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Master's Thesis

**EQUIPPING NURSES WITH BETTER KNOWLEDGE ON OPIOID
ADDICTION: HOW RECOGNIZING RISK FACTORS FOR SUBSTANCE
ABUSE LEADS TO IMPROVED PATIENT CARE**

Master of Science in Nursing

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Abstract:

Opioid abuse and addiction has become a rampant epidemic in the United States, and the entire world within the last few decades. This healthcare crisis is particularly contemptible due to the inadvertent involvement of healthcare providers in its perpetuation. Although the crisis was initiated as a result of misinformation spread by pharmaceutical companies, the medical community is now responsible for treating and preventing opioid abuse. Nurses in particular, participate in direct patient care. They are most often best equipped to determine a patient's pain and provide pharmacological relief. Thus, it is vital that nurses are strongly educated on the ways in which their patients may be impacted by opioid abuse. A medically-based understanding of the history of opioid addiction can reduce the stigma around substance abuse and allow nurses to provide the best care possible. Awareness and mindfulness of contributing risk factors to opioid addiction is also key in treating and preventing this disorder. Genetic risk factors in the form of single nucleotide polymorphisms (SNPs) on the OPRM 1 and COMT genes, psychological risk factors of Major Depressive Disorder, Post Traumatic Stress Disorder and other non-pathological life stressors, and sociodemographic parameters of race, education and socioeconomic status, have all shown to increase susceptibility to opioid abuse and addiction. By equipping nurses with this knowledge, they can play an integral role in prevention, early recognition, and early intervention of analgesia issues. Therefore, nurses can be vital in establishing an interdisciplinary approach to pain management that reduces the risk of opioid addiction.

Objectives and Aims: To analyze the ways in which nursing personnel can play an integral role in prevention, early recognition, and early intervention of analgesia issues by learning about the genetic, psychological and socio-demographic risk factors that predispose patients to opioid use disorder.

Research Question: In nurses that provide direct patient care, how does understanding the genetic, psychological, and socio-demographic risk factors that predispose patients to opioid use disorder assist in providing better healthcare services?

Introduction:

Why should opioid abuse be such an important topic for nursing personnel?

Nursing programs of various educational levels often provide a fundamental understanding of the basics of pharmacology. However, in the wake of the opioid epidemic, it is vital to equip nurses with a much more detailed understanding of opioid addiction. As healthcare workers that provide some of the most vital direct patient care, nurses should be well versed on the mechanisms by which opioid addiction can occur, as well as the various risk factors that can predispose patients to opioid abuse. Thus, knowing the genetic, psychological, and socio-demographic risk factors that can lead to opioid use disorder can allow nurses to provide better healthcare services and limit the opioid abuse epidemic.

What are the defining characteristics for substance abuse and drug addiction?

The DSM-5 states that a patient must exhibit ≥ 2 of the following features within 1 year in order to qualify for a diagnosis of substance abuse disorder. The criteria are broken up into three general categories of impaired control, social impairment, risky use, and pharmacological indicators. Impaired control is defined as substance use in larger amounts and/or for a longer time than originally intended, ongoing failed attempts to cut down on use, a large amount of time spent on substance-related activities including seeking out, buying and recovering from substance, as well as an intense craving for the substance (Hasin et al., 2013). Social impairment includes issues with fulfilling work, school, family, or social obligations such as not attending work or school, neglecting children or their partner, issues with interpersonal relationships directly related to substance use such as withdrawal from relationships or marital issues, decreased social, occupational, and recreational activities. Risky use implies utilizing the substance under hazardous situations such as driving a car or when operating heavy machinery, as well as continued use despite awareness of the problems surrounding the substance. (Hasin et al., 2013) (Table 1.1).

Pharmacological indicators include drug tolerance which is the need to continuously increase the dose of the substance in order to achieve the same desired effect, drug withdrawal such as a substance-dependent group of symptoms that occur after a period of prolonged cessation of the drug use accompanied by the urge to readminister the substance. Withdrawal symptoms can often present as the opposite of the intoxicating effects such as when heroin intoxication causes sedation and constipation, while heroin withdrawal results in anxiety, insomnia, and diarrhea. Other signs of withdrawal can include flu-like symptoms such as

myalgia, or piloerection. A patient can also present with mydriasis, tachycardia, or agitation during withdrawal. In contrast, an individual who is under the influence of opioids can present with miosis, depression of the central nervous system, euphoria, seizures, or absent gag reflex (Hasin et al., 2013) (Table 1.1). Since nurses generally spend the most time observing and caring for patients, it is vital for them to properly assess and analyze these symptoms of drug abuse or withdrawal in their patients.

Table. DSM-5 Diagnostic Criteria for Opioid Use Disorder*	
<ol style="list-style-type: none"> 1. Opioids are taken in larger amounts or duration than intended 2. Persistent desire/unsuccesful efforts to cut down or control opioid use 3. A great deal of time is spent obtaining, using, or recovering from the effects of opioids 4. Craving 5. Recurrent use of opioid results in failure to fulfill major role obligations at work, school, or home 6. Continued use despite social/interpersonal substance-related problems 7. Important social, occupational, or recreational activities are given up or reduced because of substance use 8. Recurrent use in hazardous situations 9. Continued use despite knowledge of having a persistent or recurrent opioid-related physical or psychological problem that is likely caused or exacerbated by opioid use 10. Tolerance^b 11. Withdrawal^b 	
Severity: Mild: 2-3 symptoms, Moderate: 4-5 symptoms, Severe: ≥ 6 symptoms	

* The information above is only an overview of the criteria used. Consult the DSM-5 before making a diagnosis.
^b Note: This criterion is not considered to be met for patients taking opioids solely under appropriate medical supervision
 Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Washington, DC: American Psychiatric Association; 2013:541.

Table 1.1-DSM-5 Diagnostic Criteria for Opioid Use Disorder- *American Psychiatric*

Association

Mechanism of Action of Addiction:

Society often ostracizes individuals who suffer from substance abuse due to subjective misconceptions that addiction comes about as a purposeful or malicious neglect or disregard for one’s health and quality of life. Thus, these ideas often create an atmosphere of taboo around the

subject of addiction, preventing those who are affected from seeking out the help they need. Unfortunately, nursing staff and the nursing community are not immune to negative attitudes about opioid use in patients. A study by Broekmans et al., in 2004 found that nurses had a very poor perception of pain treatment with opioids. Despite a neutral to positive score on the Opioid Attitude Scale (mean=69.4%), it was found that nurses had personal negative biases towards the use of opioids during a diagnostic phase and the risk of possible addiction. The researchers believe that such bias can stem from a lack of understanding about the mechanisms of addiction and can hinder proper treatment of pain (Broekmans et al., 2004). In reality, substance abuse can occur due to a culmination of neurobiological processes that impact the brain and alter its chemistry. Therefore, it is vital to understand the science behind the concept of addiction in order to best prevent and assist individuals who may suffer from this condition (Koob 2021).

Upon ingestion of an opiate, the drug begins to travel through the blood stream and binds to the mu, delta, or kappa receptors respectively. Although some opiates can bind to more than one receptor, the one most commonly associated with eliciting feelings of reward and pleasure is the mu opioid receptor. Therefore, once the drug binds to the receptor, individuals experience these positive of rewarding feelings that would otherwise only be activated during certain activities such as food or sex. Although opioids are prescribed as a method of therapeutic pain relief, the pleasant feelings of the drug in absence of pain can encourage repeated use without medical need (Paul et al., 2021)

In order to achieve the feelings of reward that are perceived by the brain, opioids activate the mesolimbic (midbrain) pathway. This pathway activates signals in the ventral tegmental area that result in the release of the dopamine in the nucleus accumbens. This release of dopamine causes feelings of pleasure that become associated with the circumstances and environment in

which they occur. Such perceptions are then recorded and stored in the brain for later use. However, these memories can soon become conditioned associations that can contribute to cravings for the pleasurable feelings when an individual comes in contact with the circumstance or environment that originally created this dopamine release. Ultimately, this process can create a precursor for the development of drug liking and craving that can become more solidified with repeated encounters of conditioning. Nevertheless, tolerance, dependence, and withdrawal are also significant motivators for repeated drug use regardless of negative consequences (Meier et al., 2021).

Clinicians believe that opioid withdrawal is one of the strongest driving forces in opioid dependence and addiction. Thus, one of the most vital treatments of opioid addiction is assisting a patient in battling with their withdrawal symptoms. In order to accomplish this task, one must have a concrete understanding of how withdrawal impacts the function of the brain (Koob 2021). Overtime, an individual exposed to the effects of opiates becomes tolerant of their initial dose and must increase their drug quantity in order to elicit the feelings of pleasure that originally resulted from a lower dose of the drug. Tolerance for opioids occurs due to desensitization of opioid receptors that become less responsive to stimuli from lower drug doses. Therefore, an increased quantity of the drug is needed to produce the previous effects. Opioid tolerance can also present as a reduction in the release of dopamine from the ventral tegmental area into the nucleus accumbens during everyday activities that previously brought pleasure such as eating.

Although the mechanism of this is not fully understood, researchers believe this contributes to the psychological aspects of craving and compulsive drug use (Paul et al., 2021). Constant exposure to increased dosages of opioids soon alter the brain chemistry so that the baseline for normal brain function occurs in the presence of the drug, but becomes abnormal in

its absence. This abnormal function of the brain in the absence of the drug causes withdrawal symptoms to occur. It is vital to note that withdrawal symptoms can only occur in patients who have developed a tolerance (Browne et al., 2020).

Opioid dependence and withdrawal occur as a direct result of symptoms stem from changes to the locus ceruleus, a nucleus located in the pons near the floor of the fourth ventricle. Neurons in the locus ceruleus produce noradrenaline which stimulates respiration, alertness, wakefulness, blood pressure, and other functions. In contrast, when opioids bind to the mu receptors in the locus ceruleus the release of noradrenaline becomes inhibited causing drowsiness, slowed respiration, and low blood pressure—symptoms of opioid intoxication as described in DSM-V (Hasin et al., 2013) (Browne et al., 2020).

Nevertheless, the human body is masterful at compensatory mechanisms. Thus, the neurons in the locus ceruleus increase their levels of activity and release of noradrenaline after repeated opioid influence. Therefore, the suppressive effects of the opioids are offset by the increased presence of noradrenaline. This creates the new normal for the body as it balances the contradictory hormones. However, the absence of opioids in the system tips the carefully balanced scale that the body has established. This results in an excessive amount of the stimulating noradrenaline hormone in proportion to the missing suppressive effects of the opioids. In turn, this imbalance presents as withdrawal in the form of increased anxiety, tremors, muscle cramps, and diarrhea (Koob 2021).

Overall, the combined effects of drug liking, tolerance, dependence, and withdrawal lead to addiction. These processes can occur simultaneously or separately over a period of time due to repeated drug use. Ultimately, the human body functions as an intricate balance of hormones and their respective receptors. Continuous opioid use alters the careful balance created by the body

which can present as drug addiction. At its core, opioid addiction is driven by the increased desire to elicit the pleasurable effects of the medication while minimizing symptoms of withdrawal. This creates a constant interdependent positive feedback loop that can become challenging to break.

Nevertheless, opioid addiction remains a complex disease that is also impacted by other sociodemographic, psychological, environmental and genetic factors. An in-depth analysis of the symbiosis of these influences can improve awareness and better prepare nursing healthcare professionals for preventing and treating opioid addiction in patients. As analgesic therapies continue to develop in complexity, the priorities of nursing care must shift to balance pain management with minimizing adverse events. Opioid analgesia continues to be a primary pharmacological intervention in hospitalized patients that spend most of their time under nursing care.

Ultimately, unintentional advancing sedation and respiratory depression are two of the most serious opioid-related adverse events. A multitude of factors can contribute to such adverse events including opioid dosage, route of administration, duration of therapy, patient-specific factors, as well as desired goals of therapy. Once again, it is vital to note that most of these therapeutic practices are administered by nursing staff. Therefore, it is vital to improve nursing education on the topic of administering necessary analgesic agents while remaining knowledgeable of potential risk factors for addiction and adverse events (Jarzyna et al., 2011).

Background and Significance:

In the last 30 years, opioid addiction has become an increasingly prevalent social and medical dilemma all over the world. However, its effects have been most pronounced in North America and parts of Europe (Hoffman et al., 2019). In the 19th century, opioid analgesics were introduced as a medical treatment used to relieve moderate to severe pain (Rosenblum et al., 2008). Although beneficial for patient comfort, medical professionals soon realized that these medications carry serious risks of developing addiction when used for extended periods of time, or consumed in large doses. Nevertheless, in the 1990s, the use of opioids for chronic pain management became much more widespread. This soon led to the use of opioids without legitimate medical need, categorizing this group of medications as possible illicit drugs. Soon enough, opioid addiction became a widespread phenomenon resulting in the increased use of other illicit drugs, overdose, and death. In the United States, opioid addiction is now considered one of the leading causes of preventable death. However, acknowledging risk factors that may contribute to addiction can potentially reduce the chances of substance abuse.

As the number of deaths due to opioid addiction continued to rise in the 20th century, the United States became faced with a \$78.5 billion financial burden to the healthcare system (Florence et al., 2016). Between 1999 to 2017 more than 700,000 people died from drug overdose, with almost 400,000 deaths being related to opioid abuse (Hoffman et al., 2019). In 2017 over 70,000 deaths were due to overdose and 68% of those deaths were due to opioid abuse (Hoffman et al., 2019). From 2016 to 2017, the prescription opioid-involved death rate decreased 13.2% among males aged 15–24 years, but increased 10.5% among people 65 and older; while death rates involving opioids remain highest among whites with a significant increase among blacks (Scholl

et al., 2013). In 2017, opioid addiction was officially declared an epidemic in the United States. It is important to recognize that nurses play an important role in identifying patients at risk for excessive sedation and respiratory depression due to opioids, as well as establishing treatment and care plans, intervening during adverse events, and other aspects of patient care. Despite the frequent use of opioids in hospital settings, there are virtually no universal guidelines in safely assessing and monitoring patients using opioids. There is also limited understanding of the benefits by which supportive monitoring via pulse oximetry (measuring oxygen saturation) and capnography (measuring end-tidal carbon dioxide), can assist nurses in patient care. In fact, as of the present day, randomized clinical trials on the value of using such monitoring devices to prevent and limit adverse opioid-induced events exist. Therefore, the task of minimizing adverse events and poor patient outcomes once again largely relies on the direct knowledge, skills, experience of nursing staff to intervene when necessary.

For the first time in 2011, the American Society for Pain Management Nursing approved the development of an expert consensus panel to analyze the scientific basis and state of practice for assessment and monitoring of hospitalized patients who receive pain control via opioids. This plan was the tentative start of official proposed practices for patient care, education, and systems-level changes to improve quality care and patient safety at the nursing level (Jarzyna et al., 2011).

Fentanyl and Oxycodone: Examples of Addictive Medically Prescribed Opioids

In order to best understand the impact of medically prescribed opioids on the addiction epidemic in America, we can briefly explore the history of two of the most commonly prescribed and abused opiates to date: Fentanyl and Oxycodone. Both Fentanyl and Oxycodone are Schedule II opioid analgesics that are commonly prescribed for acute and chronic pain management. Fentanyl is a synthetic opioid that was approved for medical use by the FDA in 1968. However, the illicit use of fentanyl is associated with the rise in overdose deaths in the US. Prescribed fentanyl and illegally acquired fentanyl are placed into the CDC's "synthetic opioids other than methadone" category due to limitations with testing which makes it difficult to know how the drug was accessed by consumers (Kahl et al., 2018). Therefore, the death rate due to synthetic opioids does not reflect the prescribing rate.

Initially introduced into the American medical system in 1963, by 2005, Fentanyl and its analogs began a surge of related fatalities due to their illicit use in the United States (Han et al.,2019). Which led to its classification as a "Schedule II" drug by the "Controlled Substances Act", due to its high potential for abuse by the U.S. Drug Enforcement Agency (Comer SD et al.,2019). It has been reported that from 2005 to 2007 an estimated 1,013 deaths occurred in six different states as a result of Fentanyl abuse (Han et al., 2019). In 2012 to 2014, another surge was recorded with an increase from 2,628 to 5,544—a twofold increase in the span of two years (Han et al.,2019). In 2016, researchers estimated that half of all opioid overdose deaths—approximately 19,547—were a direct result of the use of Fentanyl and Fentanyl analogs such as Acetylfentanyl, Furanylfentanyl, and Carfentanil (Han et al.,2019).

Pharmacologically, Fentanyl was designed to be a rapid onset drug with a short duration of action. Therefore, it is only meant to be used for acute analgesic effects (Araldi, Dioneia et al.,2018). However, researchers have found that when mixed with other drugs, the effects of Fentanyl can be prolonged. This is suspected to be a major factor in the increasing rate of fatalities due to Fentanyl abuse (Han et al.,2019). Despite the beneficial uses of Fentanyl in the medical field, the recent trends in fatalities of illicit Fentanyl use give credence to the demand for further research and study on risk factors, preventive measures and treatments.

Oxycodone is another opioid medication that is widely used to relieve moderate-to severe acute pain. Most commonly it has been used as an analgesic for paroxysmal spontaneous pain, steady pain, and allodynia related to postherpetic neuralgia. It has also become increasingly used to manage cancer-related pain. Nevertheless, Oxycodone is one of the most commonly abused opioid medications on the market. Upon its initial introduction into the pharmaceutical world, it was claimed that Oxycodone is less addictive than morphine. Soon enough, a false-claimed non-addictive formulation of Oxycodone called OxyContin entered the market, further contributing to the opioid crisis. Abuse of this medication was often carried out by crushing the pills for immediate burst release, typically administered via nasal insufflation, or by liquefying the pills for intravenous injection. Nevertheless, oral Oxycodone is found to have a higher abuse liability when compared to other oral opioids such as oral Morphine and Hydrocodone (Wightman et al.,2012). In 2011 Oxycodone was ranked as the number one overdose drug involved in deaths resulting in 5,587 fatalities (Spencer et al.,2019). Although Fentanyl and Oxycodone are only two examples of commonly prescribed opioids that contribute to the epidemic, the development and history of these medications provides a good indication of how these medically prescribed drugs have led to the opioid epidemic America faces today.

Design and Methods:

This literature review focuses on the ways in which nursing personnel can play an integral role in prevention, early recognition, and early intervention of analgesia issues by learning about the genetic, psychological and socio-demographic risk factors that predispose patients to opioid use disorder. It was completed by analysis of database resources including but not limited to EBSCO Medline, PubMed, Google Scholar, PubMed Central, and The Directory of Open Access Journals. The analysis was not restricted to peer reviewed journals. The types of studies included are experimental, descriptive, and observational. The search terms utilized include but are not limited to “nursing education,” “nurses and opioids,” “opioid receptors” and “genetics”, “mental illness”, “opioid use disorder” and signaling pathways as they pertain to the possible risk factors to be investigated. Data and information focuses mostly on the prevalence of addiction as it relates to in the United States has been excluded, as well as articles dated before 2006.

Findings:

Genetic Risk Factors:

Opioids are generally divided into two categories as endogenous or exogenous. Some endogenous opioids include enkephalins, endorphins, endomorphins, dynorphins, and nociception/orphanin. In contrast, exogenous opioids include morphine, heroin, and fentanyl. Upon entering the bloodstream via oral or intravenous methods, these substances then bind to the

same receptors as endogenous opioids. The most common binding receptors for opioids are Mu, Kappa, or Delta receptors. These can later be separated into other subcategories that will not be discussed in the context of this research. Structurally, opioid receptors are G protein-coupled receptors (GPCRs) that mediate the body's response to various hormones, neurotransmitters, and drugs. Thus, they play a significant part in sensory perception of vision, taste, and olfaction. However, perhaps their most important functions in the context of addiction relate to analgesia as well as mood and reward sensations. Despite the general commonalities that exist across the anatomy and structure of the human body, minor alterations in our genetics have proven to impact our perception of pain, pleasure, and other hormonally regulated emotions. One such genetic difference are Single Nucleotide Polymorphisms (SNPs). These slight variations in an individual's genetic sequence can result in varying understandings of pain levels, sensations of pleasure, as well as efficacies of medications and treatment of substance abuse disorders (Crist et al., 2019).

In the context of opioid use disorder (OUD), one such SNP affects the mu-opioid receptor (MOR) and is encoded by the OPRM1 gene. The activation of MOR signaling via endogenous peptides such as beta-endorphin, opioid analgesics, or opioid medications results in downstream dopamine release in ventral striatum and medial prefrontal cortex and its rewarding effects. However, researchers have found that OPRM1 polymorphisms that affect MOR function or expression can change this reward pathway and can increase risk of OUD. Two of the most common variants in this polymorphism occur on exon 1 of OPRM1 which changes the amino acid sequence of MOR. The two common variants are rs1799972, which is found predominantly in individuals of African descent, and rs1799971 which is widespread in all non-African populations. Despite the large quantity of studies that indicate that the rs1799971 genotype

affects MOR function, case-control studies of this variant in OUD have produced inconclusive results. Nevertheless, recent results on the topic seem more promising (Crist et al., 2019).

Hancock et al., 2015 conducted a study on 103 OPRM1 SNPs for association with OPRM1 mRNA expression in prefrontal cortex from 224 European Americans and African Americans of the BrainCloud cohort. They then tested the 16 putative cis-quantitative trait loci (cis-eQTL) SNPs for association with heroin addiction in the Urban Health Study and two replication cohorts, resulting in a total of 16,729 European Americans, African Americans, and Australians of European ancestry. Their results find that common OPRM1 intron 1 SNPs have significant positive associations with heroin addiction. They conclude that the haplotype structure of rs3778150 and nearby SNPs may explain the underlying inconsistencies in associations rs1799971 and heroin addiction (Hancock et al., 2015).

Another commonly studied single nucleotide polymorphism as it relates to opioid addiction is the Catechol-O-methyltransferase (COMT) gene. Located on chromosome 22q11.21, this gene is an important metabolic enzyme that is active in the metabolism of dopamine. COMT is able to catalyze the methylation of the three hydroxyl groups of catecholamine, resulting in its degradation. Therefore, COMT has a significant impact on dopaminergic nerve transmission, especially in parts of the brain with a lower density of dopamine transporters. One such part of the brain is the prefrontal cortex which contains more than 50% of the region's dopamine that is degraded by COMT (Oosterhuis et al., 2008).

The reward pathway made up of dopamine circuits is vital in analyzing the neurobiological development of substance addiction. Opioids and other addictive substances can elevate dopamine levels in the synaptic cleft by activating the mesolimbic dopaminergic pathways, which the body can perceive as a reward. The COMT gene is also known to be highly

polymorphic with a variety of single nucleotide polymorphisms (SNPs) that can further impact both how the brain perceives and tolerates pain and reward signals (Roethe et al., 2006).

One widely studied COMT single nucleotide polymorphism is the COMT (rs4680) which changes the translated amino acid from valine to methionine (Val158Met). Researchers found that this polymorphism may correlate with increased chronic pain sensitivity, which in turn can lead to increased opioid use. Some studies in particular focus on the chronic pain experienced by cancer patients. One study in particular, found that in the 24-hour period post a nephrectomy, (COMT rs4680), patients homozygous for the variant Val/Val consumed 36% (95% confidence interval, 31%-41%) more opioids than patients homozygous for the Met/Met group ($P = 0.009$) (Candiotti et al., 2014).

A commonly utilized therapy for opioid addiction is Methadone Maintenance Therapy (MMT). Researchers found that in addition to increased susceptibility to substance abuse and lower tolerance of chronic pain, individuals with certain polymorphisms of the COMT gene may be less responsive to MMT. A study conducted on Chinese opioid-dependent patients found that the haplotype A-T-A (rs737866-rs933271-rs4680) carriers of the COMT polymorphism were more likely to be unresponsive to treatment by MMT. However, patients carrying the TC or CC genotype at rs933271 had a 1.53- fold chance of responding to MMT when compared to patients with the TT genotype. In the additive model, the patients who carried the TC genotype were increasingly responsive to MMT in contrast to the CC genotype individuals. The researchers surmise that an association exists between the polymorphism of rs933271 and the response to MMT. Thus, the COMT polymorphisms can impact not only one's likelihood of becoming addicted to opioids, but also their susceptibility to treatment (Duan et al., 2020).

Researchers have often linked the polymorphism of the COMT gene to opioid addiction, as well as drug seeking behavior and impulsivity. The presence of COMT polymorphisms has also been found as a correlate with other psychiatric and substance addictions. Nevertheless, the role of COMT gene polymorphism in MMT remains controversial (Duan et al., 2020).

Ultimately, a more detailed understanding of the genetics surrounding opioid addiction can help nurses better discern clinical judgement and understanding of opioids. A knowledge of concepts such as genetic polymorphisms, the pain pathway, and the ways the brain processes opioid analgesics can improve clinical outcomes and lessen negative biases towards patients receiving such analgesia. Moreover, a clear appreciation for how addiction can occur via genetics and neurological pathways can also provide a more well-rounded healthcare approach amongst the nursing community.

Psychological Risk Factors:

Psychological risk factors have been proven as significant risk factors for the development of opioid addiction. Most specifically, these include disposition factors such as personal trauma, mental illness such as depression and stress in general. The presence of these life circumstances or disorders can further intensify any additional chronic pain condition that can present in the patient's life. Thus, their perception of pain is directly impacted by their comorbid traumas or mental illnesses. In turn, this can lead to consumption of larger opioid dosages increasing susceptibility to abuse and addiction. (Williams et al.,2020).

Although the concept of personal trauma can be quite broad, in the context of this paper personal trauma will be defined as any traumatic life experience such as partner violence, sexual assault,

and negative childhood experiences. A study that analyzed gender based violence in US women found that women who suffered from childhood violence or abusive relationships maintained an increased likelihood by 2.5-3.6 times of misusing opioids as a result of comorbid mood and anxiety disorders. Further data showed that experiencing abuse at an increasingly young age positively correlated with likelihood of opioid addiction. Individuals who experienced child abuse between the ages of 2-10 were 18 times more likely to abuse opioids in their lifetime (Walsh et al.,2015). Additional findings include that individuals with personal trauma were 3.5 times more likely to develop or suffer from the exacerbation of a congruent chronic pain condition. As a consequence, such an individual would now have double the chance of being prescribed opioids increasing their total likelihood for being prescribed opioids and developing an opioid addiction to 4.5 times greater than those who do not have a history of personal traumatic events (Williams et al.,2020).

In addition to developing chronic pain conditions, those with personal trauma are also more likely to be diagnosed with mental health conditions such as Post-Traumatic Stress Disorder (PTSD) or Major Depressive Disorder (MDD). These disorders are also contributing risk factors for opioid abuse. Major Depressive Disorder (MDD) is categorized by ongoing feelings of low mood, low self-esteem, and finding decreased pleasure in activities an individual previously enjoyed. MDD occurs due to a series of culminating factors such as a biochemical imbalance in the brain, genetic predisposition, an individual's own personality, self esteem and stress coping strategies. Environment also plays an important role as well based on the individuals living conditions, lack of emotional support, neglect and abuse (Kanter et al.,2008).

As a result, the decreased perception of pleasure from activities previously enjoyed and a general inclination towards negative emotions increase susceptibility to opioid addiction in those

who suffer from MDD by the very design of their disorder. This can be attributed to the impact of opiates on the pleasure centers of the brain which can be dulled in patients with MDD, necessitating increased drug dosages in these individuals. In contrast, those who do not suffer from MDD do not experience this precursor of decreased pleasure perception and would be less likely to suffer from opioid misuse. Therefore, patients who suffer from MDD and are also diagnosed with a chronic pain condition are inevitably more likely to feel their conditions are amplified by one another. Studies demonstrated that such patients were 5 times more likely to report opioid abuse (Williams et al.,2020).

Post-Traumatic Stress Disorder (PTSD), is another mood condition that can affect one's perception of pain and their likelihood of opioid addiction. By definition, PTSD is triggered by participating in or witnessing a terrifying event. Symptoms can include nightmares, flashbacks, severe anxiety, and an inability to control one's thoughts in regards to the event (Dahlby & Kerr 2020)

Experts find that PTSD and Opioid Use Disorder (OUD) are actually commonly co-occurring conditions. Despite this known fact, patients who seek treatment for substance abuse are rarely evaluated for PTSD. From the perspective of public health, it is vital to note that the correlation between PTSD and OUD calls for improved coordination and awareness amongst healthcare providers. However, as with other comorbidities, researchers seek to unravel the detailed relationship between PTSD and OUD.

A commonly accepted theory is the 'self-medication hypothesis' which proposes that opioids are used to alleviate the severity of PTSD symptoms, inadvertently placing patients at risk of habitual self-medication and addiction. Statistical findings support this hypothesis due to a significantly higher rating for subjective pain and a greater rate of opioid prescriptions in PTSD

patients when compared to those without. Additional medical rationale points to the combination of an overstimulated noradrenergic system and the sedating effects of opioids in PTSD patients as the underlying mechanism for substance abuse. This logic is reinforced by reports of reduced PTSD symptoms following the acute administration of morphine. As previously described, opioid addiction is controlled by the increased desire for the pleasurable effects of the medication, as well as a desire to avoid symptoms of withdrawal. Individuals who suffer from PTSD can find the effects of opioid withdrawal particularly catastrophic as the noradrenergic system becomes increasingly activated and amplifies their perception of stress. As a result, self-medication of opioids provides a type of negative reinforcement to avoid such consequences (Dahlby & Kerr 2020).

Other examples of stressors can present in the non-pathological circumstances of life such as interpersonal conflict, the loss of a job, or the death of a loved one. Financial situations can also serve as contributing stressors in an individual's life. However, the culmination of non-pathological stressors for ongoing periods of time can result in chronic stress. As a result, chronic stress can influence opioid abuse behaviors through the addiction of endogenous opioids, which plays a role in regulating physiological responses and inhibiting stress related symptoms (Bershad et al.,2018). Consumption of excessive opioids would then become an easy gateway for an individual to escape their daily stressors and develop an addiction to opioids (Preston et al.,2018).

Perhaps a possibly surprising stressor of life that has negatively impacted opioid abuse is the lack of marriage in an individual's life. Studies indicated that people who were married had a lower likelihood of opioid overdose compared to individuals who never married (HR=1.71, CI: 1.55, 1.89) (Altekruse et al.,2020). Although the exact rationale behind this is unknown, it can be

implied that perhaps marriage or having a partner brings about positive behavioral, physical, or economic benefits that would diminish the chances of fatal opioid overdose.

By knowing and recognizing such psychological risk factors, nurses can better anticipate and prepare for possible complications related to opioid use. This can also assist with increased empathy towards patients and limit bias in the healthcare environment. Providing nurses with such knowledge will allow them to appreciate the ways in which a combination of past medical history and other factors can impact their patients. This can further increase patient empathy and improve the quality of care provided.

Sociodemographic Risk Factors:

Analysis of the current opioid crisis demonstrates prescribed opioids have a large contribution to the increase in overdose in the United States. Although there are correlations to drug abuse and unemployment, which would lead to lower socioeconomic status, evidence shows those in higher socioeconomic status have more incidence with prescription overdose. The common misconception of the opioid epidemic is that primarily individuals of the lowest socioeconomic status would be most affected. However, when compared to other types of substance abuse, opioid addiction does not follow these trends. In a study that aimed to explore the relationship between socioeconomic status and opioid prescription, researchers found that opioid prescriptions were given more to those of higher socioeconomic status compared to those of lower socioeconomic status. Race was also found to be an important factor in the socioeconomic influence of opioid use. Data shows a significant disproportion between the number of opioid prescriptions given to Caucasian Americans when compared to African

Americans, with the latter receiving opioid prescriptions less frequently after accounting for factors of pain-level, age, injury-status, and other covariates. Other disparities included percent of patients prescribed opioids in the highest quartile vs lowest quartile of socioeconomic status via indicators of poverty (49.0 % vs. 39.4 %, $P < 0.001$), household income (47.3 % vs. 40.7 %, $P < 0.001$), and educational level (46.3 % vs. 42.5 %, $P = 0.01$) (Joynt et al., 2013).

Although our literature review focuses on the abuse of opioid prescriptions, it is vital to note that opioids are still a viable treatment for pain when prescribed and used as medically intended. Therefore, the study by Joynt et al., 2013 perhaps inadvertently highlights another important issue in the medical community— under prescribing necessary pain medications on the basis of racial or socioeconomic profiling. This point must be mentioned and recognized as it can skew an objective understanding of the data and understanding of opioid use and its addiction. Despite the notable differences of prescribed opioid rates for African American and Caucasians, another study found that death due to drug and opioid overdose disproportionately affected the African-American population in San Francisco. Therefore, an African American individual is less likely to receive a prescription for opioids but is more likely to die from its overdose. Researchers found that overall, deaths due to opioid overdose were concentrated in small, high-poverty, areas in central San Francisco (Visconti et al., 2015).

A more recent study showcases contradictory results when it comes to the relationship between race and opioid overdose. Altekruze et al., 2020 found that out of their initially surveyed population of 4.5 million Americans, Caucasian Americans (referenced as “Whites” in the study) accounted for approximately 80.7% of the recorded opioid overdose deaths and 66.4% of people who were alive at the end of follow-up. American Indians, Alaskan Natives and Asians, as well as Pacific Islanders each accounted for approximately 1% of the recorded opioid overdose

deaths. African Americans (referenced as “Blacks” in the study) and Hispanics accounted for approximately 8.2% and 7.3% of these deaths, respectively (Altekruse et al., 2020). Despite this data, the researchers warn that their data showcases a skew simply because a greater number of White individuals were surveyed in comparison to African Americans and other groups.

Additionally, they believe that certain socioeconomic status (SES) factors were not accounted for in the Black population. This highlights the importance of mindful statistical analysis when looking for general trends in such data. Nevertheless, the researchers conclude that the general prevailing cause for the exponential deaths due to opioid overdose in the United States can be attributed to low socioeconomic status (SES) (Altekruse et al., 2020).

In America, one’s racial group along with their educational attainment also correlate with access to employment. This also plays a role in the socioeconomics as it pertains to the opioid crisis. It was found that individuals who participate in manual labor are more likely to experience work-related injuries and suffer from chronic pain. Therefore, they are also more likely to receive an opioid prescription and become victims of addiction. Data on those who are above and below the poverty line as well as the standard income for each described demographic in the study finds a significant disparity in hazard ratio between the groups. Those who live in households five times above the poverty line (500% - 999%) maintain a hazard ratio of 1.59, while those in the lowest quartile of salaries have a hazard ratio of 5.57 (Altekruse et al., 2020). Therefore, a greater socioeconomic status is negatively correlated with risk of opioid overdose. This can be attributed to diminished access to proper medical care after overdosing, as the more affluent communities have the means to receive better medical care to mitigate an opioid overdose. Other confounding factors include location, education levels, and other opportunities for improved quality of life (Meara et al., 2008).

Recognizing social risk factors for opioid abuse can further improve nursing care. The idea that patient outcomes are frequently greatly impacted by their sociodemographic standing can allow nurses to be mindful of varying treatment results. Thus, they can tailor their treatment approach and be mindful of certain treatment barriers amongst patients. Access to proper resources and medication is not universal for patients in America. Therefore, it is important to consider this inalienable aspect of patient care.

Conclusion/Discussion:

The impact of the opioid epidemic in the United States has become one of the most prominent healthcare crises in the country. Opioid addiction is a particularly critical issue in the medical community due to the direct involvement of healthcare professionals in its perpetuation. This largely occurred as a result of misinformation provided by pharmaceutical companies in regards to the safety of these medications. Despite the known risks of opioid addiction, opioid medications as prescribed by healthcare providers remain a valid form of treatment for certain conditions, especially as they relate to chronic pain. Therefore, it is vital for the medical community to be aware of the genetic, psychological, and sociodemographic risk factors for opioid addiction. In particular, nurses are most directly involved in patient care. They are uniquely equipped to determine a patient's pain and provide pharmacological relief. Thus, it is important that nurses are strongly educated on the ways in which their patients may be impacted by opioid abuse. As a result, a medically-based understanding of the history of opioid addiction can reduce the stigma around substance abuse and allow nurses to provide optimal patient care. Ultimately, spreading knowledge and awareness of these risk factors can allow nurses to be more

mindful of addiction potential and adverse events in patient care, as well as improve their own recognition of possible confounding biases that can impact their professional judgement (St. Marie.,2019).

Genetic risk factors include various Single Nucleotide Polymorphisms (SNPs) such as the OPRM1 gene for the mu-opioid receptor (MOR). Certain variations of this gene have correlated to increased susceptibility to Opioid Use Disorder (OUD). Another commonly studied SNP is the Catechol-O-methyltransferase (COMT) gene. Some polymorphisms of COMT has been found to increase likelihood of opioid addiction as well as hinder treatment for substance abuse. As the medical community continues to explore areas of genetic alteration through epigenetics, perhaps future treatment for opioid addiction can involve further exploration of methylating or editing such polymorphisms.

Other contributing factors to opioid abuse and addiction include psychological risk factors such as personal trauma and mental health illnesses. Conditions such as Major Depressive Disorder and Post Traumatic Stress Disorder have been known to alter one's perception of pain, pleasure, and analgesia. Therefore, such individuals are more likely to utilize opioids in larger quantities that would render them vulnerable to addiction. The relationship between opioid use disorder and other mental health disorders often presents as a mutual amplification of both conditions. Other non-pathological life stressors can similarly impact an individual's proclivity to addiction. Nurses should be aware of these confounding factors so that they may properly screen and treat their patients for their respective conditions.

Sociodemographic risk factors include race, income & educational attainment, each of which present their own increased risks regarding opioid prescriptions as well as response to the medications themselves. Studies have shown that African Americans are generally the

population most susceptible to opioid overdose despite being the least likely to receive an opioid prescription. Research that supports this notion points out the issue of bias in the healthcare community in which the pain of African American patients is not acknowledged and treated as needed. Although our research focuses on opioid medications in the context of addiction, it is vital to note that patients of all races and ethnicities deserve equal treatment, validation for their healthcare concerns, and relief for their pain.

Other data shows that White individuals are most likely to suffer from opioid overdose in comparison to other races and ethnicities. However, this data is admittedly skewed due to inequalities in the population surveyed and the lack of adjustment for certain socioeconomic factors. Nevertheless, individuals who belong to a minority race, are of lower socioeconomic status, work in manual labor, or attain a lower level of education, are most vulnerable to opioid addiction and overdose. Thus, it is necessary for interventions to be administered accordingly to the communities with limited access to adequate healthcare and rampant opioid addiction.

A lack of knowledge on these risk factors for opioid addiction can cause direct implications for nurses in clinical practice of all settings. This calls for a significant improvement in exposure and education on opioid analgesia so that nurses may improve the safety and efficacy of patient care. When risk is assessed and acknowledged, strategies can be put into place to analyze opioid abuse risk that can be monitored both within the clinical setting and outside of it. One potential strategy would be an opioid risk assessment tool when patients are first admitted for care. Results from such assessments can help guide patient treatment and can be accessed by nurses as they provide daily care. can be used when patients are admitted for care. Studies have shown that risk assessments that include a thorough understanding of patient's use or abuse history and current drug use pattern can greatly improve outcomes and minimize risk. However,

such assessments must be conducted with mindfulness and empathy which can only be implemented via detailed understanding and knowledge on the topic of opioids. Providing such an education can allow nurses to lead with kindness in healthcare while improving communication and trust with patients. Overall, knowledge and education always lead to better results—allowing nurses to achieve the ultimate goal of providing the best possible medical care.

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