identify the symptom that may appear with both opioid withdrawal and COVID-19 infection.

- A) Weight Gain
- B) Increase Muscle Tone
- C) Increase Hunger
- D) Fever

2) scRNA-seq reveals the same phenomenon after a short in vitro _____ treatment was discovered

- A) Oxycodone
- B) Morphine
- C) Oxymorphone
- D) Dihydromorphone

3) Boslet, et al. use a superior prediction model. They found that 71.8% of unclassified drug overdoses in 1999–2016 involved opioids, thus translating into 99-160 additional opioid-related deaths, or approximately _____ more than previously reported.

- A) 12%
- B) 18%
- C) 17%
- D) 28%

4) Long-acting opioids with known immunosuppressive properties include all but this one agent.

- A) Methadone
- B) Fentanyl
- C) Oxycodone
- D) Morphine

5) Woolhandler and Himmelstein assert with jobs and health insurance coverage disappearing as the COVID-19 pandemic rages, states that have declined to expand _____ should urgently reconsider.

- A) Private Health Insurance
- B) Medicare
- C) Global Health Insurance
- D) Medicaid

6) _____ conducted a retrospective cohort study to investigate long-acting opioid use and the risk of serious infections

- A) Marks et al.
- B) Wiese et al.
- C) Smith et al.
- D) Block et al.

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7) Schwetz, et al. note that the increasing infection rates and demographic trends of bacterial and _____ infections appear to mirror trends observed with the opioid epidemic.

- A) Viral
- B) Protozoa
- C) Parasitic
- D) Fungal

8) Identify the correct percentage with its corresponding symptom.

- A) Fever 87.9%
- B) Dry Cough 100%
- C) Nausea and Vomiting 25%
- D) Chills 96%

9) Karagiannis, et al acknowledge that chronic opioid usage not only causes addiction behavior through the central nervous system, but also modulates the _____ system.

- A) peripheral circulation
- B) peripheral neurological
- C) peripheral immune
- D) peripheral clotting

10) Vulnerable populations, those who _____ or have a substance use disorder (SUD), may have direct challenges to respiratory health.

- A) Smoke
- B) Vape
- C) Use Opioids
- D) All answers are correct

SEE ANSWER SHEET ON PAGE 145.

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EXAM #8/20

**The Shadow at the Intersection of the
COVID-19 Pandemic and the Opioid Crisis
(Smith)**

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