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Current perspectives on the opioid crisis in the US healthcare system

A comprehensive literature review

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Abstract

Introduction: The administration of opioids has been used for centuries as a viable option for pain management. When administered at appropriate doses, opioids prove effective not only at eliminating pain but further preventing its recurrence in long-term recovery scenarios. Physicians have complied with the appropriate management of acute and chronic pain; however, this short or long-term opioid exposure provides opportunities for long-term opioid misuse and abuse, leading to addiction of patients who receive an opioid prescription and/or diversion of this pain medication to other people without prescription. Several reviews attempted to summarize the epidemiology and management of opioid misuse, this integrative review seeks to summarize the current literature related with responsible parties of this opioid abuse crisis and discuss potential associations between demographics (ethnicity, culture, gender, religion) and opioid accessibility, abuse and overdose.

Methods: We performed an extensive literature search in Google Scholar and Pub Med databases that were published between December 7, 1999 and January 9, 2018 in accordance with the Preferred Reporting Items for Systematic Reviews and meta-Analysis (PRISMA) guidelines. Searches were referenced using medical subject headings (MeSH) that included "opioids", "over-prescription", "opioid consumption", or "opioid epidemic". The final review of all data bases was conducted on July 24, 2018.

Results: A total of 7160 articles were originally identified. After 3340 duplicate articles were removed, 3820 manuscripts were removed after title and abstract screening. Following this, 120 manuscripts underwent eligibility selection with only 70 publications being selected as reliable full-texts addressing related factors surrounding the opioid crisis.

Conclusion: With approximately 100 million people suffering from both chronic and acute pain in the United States (US) in 2016, opiates will continue to remain a prominent class of medication in healthcare facilities and homes across the US. Over 66% of total overdose episodes in 2016 were opioid-related, a figure that attests to the severity and wide-spread nature of this issue. A three-point approach accentuating the prevention, treatment, and rehabilitation of both those currently affected and at-risk in the future may be the comprehensive solution.

Abbreviations: CDC = Center for Disease Control and Prevention, DEA = Drug Enforcement Administration, HOD = heroin overdose, NIH = National Institute of Health, OATs = opioid agonist treatments, OUD = opioid use disorder, PDMPs = prescription drug monitoring programs, POD = prescription opioid overdose, SOs = synthetic opioids.

Keywords: opioid consumption, opioid epidemic, opioids, over-prescription

1. Introduction

The administration of opioids has been used for centuries as a viable option for pain management.[1] Literature reported in 2016 that approximately 100 million people suffer from pain in the United States (US), 9 to 12 million of them reported chronic pain while the rest reported short-term pain from injuries, diseases, and/or medical procedures.[2] When administered at appropriate doses, opioids prove effective at not only eliminating pain but further preventing its recurrence in long-term recovery scenarios.[3] Physicians have complied with the appropriate management of acute and chronic pain; however, this short or long-term opioid exposure provides opportunities for long-term opioid misuse and abuse, leading to addiction of patients who receive an opioid prescription and/or diversion of this pain medication to other people without prescription.[2,4,5] In the last 25 years, opioid misuse, over-prescription, and unauthorized distribution have run rampant in the US, resulting in growing

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evidences of opioid prescription abuse and dependence disorders, non-medical use of pharmaceutical opioids and accidental overdose death rates at levels unseen before in the US.[4,6,7] Around 6% of the US population (15–64 years old) reported some type of opioid abuse, and an estimated deaths of 115 US citizens per day due to opioid overdose have been reported in 2015.[7] Devastating implications for the medical infrastructure and healthcare system will arise if this problem is not resolved in the coming decade.[2] The current literature related with pain and opioid misuse confirms controversial incidence, associated factors, and potential approaches to control this problem. Several reviews attempted to summarize the epidemiology and management of opioid misuse, this integrative review seeks to summarize the current literature related with responsible parties of this opioid abuse crisis and discuss potential associations between demographics (ethnicity, culture, gender, religion) and opioid accessibility, abuse, and overdose.

2. Methods

We performed an extensive literature search in Google Scholar and Pub Med databases that were published between December 7, 1999 and January 9, 2018 in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[8] Searches were referenced using medical subject headings (MeSH) that included "opioids", "over-prescription", "opioid consumption", or "opioid epidemic". Two authors screened independently the search results for eligibility and reviewed the selected articles if they were: related with crisis of prescription opioid of other illicit opioid misuse, focused on the US population and published in the English language. The manuscripts were excluded if they were: abstract publications, reviews of non-primary research, specific to specific pain (e.g., palliative pain), case reports, series of case reports, focused on the evaluation of a specific opioid brand and non-English language. The final review of all data bases was conducted on July 24, 2018.

3. Results

A total of 7160 articles were originally identified from our data base search. After 3340 duplicate articles were removed, 3820 manuscripts were removed after title and abstract screening. Following this, 120 manuscripts underwent eligibility selection with only 70 publications being selected as reliable full-texts addressing a variety of influencing factors surrounding the opioid crisis (Fig. 1). Among these 70 publications, we found 12 articles with data from a significant amount of patients and an abbreviated compilation of demographic profile and outcomes/implications from these sources can be found in Table 1.

4. Discussion

Our review identified several associated factors that are directly or indirectly related to the current opioid abuse crisis in the US. The identification of these factors could enhance our knowledge and understanding of the trends of this crisis and potential solutions that are crucial to the design of new policies and healthcare reform plans to properly reduce and/or eventually solve this problem.

4.1. Demographics and US regional distribution

Opioids were responsible for 66.4% of total overdoses in the year 2016.[9] From a demographic perspective, although this increase

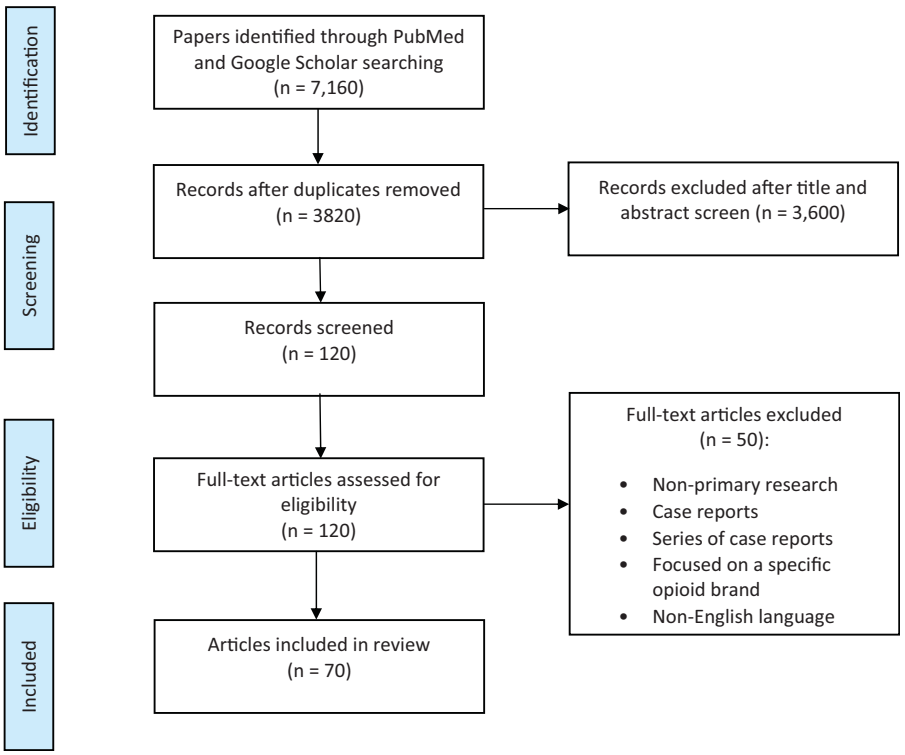

Figure 1. PRISMA flow chart diagram of manuscripts selection. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Table 1

Characteristics and overview of scientific manuscripts reviewing opioid consumption crisis.

Author	Publication Year	# of Patients	Population	Outcomes/Implications
Vivolo-Kantor A.M. et al	2018	142,557	Patients visiting emergency department	Emergency department visits related to opioid overdose increased in United States 29.7% from July 2016 - September 2017. This increased rate includes all demographic groups (males 30%, females 24% and across all age groups), higher occurrence in cities with population greater than 1 million.
Hill M.V. et al	2017	642	Patients undergoing 5 selected outpatient procedures	Wide variation of opioid medication prescribed in patient undergoing the same type of procedures. Over prescription (72% pills unused). Refills were requested in less than 2% of patients.
Cicero T.J. et al	2017	301	Patients entering opioid rehabilitation clinics	Patients with opioid use disorder for Immediate-release and extended-release formula. Immediate-release preferred (66.1%) rather than extended-release (4%), regardless of route and dependent of the quality of drug (high).
Iyiewuare P.O. et al	2017	733	Community health clinics substance misuse patients	87% of patients with known opioid or alcohol use disorder screened positive for alcohol or opioid misuse, only 7% of these patients were under treatment for substance use disorder 27% of patients that screened positive had a historical diagnosis of bipolar disorder or schizophrenia.
Han B. et al	2015	472,200	Adults 18–64 years old National Survey on Drug Use and Health	During 2003–2013 the use of nonmedical opioid prescription reduced with only 0.5% (4.9% from initial 5.4%). Yearly prevalence of prescription opioid disorder increased with 0.3% in 2013. Overdose death rates from opioid prescription in 2013 increased from 4.5 to 7.8 per 100,000 patient population. Prevalence of prescription opioid use disorders increased with 5.9% from 2003 to 2013 (11.9% to 17.8%).
Liu Y. et al	2013	3,391,599	Adults 18–64 years old with various opioid prescriptions	Patients received 3.3 opioid prescriptions with a mean annual day of supply of 47 days. 25% of enrollees had at least one sign of potential misuse and 5% at least two or more signs. Only 78.5% received less than a 30-day supply of opioids and 12% received more than 90 days' supply. Medical diagnoses/opioid prescriptions were matched for 82.3% of patients. Females (59%) of study population were more likely than males to have a misuse indicator.
Rodgers J. et al	2012	250	Adult patients undergoing upper extremity surgery	Total number of opioid medication prescribed was 30 pills per patient. An average of 10 pills per participant was used and 19 pills were reported as unused. A 79% reduction of opioid prescription was recommended.
McCabe S.E. et al.	2012	7374	Public and private high school seniors	17.6% high school seniors received an opioid prescription in their lifetime, and 12.9% reported its use for nonmedical circumstances. 80% of the nonmedical users obtained prescription opioids from previous prescriptions. Gender differences were not significant, but there were substantial racial/ethnic differences.
Puffer E.S. et al	2012	45	Adults 18–57 years old receiving opioid detoxification	Higher positive religious coping related to lower pre-admission opioid use ($P<.001$) and increased 12-step programs participation ($P<.05$). The reduction in negative religious coping after discharge is correlated with less opioid use and increased 12-step programs participation.
Birnbaum H.G. et al	2011	15,128	Medicaid and privately insured adult beneficiaries	Abuse of prescription opioids is an increasing financial burden ($55.7 billion in 2007) for: workplace ($25.6 billion), health care ($25.6 billion) and justice system ($5.1 billion)
Kelly J.P. et al.,	2008	19,150	Adults	Opioid use increased with age and decreased with education level. Polypharmacy is reported in 21% of opioid users and 4.5% in non-opioid users. 5% of the United States' adult population took an opioid in their lifetime and 4.3 million (2%) of adults in the United States took an opioid on a weekly bases (2006).
Boyd C.J. et al	2006	1086	Adolescents (7th–12th grade students)	14% prevalence of nonmedical prescription medication use and 12% were prescription opioids. Reasons for non-prescribed use: 3% sleeping problems, 2% as sedatives/ anxiety and 2% as stimulants.

Legend: % = percentage, $P = P$ value.

affected all ethnic groups, non-Hispanic whites experienced the most devastating increase with adults ages 45 to 54 suffering the highest rates of mortality according to the National Center for Health Statistics.[10] There is a significant number of bipolar and schizophrenic patients abusing opioids when compared with the general clinical population ($P < .001$).[11] The study reported that a higher proportion of men than women are testing positive for substance use disorder (SUD), including opioid use disorder (OUD) (77% vs 44%).[11]

Due to the high relapse rates among opioid-dependent patients, strategies such as positive religious coping, reducing opioid consumption, and increasing participation in related programs may be utilized for recovery treatment.[12] Negative religious coping is also associated with lower relapse rates.[12,13] Taking into account the vast amount of cultural diversity in the US, religion, and spirituality remain sensible subjects for physicians to discuss when addressing opioid addiction.[12,13] Opioid-related overdose is a leading cause of unintentional injury and thus adds significant financial and resource burden to hospital systems. From 2001 to 2012, more than 660,000 hospitalizations in the US were attributed to opioid overdose, which accrued more than $700 million healthcare dollars annually.[14]

By region, prescription opioid overdose-related (POD) hospitalizations were highest in the South region while heroin overdose (HOD)-related hospitalizations were highest in the Northeast and Midwest regions.[15] By community, hospitalizations due to HOD were higher in urban areas compared to rural areas (5.5 per 100,000 vs 2.1 per 100,000 in 2014).[16] In contrast, POD hospitalization rates were 30% higher in rural compared to urban populations.[16]

The state of Ohio has been known as an opioid battleground for many years, boasting the fifth highest rate of overdose in the US (2017).[17] An Opiate Action Team was founded in 2011 to reduce the amount of drugs being prescribed, educate the population and increase availability of naloxone.[18] The region saw a decrease in the amount of opioid-related overdoses during the period of 2011 to 2015 from 45% to 22%.[17]

4.2. Opioid epidemic

The Center of Disease Control and Prevention (CDC) defines an epidemic as, "the occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular period of time,".[19] While the abuse of prescription pills is not a disease, addiction is.[20] The hotbed of occurrences originates in the US, which has the highest rate of abuse in the world.[21] This specific outbreak is the worst drug abuse cycle the US has ever seen and is listed by the CDC as a top 5 public health challenge.[21] Since 2000, the incidence of death from drug overdose has tremendously increased (137%, including 200% of deaths related to opioids).[22] The CDC reported a total of 63,632 opioid overdose deaths in 2017 in the U.S., with an increment of 45.2% for synthetic opioid-involved overdose from 2016 to 2017; hence this epidemic continues to illustrate its severity and considerable threat to the health of American citizens.[22–24] However, a strong effort has been made to subdue the problem. Opioid prescriptions were reduced by 13.1% from 2012 to 2015 as a result of physician awareness and implementation of new policies.[25] One particular study displayed a 30% reduction in opioid prescriptions for pain management as a result.[26]

4.3. Shifting patterns from prescription opioids and heroin abuse

The high rate of opioid prescription in the US (around 50,000 prescriptions/million inhabitants, places us first in the world, in comparison to other high-income countries; With Canada being the second opioid prescriber with a much lesser value (around 30,000 prescriptions/million inhabitants) from 2012 to 2014.[27,28] Coupling this with the leniency that exists regarding the regulation of the actions of pharmaceutical companies, the problem quickly grew out of control.[29] Developed tolerance to these easily accessible and addictive drugs results in users seeking a more cost-effective drug in order to achieve similar results.[30]

The most prescribed opioids in the US include hydrocodone (a constituent in Vicodin, Lortab, Zohydro, and other commercial-name drugs), oxycodone (a constituent in Oxycontin and Percocet), and morphine.[31] The easy access to prescription opioids by the general public has shifted the trends of addiction by introducing consumers to other forms of opioid drugs such as heroin and other illegal opioid formulations, aggravating the problem by creating an interaction between the 2.[28]

4.3.1. Oxycodone. The shift to opioids being considered a national health concern started with the promotion of drugs like oxycodone by Purdue Pharma, with a bonus system applied to the sales of the drug in an attempt to influence prescription rates.[32] A marketing database with information about prescribing trends of physicians across the US was subsequently created.[32] Promotional campaigns of oxycodone portrayed the risk of addiction as an insignificant concern as sales increased exponentially during that time period.[32]

4.3.2. Synthetic opioids. Synthetic opioids (SOs) are a class of drugs commonly used for pain management due to their ability to mimic the pharmacologic pathway of true opioids such as morphine and codeine (Figure A).[33] These SOs have flooded the market in the past decade from both pharmaceutical companies and illegal sources, representing a major contribution to the opioid crisis.[34] Karila et al referred to synthetic pharmaceutical and non-pharmaceutical fentanyl that arrive illegally from main exporting countries such as China and Mexico and can be readily available on the internet at low prices and high purity.[35] There is limited data on the pharmacological properties of many SOs, which only require small doses to produce an effect, leading to a high-risk for overdose or harmful physiological and psychiatric complications.[36] SOs accounted for 19,000 deaths in the US in 2016, more than any other class of opioid drug.[34] Additionally, SOs accounted for 31% of all deaths due to drug poisoning in 2016 according to the Drug Enforcement Administration (DEA), underlying the increase in their availability and popularity on the street.[36] The DEA reports a dramatic rise in the tablet form of SOs seized, suggesting the inclusion of prescription opioid users in the market for fentanyl.[36]

4.3.3. Heroin gateway. Heroin has gained significant consideration in media outlets in the past decade as its recreational use has become an issue of national attention. A 2014 study found that for users of both opioids and heroin, the average start date of opioid usage was 2005 compared to a start date of 2008 for heroin, suggesting that the abuse of opioid medication may lead to future use of heroin.[37] A review initiated by Cicero et al demonstrated a significant shift from the 1960s to the early 2000s in regards to the method of opioid introduction.[38] Heroin was often the initial opioid abused by individuals in the 1960s with

opioids often serving as a gateway at the turn of the century.[38] Inflow of heroin into the US now predominantly arises from the Mexican and Colombian markets, affecting different geographical areas with a downward trend in their pricing on the street.[39] The complicated nature of the heroin problem in the US involves market structure and distribution.[40] A study conducted by Mars et al in 2015 analyzed these parameters in Philadelphia and San Francisco. Philadelphia's open drug markets and the existing competition drives the price of the product down.[40] This leads to purity-based competition, causing a higher risk of overdose in affected communities.[40]

4.4. Over-prescription

Health care providers' over-prescription is one of the leading factors of addiction.[41] Commonly prescribed drugs such as hydrocodone and oxycodone have risen from 76 million prescriptions in 1991 to roughly 207 million in 2013.[42] According to data from the CDC, the total number of opioid prescriptions has decreased since 2012, with a low of almost 215 million total annual prescriptions in 2016.[43] A study conducted by Liu et al found that out of 3,391,599 patients who were prescribed opioids by medical providers, almost 25% displayed characteristics of personal misuse (recreational use).[44] The study concluded that the average patient was administered three different prescriptions lasting an average of 47 days with opioid and benzodiazepine overlapping.[44]

This tendency of abuse is not only affecting adults; adolescents and children are affected as well and contribute heavily to the problem.[45] Easy access to prescription opioids in American households has led to more frequent opioid overdose among children.[46] The largest increase in hospitalization rates for opioid overdose between 1997 and 2012 was reported for children aged 1 to 4 on a retrospective analysis obtained from pediatric hospital discharge records across the US.[47] A study population of 7374 high school seniors found that 12.9% had used opioids recreationally and that 80% of these nonmedical uses originated from previous prescriptions.[48]

4.5. "Doctor shopping"

Another common method of procuring opioids is "doctor shopping" which occurs when multiple providers are visited in order to gain a surplus of medication.[49] New prescription drug monitoring programs (PDMPs) have been developed as a response to this issue in an attempt to eradicate this form of exploitation.[50] Most states have only started implementing PDMPs within the last 10 years, increasing from 16 to 49 states from 2001 to 2012.[51] These programs provide physicians with an electronic database that entails the prescription history of each patient that can be checked before and after a new prescription is written.[51] A study accessing data from the National Survey of Drug Use and Health (NSDUH) proved the usefulness of creating and using databases when addressing "doctor shopping" for opioid prescriptions in 36 states.[51] Additionally, extended-release opioids have proven to be a useful alternative compared to traditional release opioids due to their less addictive nature and lower rates of abuse.[52] A survey conducted by Cicero et al demonstrated a greater preference for instant release (95%) than extended release due to the immediate effect of the drug.[53]

4.6. Distribution

The manner of opioid distribution in the US is perhaps the root of the large-scale problem the US now faces.[54] Between 26 and 36 million individuals abuse opioids worldwide with overdose deaths in the US quadrupling since 1999.[54] The degree of economic strain the litany of abuses places on affected communities is impressive and trending in the wrong direction. Just ten years ago, the total cost of opioid-related abuses on communities was estimated to be 55.7 billion dollars.[55] Ten years later, the problem has slipped even further out of control.

Opioids are "powerful pain-reducing medications" used to treat postoperative pain following surgery.[56] A prospective study published by Rodgers et al (2012) raised awareness concerning the excessive number of opioid pills ("leftover medication") prescribed for patients undergoing hand and wrist surgeries.[57] A more recent study assessed the opioid prescription for partial mastectomy and laparoscopic inguinal hernias with 90.5% of the patients being prescribed opioids.[58] The authors commented on the large excess of pills prescribed and the lack of disposal for opioid surplus, with only 5% returning their medications to a collection site approved by the Federal Drug Agency.[58]

4.7. Healthcare and insurance responsibility

It is estimated that the total cost placed on the US healthcare infrastructure involving opioids is $72.5 billion annually.[59] Coverage for at-risk individuals often supports the prescription of opioids rather than other time-consuming pain relief alternatives.[60,61] These alternatives, such as interdisciplinary treatment programs, have proven to be clinically efficacious.[60,61] Unfortunately, these programs have decreased in number beginning in the early 2000s due to sparse coverage on insurance plans.[60,61] Several studies support the cost-efficiency of such programs despite the aggressive coverage drops exhibited by most insurance companies.[60,61] However, they have largely replaced these alternative programs to cover the use of opioids with a high potential for abuse.[60,61] The immediate impact of this trend was quickly observed when methadone was found responsible for one-third of opioid fatalities, despite representing only 5% of opioids prescribed, from 1999 to 2010.[60] The American Medical Association, the American Society of Anesthesiologists and the American College of Physicians have supported the use of non-opioid pharmacologic therapy as a preferable alternative.[62]

There is a correlation between cost management, profitability and the coverage provided to Americans by health care providers that do not respect the personal health of consumers.[63]

Additionally, financially incentivized coverage decisions made by health care providers 20 years ago play a role in the opioid crisis seen today in the US.[63]

4.8. Legal implications

Efforts to reform opioid-overdose legislation in certain states, including Good Samaritan laws and increased naloxone access, have been associated with reduced mortality rates.[64] However, suppressive policies towards supply and consumption of opioids continue to be the norm, aggravating the problem of illegal sale on the black market.[65] Criminalization of opioids creates a strong stigma towards certain societal groups including pregnant women, as legal consequences of opioid abuse when pregnant

deters women from seeking treatment and damages patient-physician relationships.[66] The devastating social impact of opioids directly affects impoverished families, as opioid-related deaths are correlated with poverty, even though prescription rates are lower for poorer communities.[67]

Many users choose to obtain narcotics via drug dealers; either in person or online.[68] Online drug dealings open the door to increased risk of overdose and death due to contamination with alternate substances or a higher potency than advertised.[68] A 2012 study surveying 50 drug dealers found that the major drugs being dealt were indeed opioids, specifically oxycodone and hydrocodone.[69] Just over half of respondents disclosed access to clinics that loosely prescribed the opioids.[69] As previously discussed, the monthly "doctor shopping" technique was used at 4 to 5 clinics on average in order to refill the dealer's various prescriptions.[69] Of those surveyed, 44% described purchasing medication in their community from patients with existing prescriptions as their preferred method of access.[69] While recreational use stemming from leftover prescriptions remains the most common method, McCabe et al reported a 38% response rate concerning the purchase of opioids from a friend or relative.[70] Obtaining these drugs from a drug dealer only accounted for 19.4% of surveyed sales.[70]

Legislation exists in the US that outlaws the unauthorized sale of narcotics online, however, these sales find ways to occur.[71] Sellers are able to do business using online markets and are adept at shipping and delivering the drugs anonymously to buyers.[72] The "dark web" is a common term for the immense section of the internet that is accessed by browsers specialized in anonymity.[73] As a result, competent drug dealers who understand how to use this section of the internet have access to high-quality drugs that can be purchased for resale.[73]

4.9. Media influence

Media portrayal of the opioid crisis has influence on the perception of the issue by American citizens.[74] While media outlets have historically correlated drug use to disadvantaged minorities, this has not proved to be the case.[74] Examples of opioid misuse have involved white, middle class, rural Americans.[75] However, tendencies to target minority doctors when running segments on prescription negligence have been observed.[74] Spikes in opioid media coverage arise in response to celebrity deaths, major federal trials, and pharmacological headlines.

Media outlets were the first to run stories about prescription misuse before many government-run programs were able to detect the scale of the problem.[75] A 2015 study addressed news headlines from 1990 to 2010 with data suggesting that media outlets had attempted to portray the issue as an isolated criminal justice problem instead of a widespread public health concern.[76] Headlines commonly focused on drug dealing, arrests, and prosecution.[76] Treatment and recovery options accounted for less than 5% of all media headlines.[76]

4.10. Rehabilitation

Lack of solutions for the increasing overdose deaths has led to alternate forms of therapy. A multimodal approach to treatment selects patients according to their risk level.[18] In order to manage chronic pain, therapy focuses on multimodal pharmacologic treatment coupled with behavioral approaches devised for long-term management with periodic monitoring of patients.[18]

Opioid agonist treatments (OATs) are preferred due to evidence of effectiveness over abstinence-based approaches when considering patient safety and treatment retention.[77] The appropriate treatment should be chosen with careful consideration of method of ingestion, variety of opioids, age, health status, psycho-social factors, and personal preferences. Methadone tends to show higher treatment retention rates and is advised for specific groups such as youth and pregnant women, whereas buprenorphine-naloxone has a lower risk of overdose for patients with ongoing treatment for a psychiatric disorder or low tolerance for opioids.[77] A study conducted in 2015 by Clark et al found that expenditure was considerably higher for behavioral treatments than OATs, which also showed 50% lower relapse risk.[78] Additionally, the study assessed risk factors for relapse, including comorbidities, showing an 80% greater risk for patients that were diagnosed with schizophrenia and bipolar disorder in manic phase.[78]

4.11. Clinician education

The most important counter to the opioid crisis is arguably the education of healthcare providers, consumers, and at-risk individuals. Due to inadequate results stemming from guidelines and programs, the resulting large scale problem has driven governments to call for change.[79] The risk evaluation and mitigation strategy (REMS) was implemented in 2012 and mandated that opioid manufacturers be required to fund prescription education programs as well as healthcare providers providing prescription data to state monitors.[79] A recent article published by Wiese et al discusses the development of "upstream" educational programs for a better understanding of the factors involved in opioid over-prescription, and a more sustainable approach to prescription that instructs future physicians at all levels of their education.[79] A clear distinction is made between "upstream" and "downstream" treatments in the form of federal regulations which are ineffective in terms of long-term behavior change and can contribute to physician burnout and moral distress.[79]

4.12. Barriers to opioid crisis control

Despite the damage inflicted by the current opioid epidemic, there is still a lack of research and public investment on areas such as opioid pain management or understanding the nature of opioid use disorder in the US.[80] Several problems have been identified as key limiting factors in basic pain research, such as selection of adequate pain models, that restrict the reproducibility of the results and ultimately waste research funding.[80] The extensive use of opioids and the epidemiology of the problem in the US has been adequately studied, but more information on the development of acute and chronic pain and how this leads to preferential opioid use is necessary to increase our understanding of opioid-related morbidity and mortality. The increase in budget funds received by the National Institute of Health (NIH) in 2018 targeted towards opioid research should support the implementation of strategies to address the abuse and enhance treatment procedures for chronic pain, a condition that received less than 2% of the NIH's annual budget before 2018 despite being so prevalent in the US population.[81,82]

5. Conclusion

While the appropriate use of opioids is an essential aspect of modern analgesia, there is no denying that the misuse and abuse of these drugs have allowed this problem to spiral out of control.[3] With approximately 100 million people suffering from both chronic and acute pain in the US in 2016, opiates will continue to remain a prominent class of medication in healthcare facilities and homes across the US.[2] Over 66% of total overdose episodes in 2016 were opioid-related, a figure that attests to the severity and wide-spread nature of this issue.[9] The unfortunate reality is that no finger can be pointed at one singular culprit, as each of the parties mentioned in this review has their share of influence and culpability by which this complex problem has evolved. The distinct associations between demographical categories (ethnicity, culture, gender, religion) and accessibility, abuse, and overdose are simply pieces of the puzzle that comprise this complex epidemic. A 3-point approach accentuating the prevention, treatment, and rehabilitation of both those currently affected and at-risk in the future may be the comprehensive solution. Further investigation of the nature of OUDs, demographical factors, rehabilitation programs and new strategies dedicated to managing an opioid crisis is required in order to effectively respond to a similar challenge in the future.[80]

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NS, AU, TW, and SB participated in design, methodology and manuscript edit. AC and LP participated in literature search, data collection, and manuscript editing.

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