The Opioid Crisis in America: Past, Present, and Future

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The opioid crisis is an ongoing epidemic that has scarred society and healthcare. Usage began from opium, and since then has evolved to more potent drugs like heroin and fentanyl. These drugs are used for their pain-relieving effects, which is sparked from the release of endorphins in the brain. OxyContin was endorsed by Purdue Pharma and other campaigns, which caused physicians to persistently prescribe. The American Pain Society promoted pain as the fifth vital sign, and the Centers for Medicare and Medicaid Services attached reimbursement for patient satisfaction. Recently, opioid use has increased across all demographics, and can be split into four possible waves: (1) prescription opioid pills, (2) heroin, (3) synthetic opioids, and (4) co-usage with stimulants. America has extremely high opioid usage, and actions have been taken to reduce the risk or usage of opioids. Prescription Drug Monitoring Programs, Enhanced Recovery After Surgery plans, naloxone promotion, and Medication-Assisted Treatment have all been enacted in most areas. Safe injection sites, where opioids are injected by doctors, may sound unethical, but research proves overdose death declined in areas with these sites. The government and other federal corporations are working to prevent another market induced crisis. Now is the time to act on the crisis and provide support to those in need.

Introduction

The opioid crisis is a widespread public health issue that has cast a shadow over the United States society and healthcare, devastating communities, individuals, and families. With prevalence beginning in 1999 and spreading country-wide, the epidemic continues to be an increasing concern requiring further research and interventions. Opioids, including heroin, morphine, and codeine, are potent pain relievers that have euphoric effects; with high rates of tolerance, they are often misused. Abuse of opioids has been reported since they were first used, but in the United States, the problem has only worsened. The first wave of the opioid crisis began in 1999 when prescription overdose deaths began to rise[1]. Recently, from 2019 to 2020 alone, it is reported that opioid-related deaths have increased by 38%, and 187 people die every day from opioids[1].

Opioids in Medicine

Opioid Development

Opioids have a long medicinal history, starting from around 8,000 years ago[2]. The most common opioid used then was derived from a poppy plant: opium. It is produced by cutting into an unripe poppy seed, and using the white fluid that leaks as a pain reliever. The prevalence of opioids was further promoted as they were used by prominent leaders and not prohibited in any religious texts. The drug sparked interest in scientists, and pharmacological developments contributed to further use and misuse. In 1803, German scientist F. W. Serturner was able to extract morphine from opium, a primary active chemical that is approximately ten times more potent than opium[3]. The drug was named after Morpheus, the God of dreams, due to its tendency to induce sleep.

Further investigation led to the extraction of a new compound from morphine: diacetylmorphine[3]. It was considered a new medical treatment with "heroic" possibilities and, therefore, was named heroin[3]. Heroin, twice as potent as morphine, was put on the market as a cough suppressant and pain reliever[3]. However, due to some complications with morphine anesthetic in surgery, the hunt for another opioid alternative began. Fentanyl was developed first in 1959 and introduced to the public as an intravenous (within the veins) anesthetic[3]. It was the most powerful opioid ever created, as it was 100 times more potent than morphine. Additionally, some chemical analogs of fentanyl are more powerful than fentanyl, such as carfentanil[3].

Opioids have been around so long that history continues to repeat itself- people have always and will continue to use drugs. Overtime, opioids have just become more powerful to adapt to society changing. Opioid addiction was present in the past just as it is now, however, due to new information and advancements in research and technology, we were just recently able to understand the severity of these drugs. We are now able to realize how harmful addiction truly is, and now have the responsibility to take accountability and act.

Medicinal Use

Endorphins function as a neurotransmitter and are associated with pain relief, like the effect of opioids. Scientists then hypoth-

esized that opioids bind to the same receptors that endorphins do, producing a similar result[4].

The three major types of opioid receptors include mu (m), delta (d), and kappa (k), and were only discovered around 1990[4]. The opioid that is naturally present in the body, b endorphin, binds to mu receptors; the strong painkillers, enkephalins, bind to d receptors; and a neuropeptide involved in pain and addiction, dynorphin, binds to k receptors[4]. When opioid molecules bind to mu receptors, they inhibit the release of noradrenaline, producing effects known as opioid intoxication- drowsiness, slowed respiration, and low blood pressure[4]. All three of these receptors produce analgesia or pain relief when activated by an opioid. Other opioid receptors may be coupled or paired with guanine nucleotide binding proteins, or G-proteins[4]. When a receptor is occupied, it forms a complex with a subunit from a G-protein and helps stimulate what needs to be stimulated to produce the symptoms of opioids[4].

The presynaptic nerve terminal (where the nerve signal begins) and the postsynaptic neuron (where the nerve signal ends) both play a role in the action of opioids. The presynaptic portion inhibits neurotransmitter release, along with inhibitory postsynaptic neurons[4]. The effect of an opioid takes place due to multiple presynaptic sites on neurons and the postsynaptic effects. For instance, presynaptic inhibition of an inhibitory or preventing neurotransmitter would result in excitatory or stimulating effects, but if a postsynaptic inhibitory effect takes place, the excitatory effect will not occur. The location and density of the opioid receptors therefore dictates the effect of opioids on the neuron.

With repeated exposure to opioids, the brain receptors take more to stimulate the same amount, as they gain tolerance over time. Tolerance is complex but can be briefly defined as a loss of analgesic pain killing efficacy after the repeated use of opioid drugs. Research suggests that there were modifications of opioid-receptor ion channels and second messenger pathways in many areas of the brain[5]. Along with those, protein kinases (enzymes that modify carbohydrates, amino acids, and other molecules), glutamate receptors (receptors that monitor excitatory synapses in the nervous system), and neurotrophic factors (molecules that support the growth of developing mature neurons) are also involved. There is evidence that multiple genes could influence adaption or tolerance at the genetic level.

As one continues to use opioids, their locus coeruleus, part of the brainstem that deals with responses to stress and panic, increases its activity, and when opioids are not detected, it releases excessive amounts of noradrenaline, creating jitters, anxiety, and muscle cramps, or the typical withdrawal symptoms. Addiction occurs as repeated exposure induces the brain's mechanisms of dependance, and so people resort to daily drug use to prevent the hurtful withdrawal symptoms[6].

Opioid Use Disorder

One can be officially diagnosed with Opioid Use Disorder (OUD) after meeting the criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)[7]. Tolerance and dependence are inevitable, so the DSM-5 removed them as a player in OUD diagnosis[7]. Nine behaviors, such as doctor shopping and repeated requests for early prescriptions, and fear of withdrawal, can help diagnose OUD. OUD can be derived from genetic, psychosocial, or environmental factors, and is a chronic disease[7].

A study conducted by the Center for Disease Control and Prevention (CDC) from 2015 to 2017 had the means of addressing the question of demographics in the opioid epidemic by measuring opioid use and overdose, including synthetic opioids[8]. It aimed to analyze any changes in drug overdose in people over 18 by race, ethnicity, and age. In large central metro areas, Black people experienced the most significant increase in rates of use. In large fringe metro areas, White people experienced the most significant increase. In medium/small metro areas, Black people had the most significant increase for any opioid, White people had the most significant increases for synthetic opioid, and Hispanics had the largest expansion of overdose. Overall, the percentage of opioid use and opioid-related deaths across all demographic groups had increased. Because of the function of opioids, access is relatively evenly distributed throughout races, but could be limited economically. Individuals with Opioid Use Disorder (OUD) can include a wide diversity as opioids are simply a pain medication and can be achieved legally.

Opioid-related hospital visits varied greatly from region to region. Large central metro and small metro areas in the Midwest had the highest number of opioid-related visits while large fringe metro and medium metro areas in Arizona, California, Nevada, and Hawaii had the highest number of opioid-related visits[9]. Both of these include the Rocky Mountain regions of the United States.

Disparities

Because of the variability of opioids, the crisis has spread across all racial and ethnic groups, but fatalities among non-Hispanic White individuals have received the most media coverage[10]. Opioid mortality was fairly similar across all racial groups starting in 1999, but has increased for non-Hispanic White individuals, with the fatality rate doubling both Black and Hispanic individuals by 2014.

The disproportionate statistic can be due to historically higher rates of opioid prescription among non-Hispanic White individuals but is more likely traced back to the under-treatment of chronic pain among racial/ethnic minorities. Black individuals were 29% less likely and Hispanic individuals 22% less likely than White individuals to receive opioids for similar pain conditions[10].

However, disparities in opioid misuse among Native American and Asian individuals are especially overlooked. Studies that have examined these groups do not have much statistical power to assess differences due to the small sample size for these groups and low prevalence of opioid misuse behaviors [10]. In order to accurately evaluate the crisis, we must have sufficient data on how it impacts every racial group. Even though rates of opioid overdose among Native Americans are second to White individuals, there are very few studies of the prevalence of misuse in these Native communities. Furthermore, national surveys claim that Asian individuals have lower rates of opioid misuses, however treatment admissions for opioid addiction increased 30% among Asian individuals from 2000-2012 [11].

Asian Americans are a highly understudied population and considered a "model minority" for health. However, data on risky behaviors and opioid use in Asian American teenagers proved that these teenagers aged 12 to 16 showed that opioid use is significantly associated with weapon carrying, risky sexual behavior, and body image [12]. Asians, especially the youth, should have their health overlooked due to the lack of inclusion in studies.

This harmful behavior possibly allows Asian Americans to underutilize opioid-specific treatment. Lack of self-help resources and stigma around substance use are especially prevalent in Asian communities, and more studies should be completed in order to fully analyze and help Asian-Americans.

Pharmaceutical Influence

The pharmaceutical industry played an extremely large role in the distribution of opioids. In 1996, Purdue Pharma released OxyContin to the public, claiming it was less addictive yet still able to alleviate chronic pain. Hearing this, both the public and physicians were persuaded, Doctors began to prescribe, possibly even overprescribe, these drugs in hopes that their patients would get better without the fear of addiction. The company that produced OxyContin distributed over 15,000 copies of their promotional video, "I Got My Life Back," which heavily influenced sales. OxyContin, nevertheless, was still extremely addictive and not as safe as advertised [13].

In order to make OxyContin more difficult to crush, reducing its ability to be abused, a abuse-deterrent formulation was created. A survey, conducted quarterly through July 2009 to March 2012 with a sample population of patients with opioid dependence, asked users to acknowledge and interpret data from the situation. OxyContin as a primary drug of abuse declined from around 36% to 12% with the abuse-deterrent. However, other opioids usage increased significantly; for example, heroin uses almost doubled [14].

Interviews with the addicts who had used both regular and abuse-deterrent OxyContin preferred the regular. 24% had found a way to alter and still abuse the newer form of the drug, and 66% claimed that they had switched to another opioid to satisfy cravings, mostly heroin [14]. Patients, however, stated that it was not that their usage of OxyContin decreased because of the abuse-deterrence, rather, they had found cheaper and more accessible drugs of choice. This data showed scientists that abuse-deterrent formulations were not as helpful as they intended and were not capable of solving an increasingly alarming problem of opioid abuse.

Physician Influence

Physicians are not totally innocent in this scenario either, as many did not have the motive to treat patients. There was a spike in malpractice, as some doctors continued to prescribe their patients opioids for monetary gain [15]. Many medical experts were under the impression that opioids helped. A doctor named Russell Portenoy was known as the "King of Pain" in the late 1900s and worked to make policy changes in state medical boards in favor of the treatment of pain [16]. Lectures were given to physicians by him and others like-minded proclaiming the safety of narcotics- but Portenoy later admitted these lectures were not truthful.

One could argue that America represents a culture of over prescription- opioids, antibiotics, and others all included [16]. In a physician's defense, they could be used to supplying multiples of thirty, for example 30 pills for 30 days or a month, and sometimes pharmacists will question the dosage and suggest increasing it. This type of over prescription could lead to an increase in abuse, but it is also the unintentional effect of leaving drugs around. The leftover pills are often the ones that are stolen by a family member and abused as well.

Around the same time as the approval of Oxycontin, the American Pain Society promoted that pain was the fifth vital sign, making it the only subjective vital sign in comparison to temperature or blood pressure. Due to this, the Centers for Medicare and Medicaid Services (CMS) now had attached significant reimbursement to patient satisfaction, and physicians had to ensure their patients had high scores on their satisfaction survey [16]. One bad score could be detrimental to the clinic, so doctors often felt pressured to prescribe opioids with the new pain scale. Furthermore, in 1980, a letter was published in the New England Journal of Medicine that challenged what physicians thought about the risk of addiction. The article mentioned that only 4 out of 11,882 patients that were given opioids become addicted to them, so this letter was used as proof that supplying opioids to patients was not bad. Pain organizations, including the World Health Organization began pushing for opioid use and curing pain. Opioids were no longer associated with short term pain, but now chronic pain as well [13].

Government Systems

The Food and Drug Administration played a large role in the crisis, beginning in the 1990's. The FDA controls advertising and promotion of prescription drugs, ensuring that the information is truthful. However, even if pharmaceutical companies send materials to the FDA for review, it is still not required for the materials to be validated and approved before their use [17]. The FDA's limited staff capacity prevents all advertising materials from being viewed before they are out on the market, allowing companies to publicize their perspectives on the addictive nature of opioids, which can often be untruthful. The Center of Disease Control in 2015 put stricter regulations to prescribe opioids, and although this was good in theory, it had unintended negative consequences- opioids were more difficult to access, so addicts began buying illicit opioids such as heroin [17].

Some states have laws in place that allow the opioid crisis to worsen. Wisconsin has the Len Bias Law- in place since 1986- where if someone dies from an opioid overdose, the law prosecutes the dealer and addict who helped the deceased acquire opioids. The Good Samaritan Overdose Law (which states that if someone calls for help during an overdose, they are exempt from prosecution) coexists with the Len Bias Law, preventing people from wanting to save addicts during overdoses. This has caused overdose rates in Wisconsin to continue to increase [17].

Socioeconomic Influence

Poverty and substance use problems usually operate together; the hardest labor jobs in poorer communities usually consist of manufacturing and service jobs, increasing workplace hazards and physical stress. Job injuries can create chronically painful conditions, resulting in disability and further poverty. Opioids may allow these individuals to maintain employment, but these individuals also appear to be at increased risk for non-medical use.

One study that covered relationships between county-level non-Hispanic white drug mortality rates and socioeconomic and opioid supply measures across urban and rural areas revealed that these mortality rates were highest and increased the most in large metro counties [18]. Rural counties in this case did not have a more direct connection to lower socioeconomic factors, as many urban counties face this as well. On average, from 2014-2016, the most rural counties had 6.2 fewer deaths per 100,000 population than large metro counties [18]. Economic distress, family distress, population loss, and exposure to opioids and fentanyl were all associated with higher drug mortality rates. However, the reason behind drug use varied from rural to urban. In rural counties, economic hardship was a stronger reason for opioid abuse, while in urban counties, the presence and availability of opioids were a stronger reason. The highest mortality rates were disproportionately in low socioeconomic areas where they were dependent on a large mining or service sector [18].

In addition, for some individuals, social disasters or stress can lead to actual physical pain. Earthquakes or other natural disasters such as Hurricane Katrina and Rita increased alcohol use and other forms of substance use, especially among those who had lower incomes [19]. Children who witness trauma when they are younger are more prone to substance use, linking them to increased opioid use years later. For example, people from one county in a deindustrialized steel production area of Pennsylvania claimed that economic hardship, social isolation, and hopelessness were reasons for their drug use, calling for jobs and building back the community to reverse overdoses [19].

Stages of the Crisis

Commercialization of Healthcare

Medicine has developed into a commercial profit as mentioned before: this can be credited by a Supreme Court decision known as Goldfarb. This unanimous decision ruled that medicine and law should be considered as simply commerce [20]. This allowed for medicine to be sold for commercial gain, allowing medical professionals or businesses to exploit opioids for their own monetary benefit. The Federal Trade Commission sued the American Medical Association afterwards and removed one of the fundamental Principles of Medical Ethics that included the original Hippocratic Oath, which stated that doctors will refrain from causing harm. These two court rulings had taken place to decrease health care costs but were attributed to the opposite. Decisions like these allowed opioids to be prescribed more, as there was less worry for the patient and more interest in healthcare professionals.

The actual aid that opioids gave patients with long term pain was put into question. Prior research has indicated that this alleviation of pain could be seen as a placebo effect. Although opioids did show relief of acute pain, most opioid trials do not extend past six weeks, and therefore, cannot sufficiently aid chronic pain [21]. To find evidence, the Agency of Healthcare and Research Policy conducted a study where they asked adults with long term pain questions such as the effectiveness of opioids or placebo, the risks of opioid use, and accuracy of risk management. Each strength of body evidence was given either a high, moderate, low, or insufficient. No study of opioid use or opioid placebo evaluated long term outcomes such as pain or quality of life.

Rates of opioid abuse or dependance range from 0.7% with low dose therapy and 6.1% with high dose therapy, compared to 0.004% with no opioids. Overdoses were much more frequent when there is recent opioid usage, with 256 out of 100,000 patients prescribed with opioids having an overdose, compared to 36 who were not [21].

Waves of the Opioid Crisis

The opioid crisis has three established waves, with the first one being prescription opioid pills. In 1980, acute pain was so often treated with opioids that propoxyphene was the second most dispensed drug in the United States[22].A decade later, US medicine was shocked with the amount of underrated chronic pain, encouraging normative practice and policy changes. Before, chronic pain was greatly managed with cognitive behavior therapy, even extremes like hypnosis[22].

Insurers only provided limited coverage of behavioral pain therapy, so pharmaceutical manufacturers saw the opportunity. The initial increase in prescription opioid is what many correlate with consequences such as opioid overdoses[23]. Pharmacy innovation included extended-release formulations, transdermal patches, nasal sprays, and oral dissolving strips, and by 2000, chronic pain was a big business. From there, pharmaceutical marketing inaccurately minimized addiction potential and promoted off-label use, allowing for physician schemes, lucrative speaking fees, and lobbying[24]. More specifically, extended release long acting (ERLAs) was a type with technological advances for analgesia and pain relief lasting longer with one pill, but these were easily abused by overuse or incorrect intake. The mechanisms that ERLAs used to prevent misuse were ignored by crushing and snorting or injecting the drugs. However, this wave may have spurred from the rise of reported pain in the elderly population, and economic and psychological distress across the United States. All these factors allowed for the increase of opioid pill consumption and allowed the crisis to worsen.

Wave two is heroin, and to explain its prevalence, it is important to acknowledge the fundamental topic of supply and demand. Heroin, for example, was only legal for so long. The beginning of illicit heroin started around the 1920s. The rise of heroin use in the 1940s and 1970s were sparked by social and cultural elements signaling the rejection of mainstream values[23]. The supply side was upheld by the Italian and French supplying heroin to the United States after World War Two, and new sources from Southeast and Southwest Asia in the 1970s. Once again in the 1990s, a new supplier emerged: the Colombian transnational criminal organizations (TCOs). The United States continues to experience waves of opioid abuse due to the amount of supply and demand. Heroin related deaths and heroin users have been increasing since the mid-2000s, sparking wave two. Heroin was easier to abuse, as there was less of a need to be supplied from illicit drug sales or prescriptions. The availability of cheaper, yet harder hitting drugs influenced new, young users, who were inclined by the economic benefits compared to opioid pills. There is a shift from opioid users' first try: what used to be prescription pills are now exchanged for heroin.

Heroin users have a different demographic compared to regular opioid prescription users. For example, the peak heroin overdose group is 20 to 34 years old, compared to the peak prescription overdose group with 50- to 64-year-old[23]. This could also be evidence for a demand driven wave two in addition to the younger population initiating first use with heroin. Wave one's overdoses were relatively even across the country, where heroin overdoses were much higher in the Northeast and Midwest[23]. There was a transformation in the US heroin supply, such as in origin, in the last decade or so. Before 2000, heroin came from four regions: Southeast Asia, Southwest Asia, Mexico, and South America/Colombia. After this, most heroin was shipped by TCOs in two countries, Colombia and Mexico. Regional distribution was then further divided with Colombian-sourced heroin in the eastern US and black tar heroin from Mexico in the western US. Mexico then monopolized the heroin market, increasing their market share from 50% in 2005 to 90% in 2016[23]. Mexican-sourced heroin is becoming more potent; "Mexican white" copied the traditional Colombian-sourced heroin and has hooked the customers of Colombian companies[25].

Wave three is especially prevalent today, which includes synthetic opioids, such as fentanyl[25]. Fentanyl is often illegally sold as "heroin" in powder form, or other fake opioids. Changes in purity and strength are a large problem, as different chemical analogues of fentanyl can be much more deadly, like mentioned before.

These synthetic opioids have sparked an emerging class of drugs, called novel synthetic opioids (NSO) that belong to new psychoactive substances (NPS)[23]. NSO has potent receptors that only require a low dosage or amount to produce the effects of a high, leading to increase in overdoses. With the newfound spread of this class of drugs, it is now the leading cause of opioid overdose in the United States. The molecules of these opioids have different pharmacological properties, with their own characteristics when it comes to pharmacodynamics and pharmacokinetics such as metabolism and absorption into the body. These NSOs pose a threat as along with being illicit, they are easily transported and concealed due to the small number of doses. NSOs have the same respiratory depression compared to other opioids, but it occurs much more rapidly.

According to the US Drug Enforcement Administration, the main provider of illicitly manufactured fentanyl is China. To get into the US, fentanyl travels by many different routes, including internet purchases routing through Canada (pill form) or Mexico (powder or pill forms). Regional discreteness can also show the impact supply has on the third wave.

Comparing drug seizure data with overdose death data can show geographical correlation between fentanyl seizures and synthetic opioid overdoses. These also overlap with areas of the wave two overdoses- the Northeast and Midwest[23]. Possibilities for this regional disparity could be that fentanyl distribution is controlled by the Sinaloa (state in Mexico) TCO or that forms of powder heroin, more common in the Northeast and Midwest, are more easily lacked with powder fentanyl than solid black tar heroin, which instead plagues the western US. These stark

differences throughout regions shows that the third wave is a supply-side event, as a demand event would have more likely to lead to more of a geographical distribution of fentanyl-related overdose.

Ethnographic research with those who use heroin confirm that fentanyl was not demand-driven and that there is a range of desirability from avoidance to enthusiasm[23]. Those who prefer fentanyl are restricted from buying it because of its concealed identity as other drugs or fake brand name pills. Cultural idioms for fentanyl have been slow to rise even though there has been years of steady supply; slang terms are available for many other illicit drugs and the lack of terms for fentanyl proves there is also a lack of demand.

To prevent the continuation of the fentanyl crisis, it seems obvious to focus on stopping supply. There is evidence that this could work with programs that include demand reduction as well, as one-sided interventions without addressing demand may cause unwanted results. Unintended consequences in the past could have sparked from the reformulation of ERLA opioids to abuse-deterrent formulas, such as OxyContin and Opana, with misuse of Opana contributing to the Scott County Indiana HIV outbreak[23].

Although the opioid epidemic is usually characterized by three waves, recent data shows that we possibly have entered a fourth one, involving stimulants, such as cocaine and methamphetamine, being used in combination[23]. The cocaine use in 2018 was estimated at 5.5 million and has increased along with methamphetamine usage. The rise in stimulant related drugs seems to connect with the opioid epidemic. Polydrug use has been a public health issue for a long time, particularly when opioids are involved, but the co-use of stimulants and opioids is becoming increasingly popular. Co-use with fentanyl is especially worrying, as like mentioned before, fentanyl is extremely easy to overdose on because of its small lethal dosage or LD50.

Combating the Epidemic

Laws and Regulations

The United States began to take action in 1914, launching the Harrison Narcotics Act, which regulated and taxed the production and distribution of opioids. This act put the control of opioid drugs in the hands of physicians, and determining whether an individual had a valid medical need for opioids was exclusively the physician's decision. This act began illegal drug use and associated drug-related crimes in the US, as increased regulation leads to increased illegal drug purchases[26]. Once the Harrison Narcotics Tax Act was established, there was an immediate change in the demographics of opioid users. Before, opioid dependence cut across all social classes. However, when they became illegal, they began to be used mainly in large cities where organized crime provided a supply. Users were primarily young, less-educated men of lower socioeconomic status[26].

Now, the United States has more opioids than any other country in the world[27], and despite being one of the wealthiest, the U.S. has increasing mortality rates. Illicit opioid sale is common all over the country: rural areas have fractured under the stress and urban cities can not completely prevent drug dealing. Opioids were abused in 80,411 overdose deaths in the United States in 2021, totaling 75.4% of all drug overdoses[28].

Due to an increase in public awareness, steps are being taken to combat the epidemic. To begin with, policy makers create interventions that prevent overprescribing. The CMS in 2017 launched the act of taking out the questionnaire mentioned before about patient pain in order to remove the benefit of hospital or physician reimbursement and treatment of pain[29].

Limiting opioid prescriptions will further reduce "pill mills," those who write prescriptions for the money, and people will be less exposed to addictive substances. To enforce this, states have already begun to use Prescription Drug Monitoring Programs (PDMPs) a statewide database that shows if the patient has received opioids, along with limits on the amount prescribed[30].

Reducing the number of illicit opioids is made possible through law enforcement, at the communal level and up to federal level. PDMPs have been available since the 1930s, but only now can technology collect information on substances and provide reports to pharmacies and prescribers efficiently.

Hospitals Regulations

As opioids are also prescribed in the surgical setting, it is important to limit opioid exposure in the operative setting. Enhanced Recovery After Surgery (ERAS) plans- which reduce the stress after surgery that leads to opioid usage- have shown a decline in opioid use along with better length of hospital stay and pain scores. With a decrease in exposure, there is a decrease in risk of addiction or abuse. Unfortunately, surgeons are not adhering or enforcing these pathways. A recent study from UCLA conducted that there was no change in the opioid prescription at discharge in pre-ERAS or post-ERAS, showing that surgeons are not changing prescription habits, counteracting the goal of ERAS completely[31]. Until prescribers limit the number of opioids or switch to safer medications, these efforts will not be replicated at a national scale in an amount to fight against the epidemic.

To combat this, another solution could be to create procedure-specific guidelines. Recommendations of the number of opioids prescribed were drawn from the number of pills that would satisfy 80% of patients and were presented at a department-wide meeting to make sure all staff were aware. This caused a 53% reduction in opioid prescribing compared to before the education, and patient pain control was not negatively affected either[31]. The guidelines combined with making the staff aware significantly decreased the potential risk of opioid abuse.

Treatment Options

Naloxone is a nasal spray that can reverse the effects of an overdose, limiting the potential mortality that could come from overdoses. It usually is available in any drugstore and carrying one can save someone's life. Each state has now passed legislation to ensure that naloxone is readily available. However, this could be a setback as research supports that increased naloxone equates to riskier drug behavior, as in some regions of the United States, increased naloxone leads to a 14% increase in opioid-related mortality[32]. This could be due to the use of more potent opioids like fentanyl, opioid related theft, and no or reduction or even a possible increase in mortality[32]. The good intention of naloxone could just promote worse abuse habits.

To help those who are battling addiction, researchers believe that medication assisted treatment is quite helpful as it decreases opioid usage, prevents relapse, and reduces the risk of fatality.

Medication-Assisted Treatment (MAT) consists of taking one or more drugs that reduce cravings for opioids and prevent them from having euphoric effects, while simultaneously blocking withdrawal symptoms. Medications that were approved by the U.S. Food and Drug Administration include opioid agonists like methadone and buprenorphine[33]. Only a small number of people get the help they need for addiction; therefore a recent focus has been applying MAT into primary care settings. The Drug Addiction Treatment Act of 2000 allowed physicians to be able to distribute buprenorphine for opioid addiction, but its use remains limited. Medicaid has now created a waiver for states to integrate MAT in primary care settings mostly financed.

Stigma associated with opioid use also affects the usage of MAT. The concept of drug recovery has clouded some opinions of methadone treatment. Other misconceptions of MAT have further led to the lack of MAT in correctional settings. MAT is physically and ideologically separate from other treatments for chronic illnesses, and is characterized by a high threshold, low tolerance model which reinforces the addict identity, hindering recovery[33].

A study of adults 18 years and older were eligible for a study for the effectiveness of MAT. After observing cognitive, occupational, physical, social behavioral, and neurological functions, it was shown that OUD patients who received MAT did not show as much benefit as those who did not[34]. In several studies, MAT patients performed worse in these areas than those of healthy people. These studies show that MAT may not have such a significant difference in opioid addicts' lives: the only claim that has substantial evidence is that those who take buprenorphine have lower levels of fatigue compared to those who take methadone. This has made it difficult to establish effectiveness but also invites more research to be done.

One of the more controversial routes to combating the opioid epidemic is safe injection sites (SISs), which consist of a space where people are injected opioids by doctors, so they can use them under the supervision of a healthcare professional. The United States Drug Enforcement Agency has stated that these sites are in violation of the Anti-Drug Abuse Act of 1986- an addition to the Controlled Substances Act that vowed that it was a crime to offer property to sell, manufacture, store, or use a controlled substance[35]. Technically speaking, there are no federal laws that explicitly prohibit these injection sites. These sites are in at least thirteen cities and states in the country, and legislation to open legal SISs have been advocated for in California, Massachusetts, Colorado, Vermont, Maryland, and New York.

Harm reduction attempts to reduce the harms associated with drug use- trying to eliminate the consequences of drug use, not the drug itself. These measures, including safe injection sites, have faced a lot of opposition due to the moral prohibition of drug use and demonization of addicts or people who use. Only until needle exchange programs showed benefit in fighting AIDS did some harm reduction strategies gain acceptance. Through all the backlash, studies prove that safe injection sites do have a positive outcome and can save lives. In Vancouver, Canada, research from a SIS revealed that greater usage of SIS was associated with safer injecting practices, reduced reuse of syringes, and safer syringe disposal. Users were also less likely to rush injections, which increases risk of overdose. Furthermore, fatal overdose deaths decreased 35% without 500 meters of the SIS, compared to a 9.3% decrease in the rest of the city[36].

One of the most effective programs has been public education and guidelines, as it is the most widespread and accepted across all states. Research has shown that people who think drugs are harmful are less likely to abuse them, therefore, interventions have been made at a variety of targets to spread awareness about drugs[37]. Some address special populations like women and adolescents, as those groups are at a higher risk for OUD. Educating primary care providers on safer opioid prescribing has led to a decrease in the proportion of overdose opioid prescription deaths. In one study, two-thirds of state agencies reported that their departments of public health, medical boards, and pharmacy had developed or were developing opioid-prescribing guidelines for providers[37]. Education and awareness allows the future to be changed, in hopes of stopping an increase of drug usage.

Methodology

This research review contains information gathered using online databases such as Google Scholar.

Conclusion

In order to prevent another market induced crisis, healthcare, specifically the pharmaceutical industry, regulators, and clini-

cians, must take large steps to reduce the influence of prescription. The 2009 Institute of Medicine (IOM) reported sixteen suggestions (for example, banning gifts and appropriate scrutiny in consulting arrangements) to diminish influence and maintain trust. Some centers have attempted to restrict interactions between sales representatives and physicians considering the opioid epidemic[37]. The Pharmaceutical Research and Manufacturers of America (PhRMA) implemented a Code on Interactions with Healthcare Professionals, but due to its leniency compared to the IOM, it has been questioned and advised to make revisions. The FDA's Office of Prescription Drug Promotion has the task of regulation of prescription drug advertisement and revision of material concerns from professionals. FDA resources should be increased in order to better detect misleading marketing and better review advertisements. This could also include expanding education for clinicians, like the Bad Ad Program, a program designed to help healthcare providers recognize misleading or false advertisements.

In order to aid our current crisis or even prevent another one, community level interventions are critical. Public education must be accessible to everyone- much of the public is advocated for education on how to teach bystanders to reverse overdoses. Increased knowledge and administration rates have shown some early evidence in decreased deaths in Massachusetts and North Carolina[38]. New York State health education curriculums now require information about opioids, changing societal perceptions about people with addiction.

The opioid epidemic has quite frankly inflamed overtime. Deaths have continued to rise, and with the emergence of a new possible wave, it does not look like much hope is on the horizon. That does not go to say that the United States isn't trying though, evident with the 2016 Comprehensive Addiction and Recovery Act which allowed education campaigns but did not give necessary funds for them[38]. The 2016 Century Cures Act authorized almost a billion dollars to states and claimed prevention strategies as a priority, but as of right now, they are underemphasized and overlooked[38].

Understanding what exactly went wrong and how to prevent and fix it are just the first steps to fighting this crisis. This crisis cannot disappear solely through government help- we must step in. Researchers should continue to accelerate their work, ensuring that everyone is equally advocated for. The youth and impressionable should be warned through accessible community resources such as papers like these or school curriculum changes. The opioid crisis has reached alarming rates- numerous lives have been lost, families torn apart, and communities damaged from the consequences of opioid addiction- affecting people from all backgrounds. Now, more than ever, we must stand hand in hand and unite to address the crisis and provide support to those in need.

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