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Missouri Opioid Crisis - A Call To Action
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The Opioid Crisis in Missouri: A Call to Action for Physicians, Legislators, and Society

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Abstract

Opioid overdose deaths in the United States increased sharply over the last decade leading the President to declare a national emergency. The neurobiology of opioid addiction is explored in conjunction with the historical events preceding the current epidemic. A patient-centric perspective is provided along with rationale for contemporary Medical Assisted Therapy (MAT) options to safely reduce overdose deaths and other preventable consequences of prescription misuse and heroin abuse. A multidisciplinary medical provider approach is essential, in addition to legislative efforts to reduce current regulatory burdens that reduce access to MAT in many settings. This review introduces a new Missouri Medicine series intended to explore key concepts to simultaneously reduce opioid prescribing, while effectively managing acute and chronic pain across complex healthcare settings.

Understanding the Scope of the Opioid Epidemic

In 2014, an estimated 2.9 million adults in the United States (US) were non-medical users of opioid pain relievers meeting the criteria for opioid use disorder. More than 50,000 people died of drug overdose in the US in 2015, and over 60,000 died from overdoses last year; more than all homicides (https://www.cdc.gov/nchs/fastats/homicide.htm) and motor vehicle crashes combined (https://www.cdc.gov/nchs/fastats/injury.htm). About 60% of these deaths are due to opioid overdoses, which have increased over 400% in the past 15 years (See Figure 1). Drug overdose is now the leading cause of death in the US in those under 50 years of age. "More than 50 people died of drug overdose in the US in 2015, and over 60 died from overdoses last year; more than all homicides (https://www.cdc.gov/nchs/fastats/homicide.htm) and motor vehicle crashes combined (https://www.cdc.gov/nchs/fastats/injury.htm). About 60% of these deaths are due to opioid overdoses, which have increased over 400% in the past 15 years (See Figure 1). Drug overdose is now the leading cause of death in the US in those under 50 years of age." According to the Missouri Bureau of Vital Statistics, there were 908 deaths from opioid overdose in Missouri in 2016 (http://health.mo.gov/data/opioids). Although opioid-related deaths are most common in eastern Missouri, people are dying across the state (See Figure 2). Because of the scope of the problem, Washington University in St. Louis recently hosted a health policy symposium on the opioid epidemic (http://emed.wustl.edu/larry-lewis-symposium).
The symposium included nurses, physicians, including several trained in addiction medicine, government officials, researchers, social workers, and a recovering patient to discuss the genesis and pathophysiology of the opioid epidemic, and pragmatic workable solutions. The problem is ubiquitous, touching numerous medical specialties, with published guidelines pertaining to emergency medicine, obstetrics, geriatrics, pain management, surgery, and anesthesiology. This essay will serve as the first in a series of Missouri Medicine reviews exploring widely available approaches from multiple disciplines to reduce the scourge of preventable opioid deaths in Missouri.

**Genesis of the Problem**

In 1999 the age-adjusted death rate from drug overdose was 6.1 per hundred thousand population, this increased to 16.3 per hundred thousand population in 2015, an average increase of 5.5% per year. The biggest increases were between 1999 and 2006, where the rate of increase was 10% per year. The increase in opioid-related deaths rose at an even steeper rate in Missouri during this period (CDC WONDER Online database, 1999-2014). Heroin use in the 1960’s was largely a minority, urban problem and almost always began with heroin as the initial opioid of use. This trend changed considerably near the turn of the millennium, both in the affected population and the initial opioid exposure. In 2005, less than 10% of heroin users had used heroin as their initial opioid; instead, nearly 80% had initiated with a prescription opioid medication. Many of these initial prescription medication exposures had been diverted for non-medical use. The causes behind the marked increase in prescription opioids being the “gateway” drug to heroin are complex, but many physicians think that a prominent factor was the well-intentioned effort to combat “oligoanalgesia” and relieve suffering. In 1995, the American Pain Society began the “Pain as the fifth vital sign” campaign and in 2001 the Joint Commission followed suit. These campaigns, coupled with a growing emphasis on patient satisfaction scores and misleading information regarding addiction potential, led to a 67% increase in prescription narcotics between 1999 and 2006. The epidemiology of heroin addiction continues to evolve. Over the last five years, a third of heroin users initiated their opioid use with that drug, while only a quarter started with prescription opioids. The transition away from narcotic analgesics towards heroin is likely a combination of development of tolerance, decreased access to opioid medication, and heroin that is more available and cheaper on the street. Even with the changing epidemiology of heroin use, the data are clear; we now have over 2 million people with opioid use disorder in the US, the majority of whom were introduced to their opiates either through legitimate or diverted use of a physician’s prescription.

**Neurobiology of Opioid Addiction**

Opioids, like most addictive drugs, induce euphoria by increasing the level of the neurotransmitter dopamine (See Figure 3). Dopamine is the predominant neurotransmitter for motivation and reward, and opioids produce dopamine levels that are significantly greater and of longer duration than any known natural reward (sex, food when hungry, or water when thirsty). The example given at the symposium that seemed to make the point compared functional MRI (fMRI) studies of “craving” between study subjects who were 1) water deprived, 2) food deprived, and 3) in early withdrawal. The affected parts of the brain differed somewhat depending on the
source of craving, but the images in opiate withdrawal show significantly more activity in many of these areas than does thirst or hunger, suggesting that the magnitude of craving in drug withdrawal far exceeds these natural cravings.11,12

Over time, opioids also reduce the brain’s intrinsic ability to produce dopamine, leading to decreased motivation, and a constant search for the one thing that now is required just to make them feel normal.10 The visual representation of the neuroscience underlying addiction, along with poignant comments from a patient with a long history of opioid addiction are telling. She related that when she was in the Emergency Department (ED), after being treated for an overdose, all she could think about was getting back out to the street to get another fix. Then one day, 11 years ago, someone gave her a dose of buprenorphine and she had in her words “a moment of clarity” which allowed her to begin the path to recovery.

Prevention Strategies


1. Evaluate the patient for potential of abuse (such as prior opioid use disorder) and have an informed risk/benefit discussion
2. If opioids are indicated, the first opioid prescription for acute pain should be no more than 20 low-dose, short-acting opioids or three days of medication, whichever is less.
3. The total dose for acute pain should not exceed 100 morphine milligram equivalents (MME). For patients presenting in acute pain, already on chronic opioids, opioid tolerant or on methadone, use the same pill and dose limits as for opioid-naive patients.
4. Other considerations, particularly for painful musculoskeletal conditions include use of multimodalities for pain control (i.e. low-dose non-steroidal analgesics along with low-dose [or no dose] narcotic analgesia) and physical modalities such as ice or heat, physical therapy, and massage. The American College of Emergency Physicians 2012 Clinical Policy on Prescribing Opioids to Adults in the ED cited several studies suggesting narcotic analgesia was not superior to non-narcotics for acute back pain, unless sciatica was present.13

Chronic pain is a more complicated issue. Opioid prescribing has markedly increased in the past decade, largely due to the extended treatment of chronic pain conditions.14 Several professional societies and organizations including the American Society of Anesthesiologists, the American Academy of Family Physicians, and the Commission on Accreditation of Rehabilitation Facilities have addressed the issue of chronic pain. Suffice it to say that patients with chronic pain will require a careful evaluation for risk/benefit and a well-integrated interdisciplinary approach. From the emergency physician’s perspective, opioids should be considered for those with chronic pain only if expected benefits (particularly for function) outweigh the potential risks. Recognizing that the majority of these patients will already be on narcotic analgesics, the question of opioid dependence is of concern. Identifying patients who have been on opioids for years may be an effective way we can identify patients with possible opioid use disorder, begin a dialogue regarding chronic pain management, and offer treatment options.
Treatment Strategies: Abstinence vs. Medication Assisted Treatment and the Concept of Harm Reduction

Abstinence programs have been around for centuries. Now known as the Minnesota Model, contemporary programs use the principles first espoused by the support group Alcoholics Anonymous, in 1935. For many years, abstinence programs were the only answer to addiction (whether alcohol or other drugs), and continue to be the most common form of addiction treatment in the United States (http://www.meaning.ca/archives/archive/art_ED_col_may_06_abstinence-addition-treatment_G_Thompson.htm). Medication assisted therapy (MAT) uses various pharmaceuticals to mitigate the neuro-hormonal imbalance which results from opioid use and leads to the cycle of addiction (See Figure 3). Research clearly demonstrates the superiority of most MAT programs over abstinence alone for opioid addiction.\textsuperscript{13-17}

Harm reduction includes interventions that reduce the potential for serious or fatal medical consequences from illicit drug use. Representative harm reduction interventions include providing clean needles (shown to reduce HIV transmission),\textsuperscript{18,19} supervised injection sites, and providing naloxone. MAT is also a harm reduction intervention since it not only increases successful remission of addiction, but also reduces rates of new HIV and perhaps hepatitis C infection.\textsuperscript{19,20,21} Large population studies in France and Baltimore, Maryland have shown a very significant reduction in overdose deaths with the widespread adoption of MAT, even when used without counseling (See Figure 4).\textsuperscript{18,22}

There are several alternative medications in the armamentarium for MAT. The oldest and best studied is methadone. A number of studies have shown that methadone programs have superior rates of remission from drug-use than abstinence programs alone. They also appear to reduce the incidence of HIV and hepatitis C transmission.\textsuperscript{23} A major disadvantage is the need for daily outpatient visits for administration, although many practitioners allow patients take-home medication after several months of good compliance. Buprenorphine, a safer partial opioid agonist, has gained popularity in MAT programs over the last decade.\textsuperscript{17} Suboxone®, which is a combination drug with buprenorphine and naloxone, has the added benefit of an opioid antagonist to lessen the risk of diversion or overdose when injected intravenously. Naltrexone is an opioid receptor antagonist that requires an initial prolonged abstinent period, ranging from a few days for heroin to as much as two weeks for Suboxone®, but it has no abuse potential and depot formulation (Vivitrol) eliminates the need for daily dosing. Which medication is preferable should be based on a number of patient
factors, including cost and accessibility, and is too broad a topic to be covered in this article. Currently the data favors agonists over antagonists, although no head-to-head trials have been published. No matter which drug is used, the attributes of a successful MAT program include: (a) identifying individuals with opioid use disorder, (b) initiating treatment as soon as possible when the opportunity presents, and (c) to continue MAT until the individual is evaluated and placed on a maintenance program.

There are obvious cautionary tales to any MAT program, which may underlie the reason why these programs have not been eagerly adopted. Many addiction experts believe that the social stigma of drug abuse and years of misinformation are the primary factors behind the slow adoption of MAT. A major focus of our symposium was to acknowledge and overcome these issues and review the evidence for MAT outcome benefits or harms. Numerous studies confirm the benefit of MAT in improving rates of recovery, reducing drug overdoses, and reducing risks of infectious disease transmission. Misuse of MAT drugs does occur with diversion rates varying between 0.2 and 62.4 per 10,000 recipients, depending on the formulation and the particular database. The French allow any physician to prescribe buprenorphine to patients with opioid use disorder with no formal psychosocial counseling or intervention. This French approach resulted in a 79% reduction in overdose deaths and a reduction in new HIV case rates from 25% to 6%, albeit with a misuse rate of 15% and a diversion rate of 39%. In fairness, this diversion rate was over their entire time of MAT, and only 6.2% said they had ever sold the medication. It appears much of the diversion (if not most) is to self-treat withdrawal. The diversion of the combination agonist-antagonist drug Suboxone® is far safer than the diversion of opioid medication, and anecdotal evidence suggests that some, if not most, of the diversion is used to self-treat dependence and reverse opioid overdose. The French and Baltimore MAT experiences can certainly inform subsequent Missouri efforts to reduce deaths and disease that results from opioid addiction, while mitigating against some of the adverse outcomes. Critically, recent evidence suggests that prescription drug monitoring programs not linked to MAT, may actually increase the number of people dying from drug overdose by pushing opioid addicts to heroin and fentanyl.

Barriers to Implementation

There are several barriers to MAT, which range from moral considerations to financial ones. Healthcare providers should be among the first to recognize that social stigma can reduce progress in both studying a disease, and in implementing the findings. With the wide-ranging demographic of the latest opioid epidemic and the emerging science demonstrating the neurobiology associated with addiction, the stigma appears to be waning. Those of us who have a friend or family member that suffers from opioid use disorder realize that this is not “a choice” but rather a disease, based on an imbalance of neurotransmitters, just as depression, mania, and Parkinson’s disease are.

Though there is still some lack of awareness regarding effective treatment strategies, the biggest barriers seem to be a lack of trained staff and cumbersome regulations. The recent explosion of coverage in the press, and the Missouri Opioid State Targeted Response Project (Opioid STR: www.missouriopioidstr.org) will serve as an impetus and a resource for healthcare providers to develop and
implement plans for prevention and treatment of opioid use disorder. Longer-term, we must emphasize education on addiction medicine in medical and nursing schools and residency programs. The four medical schools in Massachusetts recently identified ten core competencies for the prevention, identification, and treatment of substance use disorders and worked them into the medical school curriculum (Opioid and Safe Prescribing Training Immersion Program; https://umassmed.edu/opioid/). This model could be integrated in Missouri medical education as well.

Lack of access to treatment is the next hurdle to cross. Opioid STR and its related projects can help provide resources for treatment. MAT training is being offered at multiple locations and times (as well as online). Washington University has embraced the need to train a group of physicians across specialties, in order to be able to initiate therapy along the spectrum of medical care, beginning in the ED, if necessary, and continuing in both the inpatient and outpatient settings.

However, to build an infrastructure that will be ideal for the longitudinal care of these patients over an extended period will require resources and a payment system that can sustain the effort. Many of these patients are uninsured, but the cost of their addiction to our healthcare system greatly exceeds the cost of treatment, not to mention that many of them can re-enter and become productive members of society once on treatment. We need policy changes that recognize that reality and allow for the adequate treatment of all people with opioid use disorder, without regulatory rules that limit care and set up barriers to payment. Finally, we need to develop a more robust and accessible primary care system where conditions associated with chronic pain can be addressed in a more holistic and appropriate way, with the intent of preventing future opioid dependence among the millions of Americans who suffer with chronic pain.

**A Personal Message from a Patient**

Hello, my name is Shannon, and my story is not unique. I spent a good amount of my life drinking and using drugs. I did not grow up with an un-loving family, in fact I felt very loved. I’m very fortunate to have them all still loving me today! I wasn’t pretty... but now, 11 years sober, I’m here to tell you there’s hope!

Speaking on my Heroin/Opioid use, pain killers led to Heroin for me. Too much disaster and pain to cover here, so I’m just going to break it down the best I can. This is what worked for me. I confessed to my family and doctor that I was an addict. I found a nonjudgmental/Spiritual Church and was reunited with Jesus. They have an Aftercare Recovery Meeting there I started attending, along with other meetings like CA/AA/NA (Cocaine, Alcohol, Narcotics Anonymous) and began working the 12 Steps of recovery with a Sponsor. I worked closely with my psychiatrist and psychologist, and still do, but the catapult that allowed all of this to happen was when my doctor asked me if I’d be willing to try a medication called Suboxone® (buprenorphine) and my life was forever changed. It was and is still a game changer! I’ve said it before and will continue to say, “Buprenorphine gave, and still gives me, a fighting chance against Opioids!”. I had some struggles before and after starting buprenorphine, but it was Never Again with Heroin/Opioids. Buprenorphine removed all physical and mental withdrawals immediately. I now live a sober lifestyle and others can too! It breaks my heart knowing that many people could achieve what I have, but are not given or being told about all the options they have. Others may not want to take a route similar to mine, but how can you choose if you’re never given the choice? I led myself down some bad paths, sometimes knowingly, sometimes unknowingly, and many miracles have happened along the way. I consider buprenorphine to be one of them.

My Sobriety date is December 4, 2006, and I take buprenorphine to this day. One of the hardest things in Sobriety to me is, “One Day at a Time”. I have to remind myself that is how it is, and today I just try to do things that help me live a life of hope, joy, and sobriety and I am perfectly fine with that. I hope my experience can help others.

Sincerely,
Shannon G.
SCIENCE OF MEDICINE

References

On October 26, 2017, the Trump administration declared the opioid epidemic a “public health emergency.” This type of declaration allows the federal government to expend additional funds to appoint specialized personnel to address the epidemic, expand treatment at existing facilities, and provides states with more flexibility when spending federal funds targeting the epidemic. Public health emergencies are limited to 90 days, but can be renewed any number of times. The President’s Opioid Commission had previously requested such a declaration.

Acknowledgment
The authors acknowledge Lisa Hayes for her indispensable assistance organizing the 1st Annual Lewis Health Symposium, as well as her professional services obtaining requisite permissions to reproduce the figures and tables for this manuscript.

Disclosure
None reported.