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ASSESSING THE EPIDEMIC: A REVIEW OF RELEVANT RESEARCH ON THE USE AND MISUSE OF OPIOIDS

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INTRODUCTION

Research on prescription drugs and heroin has shown a surge in misuse in recent years. **This research review highlights seven articles underlining the causes and implications of this opioid epidemic.** The first five articles in this review examined a variety of defining aspects of the epidemic. In their article, Han, Compton, Blanco, Crane, Lee & Jones (2017) reported on a 2015 national survey of drug use among U.S. adults and review the prevalence, motivations, and sources of prescription opioid misuse and offer practical solutions for practitioners.

In turn, Garland, Froeliger, Zeidan, Partin & Howard (2013) described the neuropharmacologic properties of prescription opioids and their interaction with cognitive, affective, and physiological factors involved in chronic pain and addictive behavior to better understand the biobehavioral risk chain leading from pain and opioid analgesia to opioid misuse and addiction. Drazdowski (2016) conducted a systematic research review that looked at studies highlighting young adults' (18-25) motivations to engage in NMUPD and argues for a better understanding of these motivations to lead to more targeted prevention and interventions.

Meanwhile, Arria & Compton (2017) further exposed the complexities implied in comprehending the prescription drugs public health issue through scientific evidence and propose a set of potential interventions to address risk factors associated with the nonmedical use of prescription drugs. Next, a review of the relationship between nonmedical prescription-opioid use and heroin use by Compton, Jones & Baldwin (2016) explored the complex and reciprocal relationship between nonmedical prescription opioid use and heroin use through a look at empirical studies. Lastly, the final two articles in this review focus specifically on prescription drug monitoring programs (PDMPs).

The observational longitudinal study by Pauly, Slavova, Delcher, Freeman & Talbert (2018) looked at the link between specific administrative features of prescription drug monitoring programs (PDMPs) and the risks of prescription opioid-related poisoning, while Ali, Dowd, Classen, Mutter & Novak (2017) investigated the association of PDMPs and their specific characteristics with the reduction of prescription opioid misuse through state-level data on PDMPs. Each article proposed practitioner-oriented recommendations for implementation and intervention.

PART 1: AN INTRODUCTION TO OPIOID USE

ARTICLE 1: A NATIONAL SURVEY OF DRUG USE IN U.S. ADULTS

SUMMARY

The 2015 National Survey on Drug Use and Health (NSDUH) was conducted through in-person interviews with a nationally representative sample of eligible U.S. adults (N= 51,200) by the Substance Abuse and Mental Health Services Administration (SAMHSA). In this study, the authors looked at the 12-month prevalence of prescription opioid use and misuse among prescription opioid users, along with their sources and motivations for misuse, based on a variety of characteristics (e.g., socio-demographics, health conditions, behavioral health status).

Reports from the survey showed that in 2015, 91.8 million (38%) U.S. individuals used prescription opioids, and that 11.5 million (5%) misused them, while 1.9 million (1%) had a use disorder. Relief of physical pain was the most commonly reported motivation for misuse (64%). The population that reported misuse when using opioids (13%) tended to be either uninsured, unemployed, low-income, or with behavioral health issues. In addition, 60% of adults with opioids misuse were using them without prescriptions, while another 41% reported for their most recent episode of misuse having obtained prescription opioids from friends or relatives.

While the authors recognized limitations to their work, such as the exclusion of the homeless population, active-duty military, or institutionalized individuals, their findings yielded important implications for practitioners, including:

- The need to **improve access to evidence-based pain management** and to **decrease excessive prescribing** that may leave unused opioids available for potential misuse,
- **The importance of interventions** targeting medication sharing, selling, and diversion from opioid misuse,
- The need to **follow prescription guidelines** to minimize excessive amounts of leftover medications and thus the availability of opioids for consumption,
- The understanding that the promotion of **alternative pain treatments can have limited efficacy** in reducing prescription opioid misuse and could instead lead individuals to look for prescription opioids outside the traditional health system,
- The **prioritization of prevention, monitoring and screening** for opioid use disorders when opioids are prescribed to individuals with psycho-pathological conditions (e.g., other substance use disorders).

REFERENCE

Han, B., Compton, W. M., Blanco, C., Crane, E., Lee, J., & Jones, C. M. (2017). Prescription opioid use, misuse, and use disorders in US adults: 2015 National Survey on Drug Use and Health. *Annals of Internal Medicine*, 167(5), 293-301.

SUMMARY

With the emerging public health concern of prescription opioid misuse and addiction among chronic pain patients, the authors called for a need for additional studies looking at the risk factors for progression to opioid misuse and opioid use disorders among chronic pain patient as well as frameworks to better understand the biobehavioral risk chain leading from pain and opioid analgesia to opioid misuse and addiction.

As such, their article described the neuropharmacologic properties of prescription opioids and their interaction with cognitive, affective, and physiological factors involved in chronic pain and addictive behavior. They did so by reviewing how the neurobiology of opioid agents and pain processing function in the human nervous system and presenting a conceptual model of the interaction between chronic pain, affective dysregulation, and opioid use in the formation of opioid addiction.

The review looked at 1.) the neuropharmacological effects of acute opioid administration on central nervous system functions, 2.) the pain and the nociceptive and affective dimensions of opioid-induced analgesia, 3.) the neurobiological transitions from opioid use to dependence and addiction, and 3.) the link between pain, negative emotion, and opioid addiction. **Based on their review, the authors' conceptual model underlined that the issue of co-occurring chronic pain and opioid addiction relies on a cyclical escalation of behaviors** where nociception and stress prompt hypervigilance and catastrophizing, which magnifies pain and provokes recurrent self-medication with opioids. This, in turn, creates an attention bias towards opioid-related cues that trigger drug use habits in spite of ever diminishing analgesia. As a result, the combination of uncontrolled use of opioids with chronic pain dysregulates the reward processing system in the brain, which then deprives individuals from experiencing pleasure in their overall environment.

Individuals thus find themselves trapped in a compulsive drive for relief, coupled with a loss of control over opioid use and increased reliance on opioids to manage a sense of well-being. Finally, the authors discussed the clinical implications of their model in the psychological treatment and prevention of opioid misuse in chronic pain patients. They recommended that multimodal interventions targeting the complex risk chain of chronic pain and prescription opioid addiction would be beneficial in interrupting this downward spiral. **Among these multimodal interventions, the authors particularly recommended mindfulness training, cognitive-behavioral therapy (CBT), positive psychology, and a combination of these approaches as efficient interventions.**

REFERENCE

Garland, E. L., Froeliger, B., Zeidan, F., Partin, K., & Howard, M. O. (2013). The downward spiral of chronic pain, prescription opioid misuse, and addiction: cognitive, affective, and neuro-psychopharmacologic pathways. *Neuroscience & Biobehavioral Reviews*, 37(10), 2597-2607.

PART 2: NON-MEDICAL USE OF PRESCRIPTION DRUGS (NMUPD)

ARTICLE 3: PUBLIC HEALTH ISSUES RELATED TO THE NONMEDICAL USE OF PRESCRIPTION DRUGS (NMUPD)

SUMMARY

In their brief overview of research in the nonmedical use of prescription drugs (NMUPD) over the past two decades, the authors called attention to the need for scientific evidence to address the increase in overdose from prescription opioids and heroin use among nonmedical users of prescription opioids. As such, they exposed the complexities implied in better understanding this prescription drugs public health issue, which range from the use of opioid analgesics to benzodiazepines, stimulants, anxiolytics, and sedatives.

The authors first focused on two popular misconceptions regarding NMUPD:

- The first one is the idea that prescription drug problems happen to individuals who are first exposed to pain medication through a physician's prescription.
- The second is the notion that the nonmedical use of prescription stimulants give individual academic advantages.

There is however no scientific evidence for both these popular beliefs.

Instead, in the first case, the authors suggested that practitioners should carefully screen and monitor patients for prior drug history when prescribing pain medication. In the second case, the authors recommended to identify students with deficits in executive functioning and to provide appropriate assessment and intervention to reduce risks for substance abuse. **More importantly, the authors highlighted the interaction between NMUPD, excessive drinking, marijuana, and other substance usage** (i.e., nonmedical users are observed to have a history of alcohol, marijuana, tobacco, or other psychoactive substance use).

Finally, the authors referred to innovative targets for prevention of NMUPD as important implications of current research in the field. They mentioned the possible link between normative perceptions of prescription stimulants and prevention or diversion among college students; and the protective effect of orientations to decrease the risk to initiate substance use among high school students. They also referred to research showing that anxiety sensitivity in women (but not in men) was strongly linked to the nonmedical use of benzodiazepines--providing promising ground for potential interventions. In conclusion, **the authors' call for action asked for a better understanding of the risk factors, clinical characteristics of individuals, and consequences of their treatment for dependence through high-quality scientific research.**

REFERENCE

Arria, A. M., & Compton, W. M. (2017). Complexities in understanding and addressing the serious public health issues related to the nonmedical use of prescription drugs. *Addictive Behaviors, 65*, 215-217.

ARTICLE 4: MOTIVATIONS FOR THE NON-MEDICAL USE OF PRESCRIPTION DRUGS IN YOUNG ADULTS

SUMMARY

Young adults are at greater risk for use, abuse, and negative outcome of nonmedical use of prescription drugs (NMUPD)—the most commonly reported form of illicit substance use for that age group, after marijuana. **Research shows that motivations for substance use predict use patterns and ensuing issues in young adults, and that different motivations lead to different patterns of use.** As a result, better understanding motivations for use can lead to more targeted prevention and intervention.

In this systematic review, the author looked at studies highlighting young adults' (18-25) motivations to engage in NMUPD, finding 37 studies (out of 355 potential articles) that resulted from a database search of the literature provided primary research data on non-medical use of prescription stimulant in U.S. student populations.

Articles in the review showed that common reasons for non-medical stimulant use were

- **academic motivations** (i.e., cognitive enhancement to improve focus, study, work) and
- **for the purpose of prescribed effects**, although recreational purposes or weight loss were also mentioned as motives.

For instance, one emerging trend noticed by the author was that CNS depressants used for sleeping were more likely to be used as prescribed in comparison to sedatives or anxiety medication. These findings have implications for the design of prevention and intervention tools.

Unfortunately, definite conclusions about the motivations for the NMUPD were difficult to draw for the author due to the limited amount and inconsistency of the available research. For example, data regarding young adults not attending college was not found, and differences between countries were noted. **The author highlighted the need for standardization in NMUPD research, along with limitations that impeded the review, including variations in definitions of “non-medical use” and “motivation,” the lack of consistency across studies, the recorded time and frequency of NMUPD, as well as other methodological limitations** (e.g., self-reports, data collection) reduced the generalizability of results. The author concluded by underlining the need to increase this research that is, to date, limited in scope, and to combine work on motivation with prevention and intervention for effectiveness.

REFERENCE

Drazdowski, T. K. (2016). A systematic review of the motivations for the non-medical use of prescription drugs in young adults. *Drug & Alcohol Dependence*, 162, 3-25.

ARTICLE 5: NONMEDICAL PRESCRIPTION-OPIOID USE AND HEROIN USE

SUMMARY

Between 2011 and 2014, deaths caused by prescription opioid overdose quadrupled—a trend that called for prevention responses at the federal and state level aiming to reduce the rate of nonmedical use and overdose through policies and programs addressing inappropriate prescribing. **While successful efforts to reduce nonmedical prescription opioid use including education for the public and health practitioners, drug monitoring programs, enforcement and regulatory actions, and the development of abuse-deterrent technologies, data showed an increase in heroin use and heroin overdoses.** Research suggested a possible link between said policies and prevention practices and the increase in heroin use and death rates.

As a result, the authors of this article explored **the complex and reciprocal relationship between nonmedical prescription opioid use and heroin use** through a look at empirical studies addressing this phenomenon among individuals with frequent nonmedical use, abuse or dependence, as well as the pharmacologic basis for heroin use, the patterns of heroin use among users of nonmedical prescription opioids, the current trends in heroin use, and the effects of policies intended to lower inappropriate prescriptions of opioids on heroin use. In pharmacological terms, heroin is similar to prescription opioids, resulting in a comparable mechanism to induce euphoria.

Salient trends are reported by the authors from the reviewed studies:

- Heroin users have reported **increasing abuse or dependence on other substances**, with an increasing rate among 18-25 year olds, urban areas, both sexes (but more among women than men), all races and ethnic groups (but more among non-Hispanic whites),
- A key factor in recent increases in heroin use and overdose may be attributed to **its low cost, availability, and purity**,
- **The shift toward heroin use among nonmedical users of prescription opioids occurred *before* the recent policy focus on prescription-opioid abuse.**

Through this review, the authors concluded that while none of the studies could disprove a possible link between policies aiming at decreasing the availability of inappropriately prescribed opioids and heroin use, **a consistent finding among them was that the transition to heroin use happened before these**

policies were in place, which did not appear to have a direct influence on the overall increase in heroin use rates. Through this review, the authors hoped that a better understanding of these relationships could impact clinical practice and interventions to avoid shifting one problem to another.

REFERENCE

Compton, W. M., Jones, C. M., & Baldwin, G. T. (2016). Relationship between nonmedical prescription-opioid use and heroin use. *New England Journal of Medicine*, 374(2), 154-163.

PART 3: REDUCING OPIOID USE WITH PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

ARTICLE 6: REDUCTION IN HEROIN USE FROM PRESCRIPTION DRUG MONITORING PROGRAMS

SUMMARY

To respond to the current opioid epidemic, U.S. states have implemented prescription drug monitoring programs (PDMPs). **PDMPs are state-based programs that track the prescribing and dispensing of controlled substances to consumers in order to reduce misuse.** In this observational longitudinal study, the authors looked at the link between specific administrative features of PDMPs and risks of prescription opioid-related poisoning (RxORP). For that purpose, they used a natural experiment design with a national population representing privately-insured adults, where they examined inpatient hospital admissions and emergency department visits related to RxORP between 2004 and 2014.

The study included data from multiple sources to examine five aspects of PDMPs (whether the PDMP was operational; if controlled substances (CS) schedules were monitored by the PDMP; the frequency of data reporting to the PDMP central server; the requirements for unsolicited reporting of patients CS prescription history; the mandated prescriber query of PDMP data before prescribing). With this data, the authors used generalized estimated equation Poisson regression models to estimate the risk of RxORP associated with PDMP features with adjustments for demographics and clinical covariates.

Results from the study showed that:

- The increase in relative risk of prescription opioid-related poisoning over time in states with operational PDMPs was **significantly lower than in states without PDMPs**;

- Adults who were privately insured and living in states with operational PDMPs were **simultaneously exposed** to higher risks of opioid-related poisoning and were **more protected** from RxORP risk during the opioid epidemic,
- **Specific PDMP features** (requiring unsolicited reporting to prescribers, law enforcement, or professional licensure boards; more frequent data reporting from dispensers; monitoring of CS schedules) **were linked to stronger protective effects** over time in comparison to states that did not have these features.

While the authors recognized some limitations to their work (e.g., the natural experiment design demonstrates associations but not inferences about causality; there is variability in PDMPs among states; there might be a differential impact of PDMPs between privately-insured population and the American public at large), they also suggested that their study could guide PDMP best practices and improve the efficiency of current and future PDMPs worldwide.

REFERENCE

Pauly, N. J., Slavova, S., Delcher, C., Freeman, P. R., & Talbert, J. (2018). Features of prescription drug monitoring programs associated with reduced rates of prescription opioid-related poisonings. *Drug and Alcohol Dependence* 184, 26-32

ARTICLE 7: NATIONAL SURVEY OF DRUG USE AND HEALTH AND PRESCRIPTION DRUG MONITORING PROGRAMS

SUMMARY

The authors of this article based their research on the 2004-2014 National Survey of Drug Use and Health (NSDUH) to investigate state-level variations in prescription drug monitoring programs (PDMP) implementation timing and characteristics, as well as patient-level outcomes to better understand if PDMPs were associated with lower prescription opioid misuse, along with their potential effect on heroin use increase. In the data, the authors looked specifically at the nonmedical use of prescription pain relievers (NMPR), heroin use, and sources of NMPR for misuse in terms of past year NMPR use, past year DSM-IV abuse or dependence of NMPR, past year NMPR initiation, and past-year days of NMPR use; with identical measures for past-year heroin use. Moreover, they looked at respondents' answers to the sources they used to obtain their drugs in the past month.

From their analysis, the authors found no effect of PDMP status on nonmedical prescription opioid use, abuse, dependence and initiation. They did, however, find that the number of days of opioid misuse reported by survey takers in the past year had lessened. In addition, they found no correlation between the implementation of PDMP and an increase in heroin use or initiation--although they were associated with an increase number of days reported for heroin use in the past year. **The**

findings also showed that PDMPs were linked to a decline in “doctor shopping” among individuals, yet with no increase in illegal sources as a way to obtain opioids. Despite a few limitations to their study (i.e., the NSDUH does not survey the same individuals every year; enrollment varies from state to state), **the authors’ conclusion was that PDMPs can help reduce the opioid crisis by providing physicians, pharmacists, and other healthcare practitioners with access to a patient’s prescription history and by identifying those in risk of opioid misuse.** They recommended additional initiatives—such as educational efforts—to continue reducing the current level of opiate misuse in the U.S., and the need for better healthcare system related policies for individuals to receive appropriate treatment.

REFERENCE

Ali, M. M., Dowd, W. N., Classen, T., Mutter, R., & Novak, S. P. (2017). Prescription drug monitoring programs, nonmedical use of prescription drugs, and heroin use: Evidence from the National Survey of Drug Use and Health. *Addictive Behaviors*, *69*, 65-77.

CONCLUSION

The relationship between prescription drug and opioid use is complex, and research has begun to explore the causes and implications of this epidemic. This review aimed to provide an overview of national trends in opioid and prescription drug use, misuse, and abuse, as well as reviewing empirical data on environmental strategies aimed at reducing the negative effects of this misuse, though we primarily focused on the use of prescription drug monitoring programs (PDMPs).

Overall, this review found that in 2015, almost 40% of those surveyed used prescription drugs, and that almost 5% misused them (Han et al, 2017). Garland et al (2013) explored the underlying biological impulses to use opioids, proposing that chronic pain and opioid use co-exist, resulting in an escalating cycle of dependence. Meanwhile, Arria and Compton (2017) explored the prevalence of misconceptions around opioid use, suggesting that two popular misconceptions are both wrong. Meanwhile, Drazdowski (2016) surveyed young adults and found that they use prescription drugs for both their intended purposes and perceived academic benefits. Compton, Jones, and Baldwin (2016) found that the shift toward heroin use among nonmedical users of prescription opioids occurred *before* the recent policy focus on prescription-opioid abuse. Pauly et al (2018) reported on the complexities of PDMPs, finding that they may provide useful protection from negative consequences, including prescription drug related poisoning. Ali et al (2017) noted that while PDMPs had no effect on NMUPD, though they did note that it did reduce “doctor shopping” and was a vital key for informing doctors about patient history.

AUTHOR INFORMATION

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