The number of Americans we lose each year to suicide and unintentional overdose has increased more than 250% since 2000. These problems continue to worsen and have become the most pressing public health issues our nation is currently grappling with. In 2017, over 40% of suicide and overdose deaths were known to have involved opioids, and rates are likely higher due to unrecorded opioid involvement. The connection between opioids and unintentional overdose is clear, but the distinct relationship between opioids and suicide risk is lesser known and has only recently been recognized.

In this review, Amy Bohnert, Ph.D., and Mark Ilgen, Ph.D., apply the commonality of opioid use between these two problems as a crucial framework for examining what is currently known about the links between them.

What is driving the increase in intentional and unintentional opioid overdose?

There are a number of drivers of opioid use, but certain pathways have been theorized to increase vulnerability to suicide and unintentional overdose: pain, increased prescribing and availability of opioids, and socioeconomic stress.

Pain, because of its impact on neurocircuitry related to reward, makes a person more vulnerable to suicide and potentially for riskier opioid use.

There are two main theories concerning the role of opioid use in escalating rates of suicide and overdose. The first focuses on the increased supply of opioids, prompted in the early 2000s by concerns about the undertreatment of pain, which led to the development of new clinical guidelines and a reclassification of pain as the “fifth vital sign.” These changes coincided with a 600% increase in opioid dosage per person per year between 1997 and 2007. These higher prescribed dosages are directly correlated to increased rates of suicide attempts and fatal and nonfatal overdoses.1,2,3,4 Rising prescription prescribing rates, in addition to the increasing availability of heroin and other synthetic opioids, means that opioids are more widely available than ever before. However, it is not clear what amount of this increased supply was a reaction to demand.
Conclusion
Rates of suicide and unintentional overdose have risen significantly in the United States over the past few decades, and opioid use has been a key driving factor. Interventions that address shared causes and risk factors have the potential to help address both problems and lower the incidence of suicide and unintentional overdose.

Citation

Opportunities for Further Research

Opioid Tapering
Although tapering can help a patient reduce levels of prescription opioid usage, there are fears that opioid tapering can lead to a patient using heroin as a substitute, or experience increased suicidality as pain increases again. Therefore, opioid tapering should be managed carefully, with adequate pain management alternatives and a transition to medication-assisted treatment if necessary.

Risk Scores
Risk scores are only moderately successful at identifying the risk of opioids misuse. To improve this, we may consider evaluating a person’s opioid misuse and an indicator not just of overdose risk, but of suicidality.

Prevention
Despite clinical, federal, and state policy efforts, overdose and suicide to be an overwhelming issue in the United States. We may not have adequately addressed the socioeconomic factors that lead to overdose and suicide, and therefore prevention efforts have been insufficient.
The present study is the first to extend this line of research to men of childbearing age, lending additional evidence for potential intergenerational, heritable consequences, resulting from paternal marijuana use. Just as other environmental triggers, such as air pollution, cigarette smoking, certain pesticides (i.e. DDT), and exposure to radiation are known to affect sperm health, THC may also increase the potential for genetic mutations.

For Clinicians

Primary care physicians and healthcare professionals, both inside and outside of substance use disorder treatment landscapes, should take time to educate patients about the impact of THC on sperm so individuals may consider potential implications for fertility and children conceived during periods of active use.

For Researchers

This article adds to a growing literature on the potential epigenetic impact of paternal marijuana use prior to conception. Findings must first be replicated in larger samples. Additionally, future longitudinal...
studies are necessary to explore the extent to which THC induced DNA alterations in sperm are passed down to offspring, as well as their long-term consequences.

For Policymakers

Marijuana potency continues to increase rapidly, with THC level increasing 300% over the past 20 years.4 Within the current political landscape and shift towards increased access to medical and recreational marijuana, policymakers should work closely with scientists to stay informed on the extent to which increased THC levels and evolving public attitudes impact men’s reproductive health.

For General Public

The full impact of passing THC-related DNA modifications onto offspring, and whether or not these changes are reversible is still unknown. Evidence of DNA alterations to existing Hippo signaling and Cancer genetic pathways may disrupt growth, enhance the potential for miscarriage, or impede healthy embryo development.

Methods

The authors employed a quantitative genome-scale approach, referred to as reduced representation bisulfite sequencing, to compare DNA methylation alterations in sperm across human and rat samples. A number of factors including, time since last ejaculation, semen volume, pH, morphology, and motility were controlled for across participants. Pyrosequencing, a DNA synthesizing method that relies on light detection, was implemented to identify genes with significant methylation differences. Data were then analyzed to uncover specific genetic pathways potentially impacted by paternal, preconception cannabis use.

Study Limitations

- A relatively small sample size of human subjects, limiting the generalizability of study findings.
- 24 males, age 18-40 years: (12 marijuana users & 12 non-users)
- The methodological approach may fail to identify epigenetic modifications that affect multiple genes simultaneously.

Citation


References


Physical Activity May Reduce Risk of Depression

March 14, 2019

As depression becomes a leading cause of disability worldwide, it is even more imperative to focus upon effective preventative measures. Findings from a recent study strengthen the empirical support, and provide the most compelling case yet, for physical activity as an effective prevention strategy for depression. Read further to find out more on how physical activity can influence risk of depression and how this can shape the future of depression prevention and treatment.

Exercise is known to be effective stress relief - higher levels of physical activity can potentially inhibit the risk of developing mental illness. As building evidence further fortifies this theory, a new study by the research team at Harvard Medical School, led by Karmel W. Choi, PhD, postdoctoral fellow at the Harvard T.H. Chan School of Public Health and Harvard Medical School’s Massachusetts General Hospital, has discovered that robust physical activity is an effective treatment for depression.

The Exercise Effect

Exercising initiates a surge of biological circumstances that yield numerous
health benefits, such as protecting against heart disease and diabetes, improving sleep patterns and lowering blood pressure. High-intensity exercise is known to release the body’s feel-good chemicals, known as ‘endorphins,’ creating a euphoria.

However, it is long-term exercise that yields the highest value - sustained activity releases proteins called neurotrophic or growth factors, which lead to nerve cells to grow and build new connections. This improvement in brain function makes an individual feel better, especially when it comes to individuals struggling with depression. Since exercise enhances nerve cell growth in the hippocampus, it can improve nerve cell connections and consequently relieve depression.

**Physical activity: a promising avenue**

The results of this study indicated that objectively measured increased physical activity protected against the risk of depression, but not the self-reported activity. This may largely be due to the fact that self-report measures are exposed to inaccuracies stemming from mood states and cognitive biases, that also influence mental health. Furthermore, objective readings are enabled to record activity other than planned exercise, such as walking to work or climbing the stairs. Hence, a depressed individual may view themselves as more inactive and lethargic than they actually may be.

“On average,” Choi says, “doing more physical activity appears to protect against developing depression. Any activity appears to be better than none; our rough calculations suggest that replacing sitting with 15 minutes of a heart-pumping activity like running, or with an hour of moderately vigorous activity, is enough to produce the average increase in accelerometer data that was linked to a lower depression risk.”

**Looking to the Future**

One in 10 adults in the United States struggle with major depression and many others are affected to varying degrees. With so many affected, there is a need to better manage major depression and its increasing burden of disability and mortality. Antidepressants have not proven effective universally and most patients are subjected to a trial-and-error process to determine the regimen best suited to their individual needs, so while these medications are an important tool, it’s important for us to explore further any other promising options for treating depression.

More and more findings are establishing links between physical activity and mental health. Having established that exercise is beneficial, the next important step should be in the direction of increasing the uptake and encouraging conformity to exercise. This knowledge is indeed important as it will allow us to focus on and invest in preventive strategies that are actually effective.

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**Citation**

As America continues to deal with an opioid overdose epidemic of staggering proportions, public health initiatives are faced with the needs of the more than 1.7 million people who are suffering from opioid use disorder (OUD) as of 2017.¹ This crisis is exacerbated by the shortage of health care practitioners trained and able to use FDA approved medication, like buprenorphine, to treat patients with an OUD. In a nation with a population exceeding 320 million, there are only 1100 psychiatrists specializing in addiction—the need for providers who are equipped and able to treat OUD is greater than ever. In a recent paper from the Yale School of Medicine Srinivas B. Muvvala, MD, MPH, Ellen Lockard Edens, MD, MPE, and Ismene L. Petrakis, MD, call upon psychiatrists and mental health professionals to play a more active role in addressing the current opioid crisis.

**What Role Should Psychiatrists Play in Responding to the Opioid Epidemic?**

March 21, 2019

Psychiatrists are unique among physicians due to their specialty training. They are well schooled in how to deal with trauma, depression, anxiety, suicidal behavioral tendencies, and other frequent comorbid psychiatric conditions, and can deal with co-occurring disorders effectively. While psychiatrists focus on the brain and behavior, they are also medical physicians and comfortable treating complex and co-morbid diseases. The high frequency of comorbid psychiatric illnesses with OUD means that patients with OUD often end up in psychiatric offices even when their substance use isn’t the explicit reason they are coming to the practice. For example, a patient may visit a psychiatrist for an evaluation suffering from depression only to find out that they have an important co-morbid, alcohol use disorder. For this reason, psychiatrists should be screening for OUD too, and be able to enact office-based interventions grounded in medication-assisted treatment (MAT).

Unfortunately, while the data and evidence supporting the use of MAT for OUDs is overwhelming, physician prescription rates and use of MATs have been slow to gain traction. Some psychiatrists are simply too busy— their practices are full and they cannot accept new patients. For others, the lack of enthusiasm about MATs is due to inadequate prescriber education about how MAT for OUD works to stabilize brain chemistry, how it can be incorporated into practice, and its efficacy. General psychiatrists do not routinely incorporate addiction treatment in their practice, and a national survey indicated that more than 80% were uncomfortable providing office-based MAT for OUD. The authors point out that it is crucial to change this, as the level of integrated mental health care and relapse prevention counseling that can be provided by psychiatrists quite efficiently and timely in an office-based setting makes psychiatric offices an optimal place to provide care for OUD.

**Reshaping the Psychiatric Response to the Opioid Epidemic**

Considerable evidential data supports the efficacy and ease of treating OUD with buprenorphine in office-based settings, and since the Drug Addiction Treatment Act of 2000 helped expand the clinical context of buprenorphine by reducing the regulatory restrictions for prescribing, psychiatrists can begin to prescribe...
“Psychiatrists are in an excellent position to meet the requirement that buprenorphine be given in conjunction with psychosocial services. Psychiatrists can provide in-house counseling and also work collaboratively with other disciplines (e.g., psychologists, social workers, nurses, and counselors).”

- Muvvala, Edens, and Petrakis

buprenorphine after completing an 8-hour training. Between this training and established mentoring programs, the authors recommend providers begin incorporating buprenorphine treatment into already established and routine psychiatric practice.

Additionally, buprenorphine education should be prioritized in all residency programs for physicians in training. Currently, only 40% of 85 surveyed residency programs offer buprenorphine waiver training, despite the low-investment requirement of a single month of addiction treatment experience. Research has indicated that psychiatrists who acquire training to prescribe OUD medication as residents are more likely to prescribe it than those who receive training later on in their practice. Training during residency is key to increasing prescriber literacy and comfort with existing OUD medications, destigmatizing the disorder and its treatment, and stressing upon professionals the importance of integrating care.

Looking from the Past into the Future

It is worth revisiting the ground-breaking report “Addiction Medicine: Closing the Gap Between Science and Practice,” by Columbia University. Published in June of 2012, this 5-year study found that, despite the prevalence of addiction, the enormity of its consequences, the availability of effective solutions and the evidence that addiction is a disease, both screening and early intervention for risky substance use are rare. Only about 1 in 10 people with addiction involving alcohol or drugs other than nicotine receive any form of treatment. The Yale group have taken these findings and built a modern approach calling psychiatric physicians to action. The report concludes: “Of those who do receive treatment, few receive anything that approximates evidence-based care. This compares with 70% to 80% of people with such diseases as high blood pressure and diabetes who do receive treatment. This report exposes the fact that most medical professionals who should be providing addiction treatment are not sufficiently trained to diagnose or treat the disease, and most of those providing addiction care are not medical professionals and are not equipped with the knowledge, skills or credentials necessary to provide the full range of effective treatments.”2 We have made some progress, but it has been slower than we would have liked and predicted at the time this study was published.

Citation


The next logical step toward better addressing OUD and curbing the current public health crisis is looking for ways to overcome systemic barriers to ensure that treatment is easier to access. New medications have been approved by the FDA offering psychiatrists more options in detoxification, agonist maintenance, and long-acting formulations of safe and effective MATs. Psychiatrists need to keep up with these advances and provide state-of-the-art evidence-based treatments in the offices, clinics, and hospitals where they practice.

“Addressing the national opioid epidemic is the responsibility of every psychiatrist, with commitment and a modest investment in further training, the expertise of psychiatrists in treating other psychiatric disorders can be extended to the effective treatment of OUD. We can and should be part of the solution to the current opioid epidemic.”

- Muvvala, Edens, and Petrakis
Cannabis use via E-cigarette on the Rise Among Adolescents
April 2, 2019

Electronic cigarettes (e-cigarettes) are the most commonly used nicotine-delivery product among US youth and their popularity is rising - 1 in 5 high school students currently use them. Until recently, there were few regulations on how companies that sell e-cigarettes can market and sell them - although companies claim that the product was made for and is marketed to adults, there has been a major uptick in use. Aggressive marketing campaigns that position e-cigarettes as a safe alternative to smoking have worked, convincing adults and youth that e-cigarettes are harmless. Because they are new to market, E-cigarette companies can also employ types of marketing strategies that are forbidden to traditional cigarette companies due to their efficacy among adolescents, such as sponsoring film and music festivals. E-cigarettes, also called vapes, vape-pens, and e-hookahs, can be filled with tobacco products that are far more addictive than cigarettes due to their much higher nicotine concentration. Instead of being packed with tobacco, e-cigarettes use cartridges that are filled with liquid that can deliver a much higher dosage of nicotine. These cartridges can also be filled with cannabis.

The rising number of students using e-cigarettes and the high co-occurring use of cannabis and tobacco products, has prompted concern, and regulatory agencies such as the FDA are working to create new regulations that will help inform adolescents on the dangers of vaping and protect them from e-cigarette advertisements in the same way they are protected from traditional tobacco products advertisements. Trivers and colleagues from the Centers for Disease Control (CDC) have analyzed the 2016 National Youth Tobacco Survey (NYTS) to reveal the trends of e-cigarette and cannabis use in school-aged teenagers.

Findings
8.9% of all students had ever used cannabis in an e-cigarette in 2016 - that’s almost 1 in 11 students.

1 in 3 high school students, and nearly 1 in 4 middle school students, that had ever used e-cigarettes had also used cannabis in an e-cigarette.

People who already used e-cigarettes to consume other nicotine and non-nicotine substances were more likely to use cannabis in an e-cigarette.

What Effect Does Smoking Cannabis in E-cigarettes Have on Health?

E-cigarettes, contrary to popular belief, can be harmful to a person’s health, according to the US Surgeon General’s Advisory on E-cigarette Use Among Youth. Cigarette aerosol can contain carcinogenic compounds and even formaldehyde - very harmful chemicals that can put the user at a higher risk of organ failure or developing cancer.

Cannabis use in youth can have harmful effects on the memory and learning, even impairing later achievement in education - when consumed via e-cigarette, the health risks of both e-cigarettes and cannabis compound each other. Using nicotine and cannabis products in adolescence also makes a person more likely to develop a substance use disorder in life.

In 2016, 8.9% of middle and high school students reported ever using cannabis in an e-cigarette.
Coordinating Care for Pregnant and Postpartum OUD Patients

April 11, 2019

As opioid use disorder (OUD) continues to rise in women of childbearing age, it is more important than ever to focus upon the complex needs and challenges of pregnant women with OUD. A recent study highlighted important experiences, potential practices and associated challenges from the Collaborative Outreach and Adaptable Care at Hallmark Health (COACHH) program, a collaborative care team aimed at providing care coordination for patients with a substance use disorder (SUD).

Care for Pregnant Women with OUD

All pregnant women have special healthcare needs, but those with opioid use disorder often require providers to have specialized knowledge on how to best address their needs. With this in mind, the program team at COACHH adapted a segment of their program to serve pregnant women. The American College of Obstetrics and Gynecology has focused on identifying the barriers that women face in accessing both care for pregnancy and opioid use disorder. Even separately, this care can be hard to find, and not adequate in addressing all the needs of this vulnerable patient population. For these women, the American College of Obstetrics and Gynecology recommends incorporating both prenatal care and pharmacotherapy for pregnant women with opioid use disorder.

Inadequate specialized treatment facilities can limit provider education and training, as they lack financial resources and social support. This perpetuates stigma, and creates substantial hurdles in the accessibility of integrated and effective care for the pregnant women who need it. The integrated system of care that the COACHH model focuses on is beneficial for both the mother and the child, and addresses some of these critical gaps in care.

Care providers for this population also frequently run into complex and interconnected medical and social problems that have given rise to the need to go beyond the conventional realm of prenatal care and care for people with OUD. To provide quality treatment, providers need to simultaneously address pregnancy and substance use together. There is also a need to account for the many socio-economic challenges facing pregnant women with OUD, including housing uncertainty, poverty, and domestic violence.

Present Study: Potential Strategies and Challenges

A series of semi-structured interviews were conducted with COACHH team members who worked directly with pregnant and postpartum women with OUD. Program logistics and takeaways were discussed and interviews were coded to assess recurring themes.

Results revealed five recurring themes: patient-provider relationship building, delivery of service, devising a care team, assessing outcomes and the associated structural challenges.

The following needs of this population were highlighted by the study:

Establishing a relationship is fundamental to engage the patient. Building trust and support for pregnant OUD patients, given the stigma of being a pregnant woman with the disease of addiction, was considered imperative to foster a productive relationship between provider and patient. A more holistic approach was suggested that encourages regular communication between patient and provider, and focuses on individual needs, existing gaps in care, associated social and community needs.

Methodology

To determine what trends exist among students, data from the NYTS school survey were analyzed. A total of 20,675 students participated in this survey to create a representative cluster of students attending public and private secondary schools.

Looking to the Future

E-cigarettes are harder to detect than many other forms of cannabis consumption, and easier to purchase - anyone can get one online with a credit card. A lack of knowledge among the adults in these students’ lives may make the use of e-cigarettes and the consumption of nicotine and cannabis more accessible to teenagers. When parents and educators are unaware of the dangers e-cigarettes pose to health, they are unable to adequately educate their teens, and they are also unable to recognize use as it happens.

We need to increase awareness among students, their educators, providers, and parents in order to help foster an understanding of the potential health risks and repercussions the use of e-cigarettes to consume cannabis can cause.

Citation

Another key part of successful treatment was connecting patients with resources and harm-reduction.

Unique challenges of pregnant OUD patients warranted a team-based approach. The wide array of variables involved with this population required a team of diversely skilled professional, all of who shared a deep understanding of addiction and pregnancy, and a familiarity with community resources. Addiction treatment can be high-stress and time-sensitive, requiring case members working with patients to regularly meet to process emotions, and avoid bias and burnout.

Qualitative and holistic terms measure success. Given the complexities of patients’ lives and the external influences on outcomes, quantitative measures were not considered to be effective in managing outcomes and quality of care. Relationships, engagement and openness were prioritized as signals of change.

Low referral rates presented challenges in reaching those in need. Typically referred to COACHH by obstetricians, the program expected to serve more than 40 women in 2 years, but fewer than 20 patients were enrolled. This was found to be due to highly time-sensitive nature of treating pregnant women with OUD, low provider awareness of resources for these patients, and gaps in care.

**Looking to the Future**

An estimated 2.3% of pregnant women used opioids in Massachusetts alone, between January of 2012 and September of 2014, a rate much higher than national estimates. The prevalence of neonatal abstinence syndrome also increased dramatically, from 3 per 1000 births to 16 per 1000 births between 2014 to 2013. Despite the increased need for care, there is still a highly limited number of providers who understand how to evaluate and treat these mothers and children. Too few providers even have the necessary buprenorphine waivers, required to prescribe the medication which has inhibited patient access to SUD treatment.

The authors emphasize integration of medical services, SUD treatment, and social support as the best way to move forward in providing care for pregnant women with OUD. Improved integration of specialized care with obstetrics and gynecology offices, community health centers, and other prenatal care facilities can increase the number of referrals, the authors concluded. Additional outreach is crucial to engage women in early prenatal care and improve outcomes.

Future studies should involve lowering the barriers to care and improving the quality and quantity of maternal-fetal providers with OUD interests and training. Additionally, patient interviews and a broader range of metrics calculating impact on health and wellbeing are needed. Assessment tools must also aggregate individualized milestones to track success rate. The results from this study can help inform the development of future tailored strategies to coordinate care for this population.

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**Citation**

The Paradox of Diverted Buprenorphine

April 18, 2019

Buprenorphine, a μ-opioid (pronounced mu-opioid) receptor partial agonist, is a highly effective, evidence-based medication for treating opioid use disorders (OUD). In order to prescribe buprenorphine, qualifying practitioners must obtain a waiver from the Drug Enforcement Agency (DEA), which places strict limits on the number of patients they may treat annually. Previous legislation and regulation meant buprenorphine treatment existed nearly entirely outside the traditional healthcare system. Despite legislation that increases the number of patients a doctor can prescribe to, and allowing individual medical providers to become certified, there is still hesitation among many providers over becoming certified to prescribe the medication, many waivered physicians do not have many patients on buprenorphine - some waivered physicians have none at all.

The unique pharmacological characteristics of buprenorphine inhibit its potential for misuse, reduce the effects of physical dependence on opioids, and decrease the likelihood of severe respiratory depression leading to overdoses. Still, it’s diversion and misuse is commonly reported by patients and law enforcement. Buprenorphine is the most diverted medication used to treat OUD, as methadone is more closely monitored and Naltrexone has no street value. Buprenorphine diversion presents a complex medical and socio-economic issue, and may also contribute to excessive mortality. A recent study by Cicero et al. examined the motivations behind the use of diverted buprenorphine and investigated the role of unmet needs for treatment. The results reveal a paradoxical situation where in-accessibility to treatment may actually be fueling this diversion.

Use of Prescribed Buprenorphine

Of the respondents, 54% reported ever receiving a buprenorphine prescription for the treatment of OUD. Those who ceased receiving buprenorphine through a prescription cited their top reasons as choosing to stop seeing their doctor or losing the ability to attend or pay for doctor’s visits/prescription. Only 19% (one in five) patients reported stopping buprenorphine because of mutual doctor and patient agreement on completion of treatment - in fact, 12% report that their doctor cut off their buprenorphine prescription despite the patient not being ready to end treatment.

Why are People Using Diverted Buprenorphine?

Three of the four most common reasons cited for using diverted buprenorphine were for self-medicating to achieve intended, therapeutic purposes of the medication: avoiding/easing withdrawal symptoms, maintaining abstinence from other substances, and trying to taper off of drugs. The authors also learned that buprenorphine is not many people’s drug of choice. Only 3% of respondents used buprenorphine because it gave “them a better high than other drugs.”

The authors found an overwhelming number of people using diverted buprenorphine, also called bupe, were doing so to ease withdrawals or wean themselves off.
The authors called for further research at international levels and emphasized the importance of finding ways to increase access by reducing costs, unavailability of prescribers and social stigma. The team concluded that improving prescriber access is more beneficial than harmful.

To better understand the use of diverted buprenorphine, the researchers surveyed data collected from adults aged 18 and older that were diagnosed with an OUD while seeking treatment at a treatment center. The survey included closed- and open-ended questions about:

- reasons for buprenorphine use with and without a prescription,
- how respondents were accessing buprenorphine,
- how their buprenorphine was administered,
- and the barriers to treatment access.

Resolving the Paradox

More data is necessary to understand how the use of buprenorphine differs from the use of diverted opioid pain medications or heroin. In these cases, as well, opioids are often diverted ostensibly for use in self-treatment of withdrawal symptoms, but it is still not completely clear if buprenorphine is diverted only when other options are not available, or because its relatively low street value makes it affordable to buy illicitly.

Medical practices can often be full, physicians are busy, and many other reasons contribute to prescribers’ hesitation to seek a buprenorphine prescription waiver from the DEA. Some, however, do not apply because they are afraid that the buprenorphine they prescribe might become diverted. It is very important to examine and follow the trends about the motivations for using diverted buprenorphine today, and understand the impact of unmet treatment needs amid an opioid crisis.

Geographic Distribution of Opioid-Related Mortality in the Third-Wave Opioid Epidemic

April 4, 2019

The opioid epidemic is a devastating public health crisis - over 47,600 overdose deaths in 2017 involved an opioid, and this number has seen a dramatic uptick in the last decade. Opioid-related mortality emerged as a public health issue in the 1990s, which led to a common cultural understanding of the opioid epidemic as a rural issue (concentrated in the Midwest and Appalachia) caused by an increase in the prescription of oxycodone. Emerging research suggests that the narrative of the current crisis is not so simple - that in fact there are multiple co-occurring and distinct epidemics, characterized by different types of opioids as well as geographical footprint.

This study, by Kiang, Basu, Chen, and Alexander, looked at the opioid overdose epidemic as multiple distinct subgroups, defined by the types of opioids driving mortality and the regions most affected. The first wave of the opioid epidemic, as recognized by the study, began in the mid-1990’s and was driven, in large part, by the increase in the prescribing of prescription opioids, the second wave began in 2010 when the nation saw a dramatic increase in heroin-related deaths. The third and current wave, which began around 2013, is defined by the rapid increase of

Citation

illicitly manufactured synthetic opioids as well as an expanded reach from rural to suburban areas.

**Results**

- The mean age at death was 39.8 years for men and was 43.5 years for women.
- Opioid-related mortality rates, especially from synthetic opioids, rapidly increased in the eastern United States.
  - In most states, mortality associated with natural and semisynthetic opioids (ie, prescription painkillers) remained stable.
  - In contrast, 28 states had mortality rates from synthetic opioids that more than doubled every 2 years (ie, annual percent change, 41%).
    - The District of Columbia had the fastest rate of increase in mortality from opioids, more than tripling every year since 2013.
    - Eight states (Connecticut, Illinois, Indiana, Massachusetts, Maryland, Maine, New Hampshire, and Ohio) had opioid-related mortality rates that were at least doubling every three years, and two states (Florida and Pennsylvania) and Washington D.C. had opioid-related mortality rates that were at least doubling every two years.
      - Among these 28 states, the mean mortality rate was 6.0 per 100,000 people.
      - Most opioid-related deaths are occurring among young and middle-aged adults.
      - This equates to a significant loss of life. Nationally, overall opioid-related mortality resulted in 0.36 years of life expectancy lost in 2016, which was 14% higher than deaths due to firearms and 18% higher than deaths due to motor vehicle crashes; 0.17 years of life expectancy lost was due specifically to synthetic opioids.

This study focused on the location of opioid-related deaths as well as their impact on life expectancy, measured in years of Life Expectancy Lost (LEL). The findings complicate the dominant narrative—opioid-related deaths have increased two-fold every two years in 24 eastern states. The devastating loss is not confined to rural states or those with high rates of poverty. Due to the recent increase in mortality—mostly driven by synthetic opioids such as fentanyl—LEL from opioids has surpassed firearms or car crashes.

**What do These Results Tell Us?**

The states with the greatest LEL in 2016 included West Virginia, Ohio, Connecticut, Maryland, Massachusetts, Rhode Island, and Washington D.C. This list runs counter to pervasive, yet outdated narratives framing the current crisis as a rural issue that primarily affects low-income communities. This study helps substantiate a critical revision of the current narrative to account for the actual and growing impact of the overdose crisis.

**Looking to the Future**

State responses to the overdose epidemic have ranged from restricting the supply of prescription opioids to expanding access to treatment and the life-saving overdose reversal medication naloxone. The authors suggest that recognizing and responding to the changing geographic trends of opioid-related mortality can empower states to enact more effective policies and better address the specific needs of their populations.

“Policies focused on reducing opioid-related deaths may need to prioritize synthetic opioids,” writes Kiang et al, and some states already have model policies that can serve as models to other states. There is recent evidence of decreases in some types of opioid-related mortality in Ohio, and the authors suggest that Ohio’s policy of increasing access to naloxone, implementing needle exchange programs, and increasing support for those with mental health and addiction problems can serve as a guide to other states as they start to address the rise in mortality in their own states.\(^1\)
Liver Transplants and Alcohol-Associated Liver Disease

March 28, 2019

Times have changed for those suffering from alcohol-associated liver disease (ALD), an umbrella term for liver conditions like fatty liver and alcohol-related cirrhosis that are caused by heavy or excessive drinking. Liver disease is one of the major consequences of alcohol use disorder, often resulting, ultimately, in liver failure. In the past, people whose liver health had deteriorated due to ALD would not have been considered for a transplant. One reason for this was the stigma surrounding alcohol use disorders and addiction. Another was a lack of understanding among physicians on how to improve outcomes for patients with ALD and in need of a transplant. Today, attitudes amongst doctors have changed along with the outlook for people with ALD. Of the 33,000 liver transplant recipients since 2002, 36.7% of them received a transplant due to ALD, up from 24.2% in 2002. Drs. Mitchell and Maddrey examined in a recent multicenter, prospective, national cohort study what has changed in the approach to evaluating transplant candidates in recent years.

Shortly after the first National Institutes of Health Consensus Development Conference on Liver Transplantation brought senior hepatologists together in 1983, the question of whether, and how, to allocate transplant organs to patients with ALD was discussed. What was eventually agreed upon was a 6-month period of abstinence before a transplant for patients presenting with ALD, with the hope that this requirement for abstinence would encourage patients to engage in treatment for alcohol use disorder. This period of time was arbitrary, not an evidence-based requirement. Certainly, abstinence would be helpful to recovery and continued consumption might harm a new liver as it had harmed the original liver. However, research data has shown that abstinence had much less of an effect on outcomes than was previously believed. Long-term outcomes for patients with ALD were not related to a period of pre-transplant abstinence and relapse post-transplant is associated with factors other than a period of abstinence. Five years after transplantation, patients who were abstinent for six months prior to receiving a transplant and...
those who weren’t had about the same survival rates.¹

With this knowledge, and the publication of a report in France and Belgium in 2011 that showed excellent short-term survival in patients with alcoholic hepatitis who received transplants, there has been a departure from the 6-month rule and a subsequent increase in the number of patients with ALD receiving transplants. Both the bias among providers against patients with ALD, and the belief that 6 months of abstinence from drinking is necessary seems to be on the decline.

ALD now edges out hepatitis C as the most common reason for liver transplants in the United States. One reason for the shift, researchers said, is that hepatitis C, which used to be the leading cause of liver transplants, has become easier to treat with medications. Hepatitis C is treatable, even curable, today - fewer patients with Hepatitis C reach a point where they need a transplant at all.

**Looking to the Future**

In addition to the shifting trends in liver transplantation, there is promising research that can help further decrease the mortality of people suffering from ALD, and possibly prevent them from reaching the point where liver transplantation is necessary at all. Clinical trials underway at the National Institute of Alcoholism and Alcohol Abuse (NIAAA) aim to help create better behavioral and medical treatments for those suffering from ALD to help improve short-term mortality. Such advancements could give patients more time to be stabilized, negating the need for some to have transplants at all, and allowing for a more thorough assessment of those who do need transplants. Until we are able to create and administer these treatments, future study should be focused on improving disparities in access to liver transplant for ALD and optimizing short- and long-term survival among transplant recipients with ALD.

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**Citation**


**Reference**